AMJ Australasian Medical Journal [AMJ 2019;12(4):110-118]

Serum vitamin D and asthma control still a controversial link: A cross-sectional study and literature review

Majdy M. Ali Qutub

Department of Family Medicine, Faculty of Medicine, King Abdulaziz University, Saudi Arabia

RESEARCH

Please cite this paper as: Ali Qutub MM. Serum vitamin D and asthma control still a controversial link: A cross-sectional study and literature review. AMJ 2019;12(4):110–118. https://doi.org/10.35841/1836-1935.12.4.110-118

Corresponding Author:
Majdy M.A Qutub
Department of Family Medicine, King Abdulaziz University, P.O Box 53281, Jeddah 21583 Saudi Arabia
Email: mmqutub@kau.edu.sa

ABSTRACT

Background

Vitamin D is an important modulator of the innate and adaptive immune system, plays an important role in the airway hyperresponsiveness and the improved asthma control. Several studies suggest that low serum vitamin D may adversely influence asthma outcomes. However, other studies showed inconsistent relationship which increased the controversy of the link between low vitamin D and asthma control.

Aims

The aim of this study was to investigate the potential relationship between low serum vitamin D with asthma control.

Methods

A cross-sectional study of consecutive patients with the diagnosis of asthma from the outpatient clinic at King Abdulaziz University hospital was analysed between January and December 2011. They were classified according to their asthma control level. Measurement of serum vitamin D was performed. SPSS was used to examine any statistical correlation.

Results

Sixty-four asthmatic patients were included in this study; 31.25 per cent (n=20) males and 68.75 per cent (n=44) were females. Serum vitamin D (25-hydroxyvitamin D) deficiency (Less than 50nmol per litre) was found in 84.3 per cent (n=54), insufficiency (50 to 74.9 nmol per litre) in 14.1 per cent (n=9), and sufficient serum level (75 nmol per litre or greater) in 1.6 per cent (n=1) patients. Level of asthma control assessment based on GINA guideline revealed 25 (39 per cent) uncontrolled, 27 (42.2 per cent) partially controlled and 12 (18.8 per cent) controlled patients. Low vitamin D was found in 12 (19 per cent) controlled versus 51 (81 per cent) non-controlled asthmatics. There was no significant statistical correlation found between low serum vitamin D level and asthma control (p value 0.85).

Conclusion

Low vitamin D was prevalent in more than three-quarters of patients with asthma. The relationship between low serum vitamin D level and poor asthma control was not statistically significant. Further studies are needed to explore the association of low vitamin D with asthma control.

Key Words

Vitamin D, 25-Hydroxyvitamin D, asthma control, cross-sectional survey

What this study adds:

1. What is known about this subject?

There is a substantial role of vitamin D in asthma. Decreased vitamin D levels may adversely influence asthma control and account for increased susceptibility to respiratory viral infections and frequent asthma exacerbations.

2. What new information is offered in this study?

Still there is a controversy in the relationship between low serum vitamin D and asthma control.

3. What are the implications for research, policy, or practice?

Further research is needed to address clearly the relationship between vitamin D and asthma control. Vitamin D supplementation in patients with low vitamin D may have a therapeutic implication in the management of patients with increased frequency of asthma exacerbations and poor asthma control.

Background

Asthma is a common chronic inflammatory airway disease representing a significant health problem worldwide. It is characterized by recurring episodes of breathlessness, wheeze and cough; often reversible airflow limitation and bronchospasm.[1]

Asthma remain one of the most common chronic disorders in Saudi Arabia, affecting more than 3 million Saudis, and several reports indicate a rise in the disease prevalence reaching 26.5 per cent.[2,3] Control of asthma is a major concern in Saudi population. Al-Jahdali et al. demonstrated in a survey only 5 per cent of asthmatics were controlled, whereas 31 per cent partially controlled, and 64 per cent were uncontrolled.[4]

Asthma control refers to the clinical manifestations of the disease that are reduced or improved by therapy, which can fluctuate over time. The impact of the disease on lung function and intensity of treatment required to achieve good asthma control denotes asthma severity.[5]

Multiple risk factors are implicated in sub-optimal control and severity of asthma, including genetic predisposition, environmental exposure to allergens and sensitization.[6]

Vitamin D is a fat-soluble steroid hormone precursor that is acquired primarily from skin by exposure to ultraviolet B (UVB) rays in sunlight. It is also found in few dietary sources, including egg yolk, cod liver oil, oily salt water fish (tuna, salmon, sardine and mackerel) and other dietary supplements.[7,8]

The effects of vitamin D on calcium, phosphate homeostasis and bone mineralization have long been recognized. Besides, vitamin D is an essential modulator of function and regulation of both the innate and adaptive immunity, plays an important role in susceptibility to viral respiratory infections, asthma prevention and improved asthma control.[9]

Decreased vitamin D levels may adversely influence asthma outcomes. Several studies demonstrated a significant link between low vitamin D levels and poor asthma control.[10,11] In a literature review, vitamin D deficiency was associated with increased airway hyperresponsiveness, lower pulmonary function, worse asthma control, and steroid resistance.[11,12] Brehm et al. revealed in a multi-center clinical trial in children an association between low vitamin D levels in patients with mild to moderate asthma and poor asthma control, reduced lung function, and more frequent exacerbations.[13] In contrast, other studies showed inconsistent relationship which increased the controversy of the link between low vitamin D and asthma control.[14-16]

We propose that lower serum vitamin D levels may be associated with poor asthma control. The aim of this study was to examine this potential relationship in Saudi patients with asthma.

Method

Study design

The study was a cross-sectional study at King Abdulaziz University hospital (KAUH).

Study setting

This study was conducted at KAUH in Jeddah, Saudi Arabia. KAUH is a tertiary care hospital with more than 800 beds.

Study participants

We included all consecutive patients with the primary diagnosis of asthma admitted to the outpatient clinic at KAUH between January and December 2011. We classified the degree of asthma control according to the Global Initiative for Asthma (GINA) 2015 guideline into three groups: well-controlled, partly-controlled, and uncontrolled asthma based on the clinical features, lung function and hospitalization for asthma (Table 1).

Patients excluded from the study included pregnant and lactating mothers for safety reasons; and smokers to rule out confounding chronic obstructive airway disease.

Written informed consent was obtained from the study subjects for performance of serum vitamin D test. The study protocol was approved by the local research ethics committee at KAUH.

The following variables were studied: age, sex, nationality, place of residence, asthma control level and vitamin D level. Blood sample for serum vitamin D level was extracted. A single measurement of vitamin D was obtained and

measured as 25-hydroxy cholecalciferol [25(OH)D] using an electrochemiluminescence binding assay method (Elecsys 2010 Modular Analytics E170, Roche Diagnostics).

Values were used as continuous variables and vitamin D was categorized in descriptive analyses as vitamin D deficiency with a serum level of <50nmol/L (20ng/mL), whereas a level of 52 to 72nmol/L was considered a relative insufficiency and a level of 50nmol/L or greater specified as sufficient vitamin D.[7]

Statistical analysis

Quantitative data was examined by applying student t-test for comparison of two groups of normally distributed variables. Qualitative data were expressed as number and percentage and analysed by applying chi-square test. Difference between patients with controlled, partially controlled and uncontrolled asthma were examined by the chi-squared test or the Fisher exact test, when the data were sparse. A p value less than 5 per cent was considered significant. Patients with controlled and partially controlled asthma were combined together to compare them with patients with uncontrolled asthma using multivariate logistic binary regression. In this regression, the dependent variable was uncontrolled asthma (yes, no) and the independent variables were age, sex, nationality, place of residence and vitamin D level. The statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) version 16 software program (SPSS Inc., Chicago, IL, USA).

Results

In this study, we included 64 patients with asthma. 31.25 per cent (n=20) were males and 68.75 per cent (n=44) were females. About three quarters were Saudis (60.9 per cent; n=39) and more than three quarters were living in Jeddah (93.7 per cent; n=60) (Table 2).

Serum 25-hydroxyvitamin D deficiency (Less than 50nmol per litre) was found in 84.3 per cent (n=54), insufficiency (50 to 74.9nmol per litre) in 14.1 per cent (n=9), and sufficient serum level (75nmol per litre or greater) in 1.6 per cent (n=1) patients (Table 3).

The assessment of level of asthma control revealed 25 (39 per cent) uncontrolled, 27 (42.2 per cent) partially controlled and 12 (18.8 per cent) controlled patients. There was no significant statistical correlation found between low serum vitamin D level and asthma control (p value 0.85) (Table 4 and Figures 1, 2). Low vitamin D was found in 12 (18.8 per cent) controlled versus 52 (81.2 per cent) in non-controlled asthmatics (Table 5).

Discussion

The striking feature in the present study that nearly all subjects demonstrate low serum vitamin d level (98.4 per cent) which is compatible with other studies.[11,17]
Low vitamin D was prevalent in more than three-quarters (79.6 per cent) of patients with non-controlled asthma (Table5). However, there was no significant positive correlation found between serum vitamin D level and asthma control as defined by GINA.

In comparison, similar results from other countries were reported (Table 6). In Krobtrakulchai et al., 64 per cent out of 125 Thai asthmatic children had vitamin D deficiency/insufficiency, and there were no substantial differences in serum vitamin D levels between the levels of asthma control, which is almost same finding in our study, yet the percentage of not controlled asthmatics was higher in our study.[15] Kavitha et al. demonstrated in 105 Indian asthmatics also higher percentages of non-controlled asthmatics with insufficient/ deficient vitamin d with no significant correlation.[16] Brumpton et al. reported similarly in Norwegian population-based study of adults with asthma no association despite the power of prospective cross-sectional study of large sample size of adults with asthma though, study estimates were imprecise as stated by the author.[14]

In contrast, the findings in this study was inconsistent with the results of previous studies.[11,18] (Table 6). Korn et al. found that low vitamin D was positively correlated with poor asthma control scores in a large German case control study with significant association of vitamin D insufficiency or deficiency with uncontrolled asthma (p=0.030).[11] These findings are in line with other large community based randomized controlled trial in adults with multi-ethnic composition in New Zealand which reported lower vitamin D levels in asthmatics with poor asthma control compared to those with controlled asthma (p=0.03) however, ACT was used for evaluation of asthma control status which differ methodologically from our study.[17] Moreover, in a Jordanian cross-sectional case control study, Samaha et al. reported significant positive relationship between low vitamin D and reduced asthma control (P<0.001).[19] Similarly, Shahin et al. reported highly significant difference (p value <0.001) in serum vitamin D levels at different asthma control levels. The high percentage 85 per cent (59 out of 70) of Low serum vitamin D levels in asthmatics was consistent with the results in our study.[20]

The current study demonstrated that low vitamin D was prevalent in 18.8 per cent of controlled asthmatic (Table 5). In contrast, Chinellato et al. observed in the children with well-controlled asthma higher serum levels of vitamin D and significant correlation between predicted forced vital capacity (FVC) percentage and serum vitamin D.[21]
This relationship of asthma control and vitamin D could be influenced by multiple factors. It is difficult to determine from cross-sectional studies whether low vitamin D is responsible for reduced asthma control or that not controlled asthmatics associated lifestyle factors such as less dietary intake and restricted sunshine exposure which contributes for their lower serum levels of vitamin D.[21] Additionally, lack of statistical power due to low sample size could be a contributing factor.

In a cross-sectional study in western Nigeria, only one (1 per cent) of the children with asthma was vitamin D insufficient and none was vitamin D deficient.[22] This is contrary to the higher percentages of vitamin D deficiency and insufficiency observed in previous studies. Significantly vitamin D deficiency in Saudi population account for 87.8 per cent in one study. Similar results were reported in Qatar.[23] Though Saudi Arabia is located near the equator, and in spite of high sun exposure, dress code which involve covering of most parts of the body, in addition to sedentary life and low vitamin D dietary intake could be contributing factors for low vitamin D observed in current study.[24]

Sun exposure is the main source of vitamin D in humans. Solar UVB radiation convert 7-dehydro-cholesterol in the skin to its precursor pre-vitamin D3, which is then transformed to vitamin D3 (cholecalciferol), which is biologically inert and must undergo successive hydroxylation in the liver to 25-hydroxyvitamin D. Parathyroid hormone controls calcium-phosphate homeostasis by regulating hydroxylation of 25(OH)D to its biologically active form (1,25[OH]2 D3) in the kidney. Vitamin D signalling predominantly occurs through binding of 1,25(OH)2 D3 to vitamin D receptors (VDR) which are found in abundance on T cells that inhabit the respiratory epithelium, macrophages and dendritic cells with subsequent regulation of gene expression by binding to genomic sequences known as vitamin D response elements (VDREs).[25]

Vitamin D has important immunomodulatory functions by enhancing antimicrobial peptide production and influencing the activities of immune effector cells (TH 2, TH 17 and T reg).[26] Furthermore, vitamin D has a substantial role in innate immunity which may account for the increased susceptibility to respiratory viral infections particularly human rhinovirus[27] This explains why vitamin D-deficient asthmatics have an increased frequency of severe exacerbations and poor asthma control outcomes. The potential role of vitamin D as an adjunct therapy for asthmatic patients with low baseline vitamin D levels was documented in several observational studies.[27,28] A recent Cochrane review confirmed the significant role of vitamin D supplementation in the management of asthma exacerbations requiring systemic corticosteroids (RR 0.63, 95 per cent CI 0.45–0.88) and likely to offer protection against having exacerbations requiring an emergency visits or hospitalization (OR 0.39, 95 per cent CI 0.19–0.78).[29] Moreover, vitamin D has been used to treat steroid resistance in some asthmatic patients.[25]

Should we need to screen patients with asthma for vitamin D level is a matter of debate and controversial. There is no evidence to support such screening for the purpose of asthma management. However, it is advisable to measure serum vitamin D level in patients who are at high risk for vitamin D deficiency. Merely, vitamin D supplementation is recommended only for patients who have deficient serum vitamin D level less than 50nmol/L because this could compromise their musculoskeletal health.[25] Further studies are required before conclusive clinical recommendations can be made for universal vitamin D supplementation.

To our knowledge, this is the first cross-sectional study in Saudi Arabia. The study methodology and measurement of serum vitamin D level in the laboratory was universal for all patients. However, the study has its own limitations as well. The results lack the statistical power due to small sample size. A larger number of subjects may be needed to validate our findings. Also, no control subjects included in the study. The study did not assess the medication used to control asthma or the intake of vitamin D containing supplements in target subjects, as this could affect serum vitamin D levels and asthma control, thus serve as confounders which may have an impact on study results. Also, the assessment of dietary intake of vitamin D and the amount of sunlight the study subjects were exposed to per day was not evaluated. The study was conducted in a large referral center and may not be representative of patients with asthma from the general population. Larger studies are required to address clearly the relationship between vitamin D and asthma control where the results could be generalizable and undisputable.

Conclusion

The relationship between low serum vitamin D and asthma control remain controversial. Further studies are needed to elucidate the nature of this potential relationship. In conclusion, the present study showed no statistical correlation between low vitamin D and asthma control.

References

1. Global Initiative for Asthma. Gina Report, Global strategy for asthma management and prevention. GINA. 2015. https://ginasthma.org/wp-content/uploads/2016/01/GINA_Report_2015_Aug11-1.pdf.
2. Al Frayh AR, Shakoor Z, Gad El Rab MO, et al. Increased prevalence of asthma in Saudi Arabia. Ann Allergy Asthma Immunol. 2001;86:292–296.
3. Sobki SH, Zakzouk SM. Point prevalence of allergic rhinitis among Saudi children. Rhinology. 2004;42:137–140.
4. Al-Jahdali HH, Al-Hajjaj MS, Alanezi MO, et al. Asthma control assessment using asthma control test among patients attending 5 tertiary care hospitals in Saudi Arabia. Saudi Med J. 2008;29:714–717.
5. Bateman ED, Hurd SS, Barnes PJ, et al. Global strategy for asthma management and prevention: GINA executive summary. Eur Respir J. 2008;31:143–178.
6. Aldubi HM, Alissa EM, Kamfar HZ, et al. Bronchial asthma and hypovitaminosis D in Saudi children. Asia Pac Allergy. 2015;5:103–113.
7. Holick MF. Vitamin D deficiency. N Engl J Med. 2007;357:266–81.
8. Gupta A, Bush A, Hawrylowicz C, et al. Vitamin D and asthma in children. Paediatr Respir Rev. 2012;13(4):236–243.
9. Lange NE, Litonjua A, Hawrylowicz CM, et al. Vitamin D, the immune system and asthma. Expert Rev Clin Immunol. 2009;5(6):693–702.
10. Beyhan-Sagmen S, Baykan O, Balcan B, et al. Association between severe vitamin D deficiency, lung function and asthma control. Arch Bronconeumol. 2017;53(4):186–191.
11. Korn S, Hubner M, Jung M, et al. Severe and uncontrolled adult asthma is associated with vitamin D insufficiency and deficiency. Respir Res. 2013;14(1):25.
12. Sandhu MS, Casale TB. The role of vitamin D in asthma. Ann Allergy Asthma Immunol. 2010;105:191–199.
13. Brehm JM, Schuemann B, Fuhlbrigge AL, et al. Serum vitamin D levels and severe asthma exacerbations in the childhood asthma management program study. J Allergy Clin Immunol. 2010;126(1):52.
14. Brumpton BM, Langhammer A, Henriksen AH, et al. Serum 25-hydroxyvitamin D, vitamin D supplement and asthma control: The HUNT study. Respir Med. 2018;136:65–70.
15. Krobtrakulchai W, Praikanahok J, Visitsunthorn N, et al. The effect of vitamin D status on pediatric asthma at a university hospital, Thailand. Allergy Asthma Immunol Res. 2013;5(5):289–294.
16. Kavitha TK, Gupta N, Kabra SK, et al. Association of serum vitamin D levels with level of control of childhood asthma. Indian Paediatr. 2017;54(1):29–32.
17. Win SS, Camargo CA Jr, Khaw KT, et al. Cross-sectional associations of vitamin D status with asthma prevalence, exacerbations, and control in New Zealand adults. J Steroid Biochem Mol Biol. 2018. https://doi.org/10.1016/j.jsbmb.2018.11.016
18. Samrah S, Khatib I, Omari M, et al. Vitamin D deficiency and level of asthma control in women from North of Jordan: a case-control study. J Asthma. 2014;51(8):832–8.
19. Samaha HMS, Elsaid AR, NasrEldin E. Vitamin D and markers of airway inflammation in asthma. Egyptian Journal of Chest Diseases and Tuberculosis. 2015;64:779–783.
20. Shahin MYA, El-Lawah AA, Amin A. Study of serum vitamin D level in adult patients with bronchial asthma. Egyptian J Chest Diseases and Tuberculosis. 2017;66:5–9.
21. Chinellato I, Piazza M, Sandri M, et al. Vitamin D serum levels and markers of asthma control in Italian children. J Pediatr. 2011;158:437–41.
22. Omole KO, Kuti BP, Oyelami OA, et al. Serum vitamin D profile of Nigerian children with asthma: Association with asthma severity and control. Pediatr Pulmonol. 2018;53:544–551.
23. Bener A, Al-Ali M, Hoffmann GF. High prevalence of vitamin D deficiency in young children in a highly sunny humid country: a global health problem. Minerva Pediatr. 2009;61:15–22.
24. Ardawi MS, Sibiany AM, Bakhsh TM, et al. High prevalence of vitamin D deficiency among healthy Saudi Arabian men: relationship to bone mineral density, parathyroid hormone, bone turnover markers, and lifestyle factors. Osteoporos Int. 2012;23(2):675–686.
25. Paul G, Brehm JM, Alcorn JF, et al. Vitamin D and Asthma. Am J Respir Crit Care Med. 2012;185(2):124–132.
26. Jiao J, Castro M. Vitamin D and asthma: current perspectives. Curr Opin Allergy Clin Immunol. 2015;15:375–382.

27. Brehm JM, Schuemann B, Fuhlbrigge AL, et al. Serum vitamin D levels and severe asthma exacerbations in the childhood asthma management program study. J Allergy Clin Immunol. 2010;126:52–8 e55.
28. Vitamin D, Volume 2: Health, Disease and Therapeutics, Fourth Edition. http://dx.doi.org/10.1016/B978-0-12-809963-6.00112-7
29. Martineau AR, Cates CJ, Urashima M, et al. Vitamin D for the management of asthma. Cochrane Database Syst Rev. 2016;9:CD011511.

ACKNOWLEDGEMENTS

The author acknowledges and gratefully appreciates the efforts of Professor Emad Koshak; consultant allergy immunology for valuable support and guidance. Sincere thanks and appreciation also to Dr Abdel Moniem Mukhtar, associate professor of epidemiology towards his valuable contribution in biostatistical works. Additional thanks and appreciation for Dr Lujain Qutub; paediatric resident at KAUH for the invaluable contribution and the assistance, and for Majed Qutub; medical student at King Saud bin Abdulaziz University for Health Sciences, College of Medicine for enthusiastic encouragement, profound ideas and comments for my study.

PEER REVIEW

Not commissioned. Externally peer reviewed.

CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

FUNDING

None

ETHICS COMMITTEE APPROVAL

The local research ethics committee at King Abdulaziz University Hospital, approval reference number: 31562/32/D

Table 1: Classification of asthma control according to GINA 2015

Characteristics	Controlled (All of the following)	Partly Controlled (Any measure present in any week)	Uncontrolled
Daytime symptoms	None (≤ twice/week)	> twice/week	Three or more features of partly controlled****
Limitations of activities	None	Any	
Nocturnal symptoms/ awakening	None*	Any	
Need for reliever/ rescue treatment	None (≤ twice/week)**	> twice/week	
Lung function (PEF or FEV1)	Normal	< 80% predicted or personal best	
Exacerbations	None***	One or more/year	

*No nocturnal symptoms in the last 3 months
**Short-acting B2-agonists twice or less per week in the last 3 months, and no use of oral steroids in the last 12 months
***No asthma attacks in last three months
****Uncontrolled asthma was diagnosed if more than two features were absent or if asthma exacerbation had caused hospital/emergency department admissions in the last 12 months; oral steroids were used in short courses or continuously in the last 12 months; or the subject had more than 12 asthma exacerbations (1 per week or more) in the last 3 months

Table 2: General Characteristics of Study Participants

		Total = n	Percentage %
Age (years)	5-14	4	6.3%
	14-44	45	70.3%
	>44	15	23.4%
Sex	Male	20	31.25
	Female	44	68.75
Nationality	Saudi	39	60.9%
	Non-Saudi	25	39.1%
Place of residence	Jeddah	60	93.7%
	Mecca	4	6.3%

Table 3: Serum vitamin D in study subjects

Vitamin D status	Male	Female	Total = n	Percentage %
Deficient <50nmol/L	19	35	54	84.3
Insufficient 50 to 74.9nmol/L	1	8	9	14.1
Normal >75nmol/L	0	1	1	1.6

Table 4: Differences between patients with controlled, partially controlled and uncontrolled asthma

		Controlled Asthma %(n)	Partially controlled asthma %(n)	Uncontrolled asthma %(n)	Total	P value
Age	5-14 years	50 (2)	0 (0)	50 (2)	4	0.03
	14-44 years	11.1 (5)	53.3 (24)	35.6 (16)	45	
	>44 years	33.3 (5)	20 (3)	46.7 (7)	15	
Sex	Male	25 (5)	30 (6)	45 (9)	20	0.38
	Female	15.9 (7)	47.7 (21)	36.4 (16)	44	
Nationality	Saudi	20.5 (8)	38.5 (15)	41 (16)	39	0.74
	Non-Saudi	16 (4)	48 (12)	36 (9)	25	
City	Jeddah	18.3 (11)	41.7 (25)	40 (24)	60	0.83
	Mecca	25 (1)	50 (2)	25 (1)	4	
Vitamin D	<50 nmol/L	18.5 (10)	40.7 (22)	40.7 (22)	54	0.85
	50-74.9 nmol/L	22.2 (2)	55.6 (5)	22.2 (2)	9	
	>75 nmol/L	0 (0)	0 (5)	100 (1)	1	

Table 5: Vitamin D serum level in controlled and not-controlled asthmatics

Asthma control status	Low (Insufficient and deficient) serum vitamin D	Normal vitamin D
Controlled	12 (18.8%)	0 (0%)
Not controlled (partially and uncontrolled asthma)	51 (79.6%)	1 (1.6%)
Total	63 (98.4%)	1 (1.6%)

Table 6: The relationship between serum vitamin D level and control of asthma, comparison of previous studies

Author	Year	Type of the study and country	Subjects	Assessment of control level	Correlation
Brumpton et al.	1995-1997 2006-2008	Cross-sectional (Norway)	n=806	GINA	No (mean difference −0.08, 95% CI -0.70-0.54)
Iolanda Chinellato et al.	November 2008-March 2009	Cross-sectional (Italy)	n=75	GINA C-ACT	Yes P = .023
Korn et al.	September 2008 -November 2011	Case-control (Germany)	n=280	GINA	Yes P = 0.030
Krobtrakulchai et al.	July 2011- December 2012	Cross-sectional (Thailand)	n=125	GINA	No P>0.05
Kavitha et al.	January 2013-September 2014	Cross-sectional (India)	n=108	GINA	No P=0.98
Samrah et al.	2014	Cross-sectional (Jordan)	n=86	GINA ACT	Yes P = 0.046
Turkeli et al.	December 2014 - February 2015	Case-control (Turkey)	n =102	GINA	Yes P = 0.001
Shahin et al.	September 2014 - August 2015	Case-control (Egypt)	n=90	ACT GINA	Yes P= <0.001
Samaha et al.	October 2013 - September 2014	Cross sectional case-control (Jordan)	n=55	GINA	Yes P < 0.001
Omole et al.	2015	Cross-sectional (Western Nigeria)	n=206	GINA	No P=0.963

Figure 1: Association between vitamin D level (nmol/L) and asthma control status (GINA 2015 Criteria)

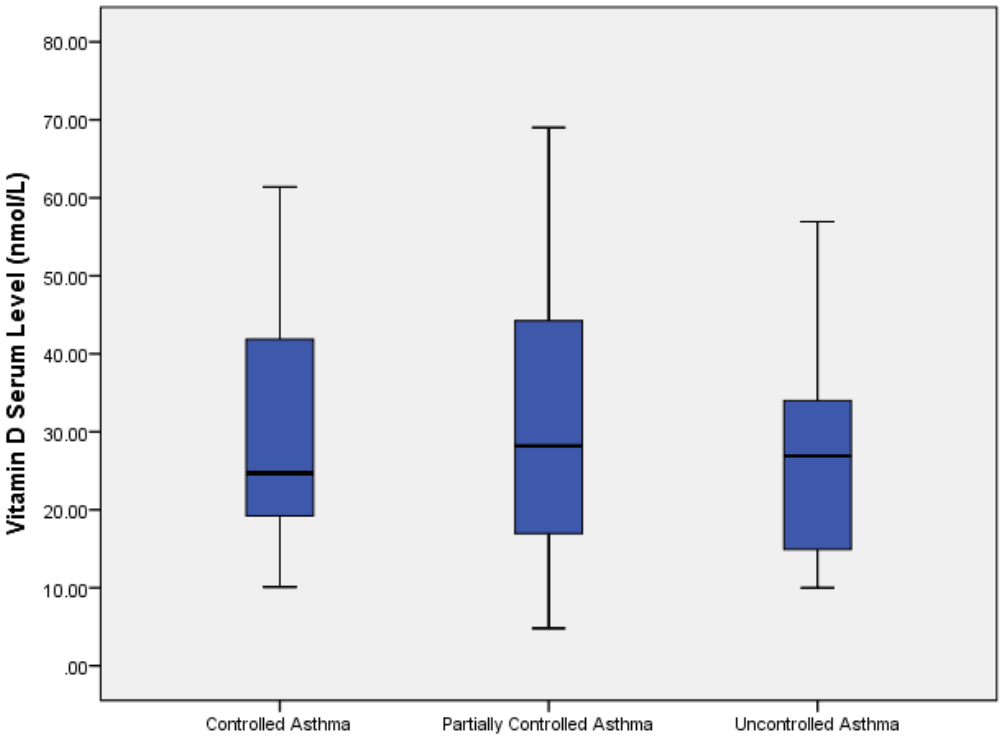

Figure 2: Association between vitamin D level (nmol/L) and asthma control status (GINA 2015 criteria)