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Original Research Article

Association between Vitamin D deficiency and lung function in asthma patients

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ABSTRACT

Background: Asthma is an inflammatory disorder, usually chronic, and is related to the hypersensitivity of the airways to allergens leading to dyspnoea, wheezing, cough and tightness in chest. Increased severity of asthma and poor control has been attributed to lower levels of Vitamin D levels.
Materials and Methods: Blood was collected from 78 patients who were diagnosed with asthma and tested for Vitamin D levels eosinophil counts, IgE levels, and regular biochemical tests. All these patients underwent Asthma Control Test, Pulmonary Function tests for FEV1%, FVC%, FEV1/FVC%.
Results: The serum eosinophil count, sputum eosinophil count and IgE levels were significantly higher in Vitamin D deficient patients compared to the sufficient patients. The most common severity of asthma among the patients was due to atopy as seen in 53.8% of the patients. In 39.6% of the patients who were Vit D deficient, the asthma was very severe as was the case in 8% of the Vit D sufficient people. The Forced expiratory volume, Forced vital capacity and FEV1/FVC1 was 92.69 ± 0.9 %, 91.3 ± 12.1% and 76.2 ± 8.7 in patients with deficient Vitamin D levels and 97.36 ± 1.1%, 99.1 ± 7.3% and 81.6 ± 13.1 in patients with sufficient Vit D levels respectively.
Conclusions: There seems to be a strong association of Vitamin D levels and asthma among patients. High vitamin D levels are beneficial to the lung function and also slow the asthma exacerbations.

1. Introduction

Asthma is an inflammatory disorder, usually chronic, and is related to the hypersensitivity of the airways to allergens leading to dyspnoea, wheezing, cough and tightness in chest. It is commonly seen to occur at night or early in the morning. In severe cases, it may be a life-threatening condition.[1] The cases of asthma have seen a rising prevalence globally, affecting 300 million people in the last few decades. This results in a huge financial burden on the human health care resources.[2,3] It is one of the very common conditions in children and one of the main causes of morbidity.[4] Asthma and its presence may be influenced by genetic factors, environmental, socioeconomical and ethnic factors.[5]

The causes of asthma are unclear as the presentation is different in adults and children.[6] Regulations of T helper cell cytokines, IL-4, IL-5, IL-13 in asthmatic patients is characterised by increased eosinophilia, increased IgE level and degranulation.[6,7]

The major source of Vitamin D is sunlight, followed by diet. On exposure to the ultraviolet rays of the sun, the 7-dehydrocholesterol, which is present in the skin is converted to previtamin D3. This previtamin D3 ultimately becomes Vitamin D3. Vitamin D3, in the liver is transformed into 25-hydroxyvtamin D(25[OH]D3), which gets activated in the kidney.[8] Activated Vitamin D3 is known to help in the regulation of the innate immune system and helps in the production of antimicrobial peptides. Then they act on macrophages, there is an increased phagocytosis and

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chemotaxis effect, which further improves the immune mechanism.[9] However, due to alteration in the lifestyle and diet, which could include more time spent indoors and unhealthy fast foods, more and more cases of vitamin D deficiency are being reported.[10,11] A distinctive link between lower levels of Vitamin D and asthma attacks with adverse outcomes have also been reported.[10,11]

Vitamin D deficiency has been seen to occur more commonly in children.[12] The incidence of Vitamin deficiency is very high globally. Almost half of the population of the world is said to be Vitamin D deficient. Some of the main causes are insufficient exposure to sunlight, pigmentation of the skin and less intake of Vitamin D in the diet.[13]

There have been studies associating Vitamin D levels with asthma. Increased severity of asthma and poor control has been attributed to lower levels of Vitamin D levels. A study showed asthmatics to have a lowered lung function with more frequent exacerbations.[14] Furthermore, Vitamin D helps in protecting the children against many diseases such as viral infections and asthma.[15,16] Taken during pregnancy, vitamin D helps in enhancing the lung capacity and protects the new born against development of asthma later on in life.[17] In non-allergic eosinophil inflammation, alarmin cytokines are regulated by Vitamin D. In case of severe asthma, where the patients are resistant to steroids and pathological interleukin (IL-17), Vitamin D3 helps in the uptake of steroids. Too much intake of vitamin D may also be deleterious.[17]

This study was therefore done to identify and assess the effect of lung function and its association with Vitamin D levels in asthmatic patients.

2. Materials and Methods

This study was done by the Department of Pulmonary Medicine at Kamineni Academy of Medical Sciences and research centre. 78 patients who were diagnosed with asthma during 14 months in between July 2018 to august 2019. This study was cleared by the institutional ethical committee and then the study was explained to the patients and an informed consent was taken from all of them.

Patients with hospitalization in the past one month, those who received immunosuppressants or steroids, other drugs such as bisphosphonates, phenytoin, sulfasalazine, omega 3 fatty acids, were excluded from the present study. Patients who had taken Vitamin D supplements were also excluded from the study.

Demographic details were taken for all the patients vide interview, including age, weight, sex, socioeconomic status etc. History of smoking, packs smoked per day, presence of asthma, family history of asthma, presence of any respiratory illness and Chronic obstructive pulmonary disease (COPD) were also taken.

All the patients were subjected to complete physical and clinical examination. Blood was collected from cubital vein and tested for complete blood picture, blood eosinophil count random blood sugar, cholesterol levels, both total and HDL, Triglycerides, and 25(OH)D levels. Sputum eosinophil count was done after sputum collected and staining with Leishman stain.

Spirometry was done on all the patients before and 10 – 15 mins after the use of inhaled salbutamol as a bronchodilator. Forced expiratory volume, Forced vital capacity were observed and FEV1/FVC ratio was calculated. Use of bronchodilators for the next 6 hours and use of theophylline for 24 hours was dissuaded. Statistical analysis was done using student t test and bar and pie charts. Asthma Control Test was done for all the patients using the standard questionnaire and the results were obtained on a sale of 5 to 25.[18]

3. Results

The number of males were 41 (52.6%) and females were 37(47.4%) (Figure 1)

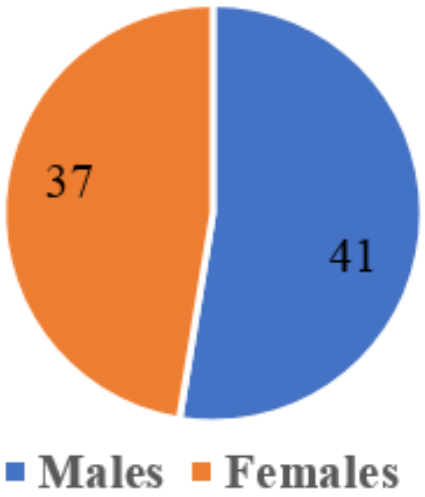

Fig. 1: Number of males and females

The most common age group to be affected was less than 10 years age group affecting 21 (26.9%), followed by >60 years with 15 (19.2%) affected. 10-20 years age group has 9 (11.5%), 51-60 years had 11 (14.1%) who were affected (Figure 2)

Most of the patients has a normal BMI between 18.5 – 24.9 kg/m^2. The mean BMI in our study was 24.4 ±2.6kg/m^2, with waist circumference being 70.4 ± 9.1 cm and hips 87.3 ± 15.6cm. 39 (50%) of the patients had a history of being regular smokers while 18 (23.1%) of them were non-smokers. 21(26.9%) were passive smokers,

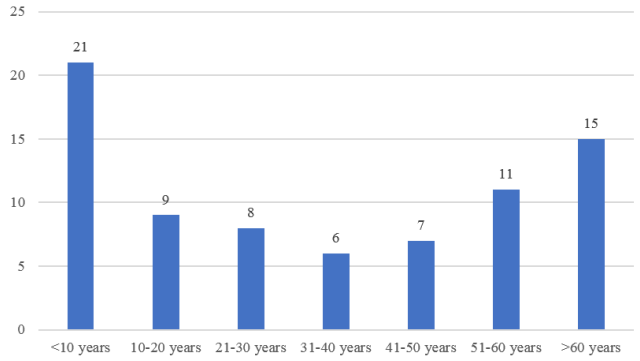

Fig. 2: Differentiation of patients based on age

having a close relative either their parent or spouse being a regular smoker (Table 3).

Table 1: Demographic details

Demographic details	Mean
BMI (kg/m^2)	24.4±2.6
Waist (cm)	70.4 ± 9.1
Hips (cm)	87.3 ± 15.6
History of smoking	
Regular	39 (50%)
Passive smoker	21 (26.9%)
Non smoker	18 (23.1%)
Systolic Blood pressure (mmHg)	124.6 ± 8.2
Diastolic Blood pressure (mmHg)	79.5 ± 5.1

53 (67.9%) of the asthmatics in our study were vitamin D deficient, with values <10mg/mL, while 21 (26.9%) were intermediate with values between 10-30 ng/mL. Only 4 patients (5.1%) had a normal value of >30ng/mL of Vitamin D values. The most common months during which asthmatic attacks were seen in these patients were in the months between Oct and Dec, when the weather was very cold or raining, followed by Jan to March, when the weather was cold, but slowly becoming warmer. During the summer months of April to June, the incidences of asthma was the least. (Table 2)

The sputum eosinophil levels among the Vitamin D deficient patients were 11.47 ± 4.1 while among the sufficient patients it was 2.19 ± 0.81, which was highly significant. The serum eosinophil levels and IgE levels also showed a similar trend, with the absolute count being 609.34 ± 38.91 among the patients with low Vitamin D levels and 211.03 ± 29.52 among the Vit D sufficient patients and IgE being 821.45 ± 49.24 and 821.45 ± 49.24 units/ml amongst eh deficient and sufficient patients respectively.Table 3

The most common severity of asthma among the patients was due to atopy as seen on 42 (53.8%) of the patients. In case of 21 (39.6%) of the patients who were Vit D deficient, the asthma was very severe as was the case in 2(8%) of the Vit D sufficient people. This was followed by moderate asthma in 15 (28.3%) of the Vit D deficient patients and 4(16%) in the vit D sufficient patients (Figure 3).

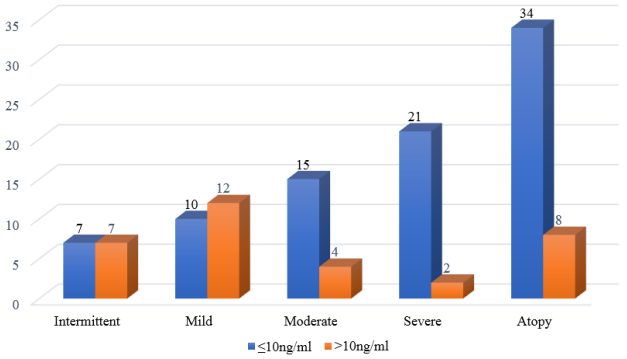

Fig. 3: Severity of asthma

After spirometry, the ACT scores of the patients was 17 ± 5 in patients with deficient Vitamin D levels and 20 ± 3 in patients with sufficient Vit D levels. The Forced expiratory volume, Forced vital capacity and FEV1/FVC1 was 92.69 ± 0.9 %, 91.3 ± 12.1% and 76.2 ± 8.7 in patients with deficient Vitamin D levels and 97.36 ± 1.1%, 99.1 ± 7.3% and 81.6 ± 13.1 in patients with sufficient Vit D levels respectively (Table 4).

4. Discussion

Asthma had become one of the most common diseases with a worldwide prevalence, with a very large economic burden. As there is a probable positive association between vitamin D and asthma, it has become one of the major topics of interest.

In the present study, 52% were males and 48% were females. In a study by Andujar-Espinosa et al, majority of the patients (78%) were women.[19] The most common age group to be affected is the paediatric age group followed by the elderly.

67% of the patients in our study were Vitamin D deficient. Out of the 33%, 26.9% had a level between 10-30ng/ml, and only 5.1% had a sufficient Vitamin D levels of above 30ng/ml. In a study by Boonpiyathad et al, a prevalence of 45% was observed for lower levels of Vitamin D levels in adults and 64% in children.[20] Mithal et al., and Palacios et al., have reported a deficiency of 69-82% in Indian population.[21,22]

Nearly 40% of the patients with vitamin D deficiency had severe asthma exacerbations. Association of Vitamin D deficiency and severe asthma exacerbations were also observed in children in studies from Puerto Rico and North America,[23,24] while in adults, similar case was found in a study by Korn et al corroborating our study.[25] A study by Confino – Cohen et al reported that asthmatic exacerbations were 25% higher in patients with Vitamin D deficiency rather than those with sufficient Vit D levels.[26]

Table 2: Incidence of URTI during seasons in asthmatics

Months	Vitamin D values		
	< 10ng/mL n=53	**10-30 ng/mL n=21**	**>30ng/mL N=4**
Jan-Mar	41(77.4%)	6 (24%)	1 (4%)
Apr-June	14 (26.4%)	3 (12%)	0 (0)
Jul-Sept	21 (39.6%)	7 (28%)	1 (4%)
Oct – Dec	46 (86.8%)	9 (36%)	2(8%)

Table 3: Eosinophil count I Vit D sufficient and deficient patients

Parameters	Vitamin D levels	Mean ± SD	P value
Sputum Eosinophil Count (%)	Deficient	11.47 ± 4.1	
	Sufficient	2.19 ± 0.81	≤ 0.001
Serum Eosinophil Count (Absolute)	Deficient	609.34 ± 38.91	≤ 0.001
	Sufficient	211.03 ± 29.52	
Serum IgE (units/ml)	Deficient	821.45 ± 49.24	≤ 0.001
	Sufficient	258.92 ± 51.54	

Table 4: Pulmonary Tests

Parameters	≤10ng/ml	>10ng/ml
ACT	17 ± 5	20 ± 3
FEV1 (%)	92.69 ± 0.9	97.36 ± 1.1
FVC1 (%)	91.3 ± 12.1	99.1 ± 7.3
FEV1/FVC (%)	76.2 ± 8.7	81.6 ± 13.1

The ACT score for patients who had deficient Vit D levels was 17 ± 5 while those with > 10ng/ml was 20 ± 3. In a study by Menon et al, the ACT score was 16.62 ± 3.18 in deficient Vit D levels patients which was lower than the control group.[27]

The FEV1%, FVC1% and FEV1/FVC% in the present study was 92.69 ± 0.9, 91.3 ± 12.1, 76.2 ± 8.7 among patients with Vitamin D levels ≤10ng/ml which was significantly lower than those with > 10ng/ml levels which were 97.36 ± 1.1, 99.1 ± 7.3 and 81.6 ± 13.1 in those above 10ng/ml respectively. In a similar study by Liu et al, it was observed that patients with low vitamin D levels had a lowered FEV1%. They also found a positive association between the FEV1% and vitamin D levels.[14] FEV1% also showed improvement in a study by Arshi et al after Vitamin D supplementation in Asthma patients.[28] Similar results were observed in a study by De Groot et al and Yadav and Mittal.[29,30] However, Castro et al did not find any association between the Vitamin D levels and asthma.[31] Alyasin et al., also found a significant relationship between the Vitamin D levels and predicted FEV1 and predicted FEV1/FVC values.[32]

There was a significantly higher levels of Serum eosinophil count and sputum eosinophil count among the patients with deficient levels of Vitamin D. The Serum IgE levels were also significantly higher in the asthmatic patients. Guru et al, in a similar study reported a higher level of eosinophils in the asthmatic patients in the Vitamin D deficient patients.[33] Higher IgE and eosinophil levels were also observed by Brehm et al in their study.[24] However a study by Hypponen et al., found a nonlinear association between the two.[34]

The most common severity of asthma among the patients was due to atopy as seen on 42 (53.8%) of the patients. In case of 21 (39.6%) of the patients who were Vit D deficient, the asthma was very severe as was the case in 2(8%) of the Vit D sufficient people. Similar results were observed in a study by Guru et al where the severity of asthma was inversely proportional to the Vitamin D levels.[34]

5. Conclusions

There seems to be a strong association of Vitamin D levels and asthma among patients. High vitamin D levels are beneficial to the lung function and also slow the asthma exacerbations. Therefore, Vitamin D supplementation among patients with asthma can help in its management. However, since our sample size is small, more studies need to be done to corroborate these findings and estimate the cut off for the optimal dose of Vitamin D to be given to asthmatic patients.

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None.

7. Conflict of interests

The authors declare that there are no conflicts of interest in this paper

8. Source of funding

None

References

1. Lange P, Parner J, Vestbo J, Schnohr P, Jensen G. A 15-year follow-up study of ventilatory function in adults with asthma. *N Engl J Med*. 1998;339(17):1194–200.
2. Moore WC, Meyers DA, Wenzel SE. Identification of asthma phenotypes using cluster analysis in the Severe Asthma Research Program. *Am J Respir Crit Care Med*. 2010;181(4):315–23. doi:10.1164/rccm.200906-0896OC.
3. Boulet LP, Fitzgerald JM, Levy ML. Asthma guidelines implementation: a guide to the translation of GINA guidelines into improved care. *Eur Respir J*. 2012;39:1220–9. doi:10.1183/09031936.00184511.
4. Masoli M, Fabian D, Holt S, Beasley R. Global Initiative for Asthma (GINA) Program. The global burden of asthma: Executive summary of the GINA Dissemination Committee report. *Allergy*. 2004;59(5):469–78. doi:10.1111/j.1398-9995.2004.00526.x.
5. Yin GQ, Jiang WH, Wu PQ, He CH, Chen RS, Deng L, et al. Clinical evaluation of sublingual administration of dust mite drops in the treatment of allergic asthma and allergic rhinitis of children. *Eur Rev Med Pharmacol Sci*. 2016;20(20):4348–53.
6. Holt PG, Strickland DH. Interactions between innate and adaptive immunity in asthma pathogenesis: new perspectives from studies on acute exacerbations. *J Allergy Clin Immunol*. 2010;125(5):963–72. doi:10.1016/j.jaci.2010.02.011.
7. Bradding P, Walls AF, Holgate ST. The role of the mast cell in the pathophysiology of asthma. *J Allergy Clin Immunol*. 2006;117(6):1277–84. doi:10.1016/j.jaci.2006.02.039.
8. Searing DA, Leung D. Vitamin D in atopic dermatitis, asthma and allergic disease. *Immunol Allergy Clin N Am*. 2010;30(3):397–409. doi:10.1016/j.iac.2010.05.005.
9. Bouillon R, Carmeliet G, Verlinden L. Vitamin D and human health: lessons from vitamin D receptor null mice. *Endocr Rev*. 2008;29(6):726–76. doi:10.1210/er.2008-0004.
10. Ginde AA, Mansbach JM, and CACJ. Association between serum 25-hydroxyvitamin D level and upper respiratory tract infection in the Third National Health and Nutrition Examination Survey. *Arch Intern Med*. 2009;169(4):384–90.
11. Uysalol M, Mutlu LC, Saracoglu GV, Karasu E, Guzel S, Kayaoglu S, et al. Childhood asthma and vitamin D deficiency in Turkey: is there cause and effect relationship between them? *Ital J Pediatr*. 2013;39:78. doi:10.1186/1824-7288-39-78.
12. Ehlayel MS, Bener A, Sabbah A. Is high prevalence of vitamin D deficiency evidence for asthma and allergy risks. *Eur Ann Allergy Clin Immunol*. 2011;43(3):81–8.
13. Brehm JM, Celedn JC, 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(9):765–71. doi:10.1164/rccm.200808-1361OC.
14. Liu J, Dong YQ, Yin J. Meta-analysis of vitamin D and lung function in patients with asthma. *Respir Res*. 2019;20:161. doi:10.1186/s12931-019-1072-4.
15. Tolppanen AM, Sayers A, Granell R, Fraser WD, Henderson J, Lawlor DA, et al. Prospective association of 25-hydroxyvitamin d3 and d2 with childhood lung function, asthma, wheezing, and flexural dermatitis. *Epidemiology*. 2013;24(2):310–9.
16. Devereux G, Macdonald H, Hawrylowicz C. Vitamin D and asthma: time for intervention. *Am J Respir Crit Care Med*. 2009;179(9):739–40.
17. Camargo CA, Rifas-Shiman SL, Litonjua AA, Rich-Edwards JW, Weiss ST, Gold DR, et al. Maternal intake of vitamin D during pregnancy and risk of recurrent wheeze in children at 3 y of age. *Am J Clin Nutr*. 2007;85(3):788–95.
18. Schatz M, Sorkness CA, Li JT, Marcus P, Murray JJ, Nathan RA. Asthma control test: reliability, validity, and responsiveness in patients not previously followed by asthma specialists. *J Allergy Clin Immunol*. 2006;117(3):549–56. doi:10.1016/j.jaci.2006.01.011.
19. Andújar-Espinosa R, Salinero-González L, Illán-Gómez F. Effect of vitamin D supplementation on asthma control in patients with vitamin D deficiency: the ACVID randomised clinical trial. *Thorax*. 2021;76(2):126–33. doi:10.1136/thoraxjnl-2019-213936.
20. Boonpiyathad T, Chantveerawong T, Pradubpongsa P, Sangasapaviliya A. Serum Vitamin D Levels and Vitamin D Supplement in Adult Patients with Asthma Exacerbation. *J Allergy*. 2016;p. 4070635. doi:10.1155/2016/4070635.
21. Mithal A, Wahl DA, Bonjour JP, Burckhardt P, Dawson-Hughes B, Eisman JA, et al. IOF Committee of Scientific Advisors (CSA) Nutrition Working Group. Global vitamin D status and determinants of hypovitaminosis. *Osteoporos Int*. 2009;20(11):1807–20. doi:10.1007/s00198-009-0954-6.
22. Palacios C, Gonzalez L. Is vitamin D deficiency a major global public health problem? *J Steroid Biochem Mol Biol*. 2014;144 Pt A:138–45. doi:10.1016/j.jsbmb.2013.11.003.
23. Brehm JM, Acosta-Pérez E, Klei L. Vitamin D insufficiency and severe asthma exacerbations in Puerto Rican children. *Am J Respir Critical Care Med*. 20121;86(2):140–6.
24. Brehm JM, Schuemann B, Fuhlbrigge AL. Serum vitamin D levels and severe asthma exacerbations in the Childhood Asthma Management Program study. *J Allergy Clin Immunol*. 2010;126(1):52–8.
25. Korn S, Hübner M, Jung M, Blettner M, Buhl R. Severe and uncontrolled adult asthma is associated with vitamin D insufficiency and deficiency. *Respir Res*. 2013;14(1):25. doi:10.1186/1465-9921-14-25.
26. Confino-Cohen R, Brufman I, Goldberg A, Feldman BS. Vitamin D, asthma prevalence and asthma exacerbations: A Large Adult Population-Based Study. *Allergy*. 2014;69(12):1673–80.
27. Menon GB, Nima V, Dogra A, Mittal C, Kaur U, Mittal. *European Respiratory Journal*. 2014;44:40–49.
28. Arshi S, Fallahpour M, Nabavi M. The effects of vitamin D supplementation on airway functions in mild to moderate persistent asthma. *Ann Allergy Asthma Immunol*. 2014;113(4):404–9.
29. Groot JCD, Roon EV, Storm H. Vitamin D reduces eosinophilic airway inflammation in nonatopic asthma. *J Allergy Clin Immunol*. 2015;135(3):670.e3–5.e3.
30. Yadav M, Mittal K. Effect of vitamin D supplementation on moderate to severe bronchial asthma. *Indian J Pediatr*. 2014;81(7):650–4.
31. Castro M, King TS, Kunselman SJ. Effect of vitamin D3 on asthma treatment failures in adults with symptomatic asthma and lower vitamin D levels: the VIDA randomized clinical trial. *J Am Med Assoc*. 2014;311(20):2083–91.
32. Guru H, Shah S, Rasool R, Qadri Q, Guru FR. Correlation between Asthma Severity and Serum Vitamin D Levels: Experience from a Tertiary Care Centre in North India. *J Biomedical Sci*. 2018;7(3):12. doi:10.4172/2254-609X.100091.
33. Hypponen E, Berry DJ, Wjst M, Power C. Serum 25-hydroxyvitamin D and IgE - a significant but nonlinear relationship. *Allergy*. 2009;64(4):613–20. doi:10.1111/j.1398-9995.2008.01865.x.
34. Alyasin S, Momen T, Kashef S, Alipour A, Amin R. The relationship between serum 25 hydroxy vitamin d levels and asthma in children. *Allergy Asthma Immunol Res*. 2011;3(4):251–5. doi:10.4168/aair.2011.3.4.251.

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