

Asthma Control in Oman

National Results within the Asthma Insights and Reality in the Gulf and the Near East (AIRGNE) Study

*Nasser Al-Busaidi¹ and Joan B Soriano²

السيطرة على الربو في عُمان النتائج الوطنية حول «الفهم العميق والحقيقة للربو» في الخليج العربي والشرق الأدنى

ناصر حمد البوسعيدي، جوان سوريانو

المخلص: الهدف: «الفهم العميق والحقيقة للربو» في الخليج العربي والشرق الأدنى عبارة عن سلسلة من الدراسات العالمية لتقييم السيطرة على الربو عند الكبار والصغار، وقد أجريت هذه الدراسة في عُمان لتقييم مطابقة السيطرة على الربو فيها مع الدليل والتوصيات العالمية. الطريقة: تم اختيار 102 من مرضى الربو الذين هم تحت العلاج أو الذين يعانون من أعراض الربو حاليا بصورة عشوائية بين يناير 2007 و مارس 2008 من مسقط وصحار ونزوى (سلطنة عُمان)، وتم استعمال الاستبيان القياسي المستعمل في «الفهم العميق والحقيقة للربو» لتقييم شدة الأعراض واستخدام مؤسسات الرعاية الصحية ومدى تقييد النشاط الجسدي واستعمال الأدوية. النتائج: كان 21% من مجموع 201 مريضا أقل من 16 سنة و 43% من الإناث. وكانت نسبة التدخين متدنية في العينة. كما ظهر تفاوت كبير في إدراك ماهية الربو ومدى السيطرة عليه في عُمان، إذ أدرك 57% من المرضى بأن حالة الربو حسنة أو تمت السيطرة عليها تماما، وفي الحقيقة أن حالة الربو عند 45% منهم لم يتم السيطرة عليها نهائيا أو كانت السيطرة عليها بشكل ضعيف. لم تلب كل التوصيات العالمية فيما يخص السيطرة على الربو بشكل كبير في عُمان، وبالأخص عند الأطفال المصابين بالربو، حيث ظهر أن 44% منهم يعانون من الاستيقاظ ليلا بسبب أعراض الربو في الأسابيع الأربعة المنصرمة، وأن 47% يعانون من الربو الناتج عن الرياضة خلال السنة الماضية. وعلى العموم كان هناك غياب عن الدراسة أو العمل في 32.6% من الأطفال و 34.8% من الكبار المصابين بالربو بسبب المرض خلال السنة الماضية. تبين أن 5% فقط من مرضى الربو يستخدمون البخاخ الوقائي (كورتيزون) وهذا يشكل أدنى نسبة من بين دول الخليج العربي والشرق الأدنى، والذي يعطي نسبة غير مقبولة بين استخدام البخاخ الوقائي (كورتيزون) / استخدام البخاخ الموسع للشعب الهوائية، وهي 0.054 لدى مرضى الربو العُمانيين. الخلاصة: السيطرة على الربو في عُمان بعيدة جدا عن المعايير العالمية المتبعة وهذا يتطلب إيجاد استراتيجيات تصحيحية.

مفتاح الكلمات: ربو، عُمان، مسح صحي، منع الربو والسيطرة عليه، بالغ، طفل.

ABSTRACT: Objectives: The Asthma Insights and Reality (AIR) study in the Gulf and Near East (one of a worldwide series of surveys conducted in adults and children to assess asthma control) was conducted in Oman to assess how closely asthma control meets international guidelines recommendations. **Methods:** From January 2007 to March 2008, asthmatics receiving treatment or currently suffering from asthma symptoms were interviewed among nationals randomly surveyed from the most populated urban areas in Oman (Muscat, Sohar and Nizwa). The standard AIR questionnaire was used to assess symptom severity, health care utilisation, limitation of activity and medication use. **Results:** From 201 asthmatic participants, 21% were under 16 years and 43% were female. Tobacco use was low in our asthmatics. Disparity in asthma perception was wide in Oman; while 57% of asthmatics perceived their asthma as well or completely controlled, actually 54% had poorly or not well controlled asthma. All recommendations for asthma control by the Global Initiative for Asthma were largely unmet, especially in child asthmatics, with 44% reporting night awakenings due to asthma during the previous 4 weeks and 47% exercise-induced asthma in the previous 12 months. Overall, 32.6% of children and 34.8% of adults reported absence due to asthma from school/work during the previous year. Use of preventive inhaled corticosteroids was only 5.0%, one of the lowest even within the AIR Gulf and Near East study, producing an unacceptable ratio ICS/SABA (inhaled corticosteroid/short acting beta-agonist) of 0.054 in Omani asthmatics. **Conclusion:** Asthma control in Oman falls far below the goals of current international guidelines therefore corrective strategies are needed.

Keywords: Asthma; Oman; Health survey; Asthma Prevention & Control; Adult; Child

ADVANCES IN KNOWLEDGE

1. Current international asthma initiatives, both for children and adults, recommend to measure the asthma burden worldwide. However,

¹Department of Medicine, Royal Hospital, Muscat, Oman; ²Epidemiology and Clinical Research, Fundación Caubet-Cimera (Centro Internacional de Medicina Respiratoria Avanzada), Islas Baleares, Spain.

*Corresponding Author email: enhsa@hotmail.com

to date there were few studies conducted in the Gulf and none in Oman focused on measuring asthma control and asthma severity.

2. The current use of preventive medications in Omani asthmatic children and adults appear to be one of the lowest in the Gulf region, and even worldwide.

APPLICATION TO PATIENT CARE

1. Doctors in Oman should be aware of the burden of asthma.

2. Educational and corrective strategies should be implemented in Oman to improve individual and population asthma management.

THE GLOBAL INITIATIVE FOR ASTHMA (GINA) guidelines, which were introduced in 1995,¹ followed by many other local guidelines, all aimed at improving asthma patient care and ensuring better long-term control of the disease. Control was the cornerstone of the latest GINA update in 2006.² Studies have shown that total asthma control is achievable in most patients.³ There exists, however, a wide gap between the goals of treatment as set out in the guidelines and actual real-life clinical practice outcomes. Recently, several Asthma Insights and Reality (AIR) surveys were conducted in various countries around the world, including the USA, Canada, the Asia-Pacific region, Western and Central-Eastern Europe, Japan, Latin America, Saudi Arabia, and most recently in the Gulf and the Near East. They all aimed to determine variations in asthma severity and control, both from the patient perspective and objectively, compared to what is recommended by the guidelines. Consistently, these surveys demonstrated a poor level of asthma control in all the above mentioned countries and regions, with local variations specific to each country.

Oman is in the Middle East at the northern edge of the Gulf with a population of about 2.6 million inhabitants. There is a paucity of statistics about asthma prevalence and asthma burden in Oman. By using the International Study of Asthma and Allergies in Childhood (ISAAC) methodology 2003, Al-Riyami *et al.* reported prevalence rates of diagnosed asthma in Oman of 20.7% in 13–14 year-olds, whereas in younger children (6–7 years) it was 10.5%.⁴

The prevalence of severe asthma (sleep-disturbing wheeze and speech-limiting wheeze) and frequent symptoms in Omani schoolchildren (age between 6–7 years), compared with other ISAAC participating countries in the East Mediterranean region, was higher than in any other country in the study. Similarly, the prevalence of sleep-disturbing wheeze among Omani children was nearly four

times that of Iran and almost double that of Malta.⁴ We also previously reported that more than 50% of our adult asthmatic patients felt that their asthma had a negative impact in their work, school or home duties.⁵ Nocturnal symptoms were common in our studied patients, only 44% reported having had no night-symptoms in the previous 4 weeks, while the rest felt their asthma often disturbed their sleep. This ranged from 4% reporting two to three wake-ups per night to 28% reporting one to two wake-ups due to asthma in the last 4 weeks.⁵

The GINA guidelines have been developed to promote standardised methods of diagnosis and treatment of asthma that now are generally accepted worldwide. Research published since the release of the GINA guidelines indicates that in many countries patients with asthma are unequally treated and that adherence to asthma treatment guidelines is poor.^{6,7}

All AIR studies aimed to assess the discrepancy between perceived symptoms and subjective assessments versus objective control and the burden of asthma in order to determine the implementation status of the goals and management recommendations advocated by GINA. They also have helped to shed light on the perceptions, knowledge and attitudes related to asthma at the local level in order to assist in future national policy development. Oman was one of the Gulf and Near East countries included in the AIR Gulf and Near East (AIRGNE) study, together with Jordan, Kuwait, Lebanon, and the UAE. The summary results have been published elsewhere,⁸ but the specific Omani data results warrant a closer look and are presented in this paper.

Methods

The AIRGNE survey was conducted between January 2007 and March 2008. The most populated urban areas in Oman were surveyed in AIRGNE, namely the capital area, Muscat/Seeb/Mutrah, with

60% of the sample; Sohar, a port city on the northern coast of Oman with 25%, and Nizwa, a city 120km south west of Muscat in the Dakhiliyah region with 15%. The sampling was structured by gender and age within each city or urban area.

Asthma patients were identified by systematically screening a sample of households for persons who had been diagnosed with asthma. A sampling plan was designed to provide a nationally representative sample of households that could be screened to identify a community sample of current asthma sufferers for Oman. A geographically stratified sample of households, proportionate to the population, was drawn within the three designated areas. The survey design required a sample of 200 asthma patients. In each household, an adult was asked whether a physician had ever diagnosed any member of the household as having asthma. If the answer was “yes”, the interviewer asked whether any of these individuals were currently taking medication for their asthma, or had suffered an asthma attack or experienced asthma symptoms in the past year. The number of persons in the household, as well as the number who had been diagnosed with asthma and met the survey criteria for current asthma, were collected to provide estimates of comparative prevalence. If more than one household member qualified as a current asthma patient, the interviewer randomly selected one as the designated respondent. Only one respondent was interviewed per household because multiple interviews in the same household would have created a bias. If the selected respondent was 16 years of age or older, the interview was conducted with the patient; if he/she was 15 years or younger, the interview was conducted with the parent or guardian most knowledgeable about the child’s asthma condition and treatment.

The study was approved by the Ethics Committee of the Ministry of Health, Oman. This study was non-interventional and anonymous, and no individual identifiers were obtained or stored. Following the advice of the coordinating team in Europe (JB Soriano) it was considered that the verbal authorisation from individual asthmatics (or his/her parent) would be sufficient consent.

The core questionnaire was that used in previous AIR studies in Europe and elsewhere,⁸ which was based on the original ATS (American Thoracic Society) questionnaire.⁹ The questionnaire

was translated into Arabic and then translated back again; any discrepancies or inconsistencies discovered by this process were solved by consensus. In addition, the following items were included: self-completion of the asthma control test (ACT) questionnaire,¹⁰ various questions modified to reflect the local conditions and characteristics of asthma in Oman and some additional questions to reflect the latest GINA guidelines. It was administered with an English-Arabic side-by-side layout,⁸ available online from the International Journal of Tuberculosis and Lung Disease (IJTLD) website.¹⁰

As per standard quality control procedures, all materials were piloted. There was also a personal briefing of all interviewers in each region, and each interviewer conducted two pilot interviews and reviewed the completed questionnaires with a supervisor before starting fieldwork. Completed questionnaires were checked locally and again centrally, and a random double check of interviews in all regions was conducted by telephone. Finally, all data were included in a database after independent double typing.

The frequency and severity of daytime and night-time symptoms, exercise-induced symptoms and severe episodes, and total symptom frequency, were used to develop a symptom severity index similar to the GINA asthma severity scale.¹¹ In addition, events such as hospitalisations and emergency care utilisation were documented, as well as the impact of days of school/work lost due to asthma. Patient demographic and asthma severity characteristics were compared using chi-squared analysis to identify factors that might account for differences in asthma management across the country, or analysis of variance for quantitative variables whenever required. Statistical comparisons within the country versus the published international AIR estimates were explored. All statistical tests were two-sided and comparisons with <5% probability of error were considered statistically significant.

Results

A total of 201 valid interviews with Omani asthmatics in the three participating cities were completed, of whom 115 (57%) were male. The age distribution was very young, with 21% of the sample being 5–15 years old and 33% 16–29

Table 1: Demographic characteristics of asthma patients. Values correspond to numbers (percentages) of patients in the corresponding category except for age of adults and children at inclusion and age at diagnosis which are represented as means \pm standard deviation (13.5 \pm 6.7)

Parameter	Population N = 201
Interval age distribution	
5–15 years	43 (21%)
16–29 years	67 (33%)
30–49 years	71 (35%)
> 50 years	20 (10%)
Age at diagnosis, mean;	13.5
Gender	
M	115 (57%)
F	86 (43%)
Level of education	
Primary	77 (38%)
Secondary	62 (30%)
University	62 (30%)
Income	
<1000 \$	152 (75%)
1000–2000 \$	36 (18%)
>2000 \$	13 (6%)
Region	
Muscat	121 (60%)
Sohar	50 (25%)
Nizwa	30 (15%)
Smoking habits in adults	
Never smoked	173 (96%)
Former smokers	7 (3%)

years old. Most participants had only completed primary (38%) or secondary (30%) education. Reported income was lower than \$1,000 per year in 75% of surveyed participants, while reported smoking in adults was minimal [Table 1].

A total of 90 (57%) of adult asthmatic responders (n = 158) perceived their asthma as "well" or "completely" controlled. The actual figures show, on the contrary, that 54% of adult responders had "poorly" or "not well" controlled asthma. ($P < 0.05$).

A total of 71% of participating Omani asthmatics reported day-symptoms during the previous 4 weeks. Similarly, 44% reported night awakenings due to asthma during the previous 4 weeks and 47%

Table 2: Comparison between objective and subjective evaluation of asthma control

	Subjective asthma control§	Objective asthma control*	P value
Poorly and not well controlled	68 (43%)	86 (54%)	<0.05
Well/ completely controlled	90 (57%)	72 (46%)	

Note: § = Adult responders only (n=158); * = objective evaluation of asthma control relies on the asthma control test (ACT). An ACT of 5 to 19 corresponds to a poorly and or not well controlled asthma, and an ACT of 20 to 25 corresponds to a well controlled asthma for adult responders only (n=158).

exercise-induced asthma in the previous 12 months, both were particularly frequent in child asthmatics [Table 3]. Exacerbations and use of health services were equally high, and limitations of daily activities due to asthma were widespread both in children and adult asthmatics. One in three asthmatics had never had their lung function tested and few owned a peak flow meter.

A total of 32.6% of children reported school absence due to asthma during the previous year, with a mean standard deviation (SD) of 6.1 (8.5) days. In adults 34.8% reported work absence due to asthma during the past year, with a mean SD of 9.9 (9.8) days [Table 4]. Use of health services was similarly high compared to other AIRGNE participating countries, with 30% of hospitalisations and 58% of emergency (unscheduled) medical visits.

Finally, current use of preventive inhaled corticosteroids was 5.0%, one of the lowest even within the AIRGNE study, with a mean of 14.6%. Most (92%) patients relied rather upon quick relief medications, producing an unacceptable ratio ICS/SABA (inhaled corticosteroid/short acting beta-agonist) of 0.054 [Table 5]. As mentioned above, there was a low prevalence of both ownership of a peak flow meter (25.4%) and ever having had a lung function test (35.0%) in the Omani asthmatics in this study.

Discussion

AIRGNE-Oman was the first survey in the country to assess objectively the level of control and severity of asthma. It demonstrated that asthma management was poor in 2007–2008 compared to recommendations in published guidelines. As in

Table 3: The Global Initiative for Asthma (GINA) recommendations for asthma control and the Asthma Insights and Reality in Oman (AIRO) results

GINA definition for control of asthma	AIRO findings	Adults (%)	Children (%)	All (%)
Minimal (ideally no) chronic symptoms, including nocturnal symptoms	Asthma symptoms			
	During day (past 4 weeks)	73	81	71
	Night wakening (past 4 weeks)	45	60	44
	Exercise-induced asthma (past 12 months)	51	60	47
Minimal exacerbation	Sudden severe episodes in past 12 months	95	84	93
No emergency visit for asthma	Hospitalisation (past 12 months)	35	42	30
	Emergency department visit (past 12 months)	18	36	21
Minimal need for short-acting β 2-agonists	Current use of quick-relief bronchodilators	-	-	85
No limitation on activities, including exercise	Asthma restricts			
	Sports and recreation	38	77	46
	Normal physical Activity	35	70	43
	Choice of jobs/careers	18	14	17
	Social activities	32	42	34
	Sleeping	22	56	29
	Lifestyle	21	49	27
Normal or near-normal lung function (PEF variability 20%)	Household chores	20	49	26
	Never had a lung-function test	42	19	35
	Owens a peak flow meter	17	35	25

Legend: PEF = peak expiratory flow.

all previously published international AIR studies, asthma is poorly managed in Oman with the performance far below the recommended goals of any guidelines. This was obvious when the actual GINA recommendations of control were compared to the AIRGNE-Oman findings [Table 2], clearly showing that guideline-based control was not achieved at the time in of our study.

In the European and Asia Pacific AIR studies approximately half of the adult patients reported daytime symptoms. The overall figure in the AIRGNE study was 68%, and it was equally high in Oman (71%) in the present study. These results are close to the findings of Rawas *et al.* as they found nearly 60% of all current wheezers reported at least one of the symptoms indicating severe or uncontrolled asthma.¹⁴ Night awakenings were also frequent in the AIRGNE-Oman study (44%), and this finding is compatible with the study of

Al-Riyami *et al.*⁴ where the prevalence of sleep-disturbing wheeze in Oman was nearly four times that of Iran (3.5% versus 0.9%) and more than double that of Malta (3.5% versus 1.5%). It was even higher than that of Australia (3.5% versus 2.8%), a country with the highest prevalence rate of wheeze among all ISAAC participating countries, being more than three times that of Oman.

The frequency of hospitalisation in Oman in the previous twelve months was also high, reaching 30%. Emergency department visits were high in Oman, as in other AIRGNE countries, the figures being 58% and 51% respectively. These figures were much higher than those in the study conducted by Al Rawas *et al.*¹² Of the asthmatic patients in his study, who were attending asthma specialty clinics, only 31.9% had visited the emergency department and 15.0% patients had been hospitalised at least once during the previous year.

Table 4: Evaluation of asthma burden in the past year in Oman by comparison to Asthma Insights and Reality in the Gulf and Near East (AIRGNE) study results

	Oman (N = 201)	AIRGNE (N= 1,000)	P value
Asthma burden in the past year			
School absence in children, %	32.6	51.7	<0.05
Mean number of days (SD)	6.1 (8.5)	7.9 (9.6)	
Work absence in adults, %	34.8	29.7	0.420
Mean number of days (SD)	9.9 (9.8)	7.3 (8.1)	
Use of health services in the past year			
Hospitalisation, %	30.0	22.5	0.723
Emergency medical visit, %	58.0	51.5	0.571

Legend: SD= standard deviation.

On the other hand, school absence in children was significantly less frequent in Oman than in other AIRGNE countries (32.6% versus 51%; $P < 0.05$, Chi 2 p statistic when compared to AIRGNE results.) Another positive finding among adult asthmatics in AIRGNE-Oman study was the very low prevalence of smoking, with only 3% of respondents reporting either a current or previous smoking habit. This is probably one of the lowest figures recorded worldwide,¹³ and indeed an achievement to be sustained in the future.

The current use of asthma medications in Oman is disappointing. According to the findings in this study, only 5% of asthmatics were using inhaled corticosteroids compared to 14.6% in other AIRGNE countries ($P < 0.05$). On the other hand, the use of rescue medication was strikingly high, with 92% of asthma patients reporting daily use of them compared to 55.5% in other AIRGNE countries. Interestingly, these findings totally differ from Al Rawas *et al.* where 92% of asthma patients attending asthma specialty clinics used inhaled corticosteroids.¹² The discrepancy is likely due to

the fact that patients in asthma specialty clinics are seen by chest specialists who are aware that steroid inhalers are the cornerstone of asthma treatment; it is also possibly due to the fact that these patients have more severe asthma.

Most patients overestimated their level of control and underestimated their disease severity, as there was a disparity in the patient subjective versus objective asthma severity perception. While 90 (57%) of asthmatics perceived their asthma as well or completely controlled, actually 54% had poorly or not well controlled asthma as objectively identified by an ACT score of 5 to 19 ($P < 0.05$). The frequency of lung function tests was generally low in Oman, being at similar levels to other AIRGNE countries, as only 35% reported their lungs ever tested, and only 25% owned a peak flow meter.

Overall, when comparing the Omani results with the AIRGNE average, the management of asthma in Oman was worse in terms of reporting a higher use of rescue medications and very low uses of inhaled corticosteroids, as well as unacceptably frequent visits to emergency departments.

Table 5: Current use of preventive inhaled corticosteroids and quick relief medications, and evaluation of lung function in Oman by comparison to Asthma Insights and Reality in the Gulf and Near East (AIRGNE) study results

	Oman (N = 201)	AIRGNE (N= 1,000)	P value*
Current use of medication (previous 4 weeks)			
Use of ICS, %	5.0	14.6	<0.05
Use of quick relief, %	92.0	55.5	<0.05
Ratio ICS/SABA	0.054	0.26	<0.05
Lung function			
Own a peak flow meter, %	25.4	17.1	<0.05
Ever had a lung function test, %	35.0	32.7	0.746

Legend: ICS= inhaled corticosteroids; SABA= short acting beta-agonist.

There are some potential limitations of this survey. First, sampling was not performed according to Random Digit Dialing (RDD) as in most other AIR surveys. In countries where telephone ownership levels approach 100% and comprehensive databases are available, RDD can approximate a representative random sample of the population. However, RDD was not considered appropriate in Oman, and overall in the GNE, because of the low penetration of telephone coverage.

Second, there are problems associated with the term asthma in our country, therefore many doctors avoid using this term, and use instead the term allergy, with an intention to making it milder and more acceptable to patients themselves or to their parents. Perhaps third, the sample size of 201, while being considerable enough, gives some subgroup analyses (by young children or in severe asthma) reduced statistical power. Therefore, more studies are needed to monitor all trends and assess current interventions.

Conclusion

The AIR study in Oman highlights the gap between the recommended long-term asthma management guidelines and the reality in Oman. International guidelines recommend treating inflammation and not symptoms, but the trend of poor inhaled corticosteroid utilisation among Omani patients with persistent asthma suggests undertreatment. This implies an immediate need to improve communication and awareness among patients and physicians, specifically to reinforce the use of anti-inflammatory medications. Underestimation of the severity of asthma and overestimation of asthma control by both patients and physicians are important factors contributing to poor asthma control.

CONFLICT OF INTEREST

The AIRGNE survey was sponsored by GlaxoSmithKline. All authors had access to the database and discussed and drafted this report independently from the sponsor.

References

1. Global Initiative for Asthma (GINA). Global strategy for asthma management and prevention. NHLBI/WHO workshop report. National Institute of Health, National Heart, Lung and Blood Institute; 1995. National Institute of Health publication no. 95-3659.
2. Bateman ED, Hurd SS, Barnes PJ, Bousquet J, Drazen JM, FitzGerald M, et al. Global strategy for asthma management and prevention: GINA executive summary. *Eur Respir J* 2008; 31:143–78.
3. Bateman ED, Boushey HA, Bousquet J, Buss WW, Clark TJ, Pauwels RA, et al. Can guideline-defined asthma control be achieved? The Gaining Optimal Asthma Control study. *Am J Respir Crit Care Med* 2004; 170:836–41.
4. Al-Riyami BMS, Al-Rawas OAS, Al-Riyami AA, Jasim LG, Mohammed AJ. Relatively high prevalence and severity of asthma, allergic rhinitis and atopic eczema in schoolchildren in the Sultanate of Oman. *Respirology* 2003; 8:69–76.
5. Al-Busaidi N, Al Mokhaini S. Level of control of asthma patients in chest specialist clinics. *Oman Med J* 2009; 24:195–8. doi:10.5001/omj.2009.38.
6. Rickard KA, Stemple DA. Asthma survey demonstrates that the goals of the NHLBI have not been accomplished. *J Allergy Clin Immunol* 1999; 103:S171.
7. Largelov P, Veninga CC, Muskova M. On behalf of the Drug Education Project (DEP) group. Asthma management in five European countries: Doctors' knowledge, attitudes and prescribing behavior. *Eur Respir J* 2000; 15:25–9.
8. Khadadah M, Mahboub B, Al-Busaidi NH, Sliman N, Soriano JB, Bahous J. Asthma insights and reality in the Gulf and the near East. *Int J Tuberc Lung Dis* 2009; 13:1015–22.
9. Ferris BG. Epidemiology standardization project. *Am Rev Respir Dis* 1979; 118:S1–120.
10. International Journal of Tuberculosis & Lung Disease. GINA questionnaire. From: <http://www.theunion.org/about-the-journal/about-the-journal.html> Accessed: July 2010.
11. Rabe KF, Vermeire PA, Soriano JB, Maier WC. Clinical management of asthma in 1999: the Asthma Insights and Reality in Europe (AIRE) study. *Eur Respir J* 2000; 16:802–7.
12. Schatz M, Sorkness CA, Li JT, Marcus P, Murray JJ, Nathan RA, et al. Asthma Control Test: reliability, validity, and responsiveness in patients not previously followed by asthma specialists. *J Allergy Clin Immunol* 2006; 117:549–56.
13. Rabe KF, Vermeire PA, Soriano JB, Maier WC. Clinical management of asthma in 1999: the Asthma Insights and Reality in Europe (AIRE) study. *Eur Respir J* 2000; 16:802–7.

Vitamin D Status in Pregnant Omanis

A disturbingly high proportion of patients with low vitamin D stores

Moza Al Kalbani,¹*Omayma Elshafie,² Mohammed Rawahi,² Ali Al-Mamari,² Abdullah Al-Zakwani,³
Nicholas Woodhouse⁴

حالة فيتامين (د) عند العُمانيات الحوامل وجود نسبة منخفضة من فيتامين (د) عند نسبة عالية من المريضات تثير القلق

موزة الكلباني، أميمة الشفيق، محمد الرواحي، علي المعمرى، عبد الله الزكواني، نيكولاس ودهاوس

الملخص: الهدف: تحديد نسبة فيتامين (د) عند النساء العُمانيات الحوامل بقياس نسبة 25 هايدروكسي فيتامين (د) في الدم. الطريقة: تم أخذ عينات من الدم من 100 من النساء العُمانيات الحوامل اللواتي يتمتعن بصحة جيدة، والمترددات إلى المستشفى العسكري في مسقط في زيارتهن الأولى بعد الحمل. أجريت الدراسة خلال فترة الصيف مايو-يونيو-يوليو سنة 2010. النتائج: أثبتت هذه الدراسة أن هناك نقصاً في نسبة فيتامين (د) عند 34 (35%) امرأة (≥ 25 نانومول/ليتر). وعدد اللواتي يشكلن خطورة 67 (69%) امرأة (مستوى 25 هايدروكسي فيتامين (د) بين 25-50 نانومول/ليتر). ولا يوجد لدى أي من المراجعات النسبة الطبيعية للفيتامين (< 75 نانومول/ليتر). الخلاصة: أثبت هذا البحث وجود حاجة لإعطاء فيتامين (د) أثناء الحمل وفترة الرضاعة وذلك بتناول فيتامين (د) 3 يومياً وبجرعة لا تقل عن 1000 وحدة عالمية.

مفتاح الكلمات: حمل، عُمان، 25 هايدروكسي فيتامين (د) 3، نقص فيتامين (د).

ABSTRACT: Objectives: The objective of this study was to determine the vitamin D status of pregnant Omanis by measurement of their circulating 25 hydroxy vitamin D levels. **Methods:** Blood samples were obtained from a cohort of 103 consecutive healthy pregnant Omanis at the Armed Forces Hospital, Muscat, on their first antenatal visit. The study took place in May, June and July 2010. **Results:** Vitamin D deficiency was present in 34 (33%) of patients (25OHD3 <25 nmol/L), 'at risk' levels were found in 67 (65%) patients (25OHD3 25-50 nmol/L); two patients (1.9%) had values between 50 and 75 nmol/L, and no patients in the optimal range >75 nmol/L. **Conclusion:** If confirmed, these findings indicate the need for vitamin D replacement during pregnancy and lactation. Although not evidence based we recommend at least 1000 IU of cholecalciferol, (vitamin D3) daily.

Keywords: Pregnancy; Oman; 25 hydroxyvitamin D3 (25OHD3); Vitamin D deficiency

ADVANCES IN KNOWLEDGE

This article is the first to draw attention to the possibility of widespread vitamin D deficiency among pregnant women in Oman.

APPLICATION TO PATIENT CARE

Until more is known about the vitamin D status in Omanis, we recommend that all pregnant women and lactating mothers should receive vitamin D supplements with at least 1000 IU vitamin D3 daily.

DEFICIENCY OF VITAMIN D IS COMMON worldwide¹ including the Gulf states.^{2,3} The latter is surprising as sunlight is abundant in the Middle East. More than 90% of our vitamin D is provided by sunlight⁴ and it is therefore obvious that those persons affected in Arabian countries have little sunlight exposure and a diet deficient in vitamin D.

The role of vitamin D in normal physiology is complex and wide ranging. It has important

immune modulating effects protecting against infection,^{4,5,6} autoimmune disorders⁷ and certain cancers, in addition to its well documented effects on the prevention of osteoporosis, fractures, falls in the elderly^{4,5} and impaired cognitive function.⁸

As we continually see patients with vitamin D deficiency in our clinics, it became important to establish whether or not vitamin stores (25OHD) are normal in a healthy Omani population. For this reason, we chose patients in their first and second

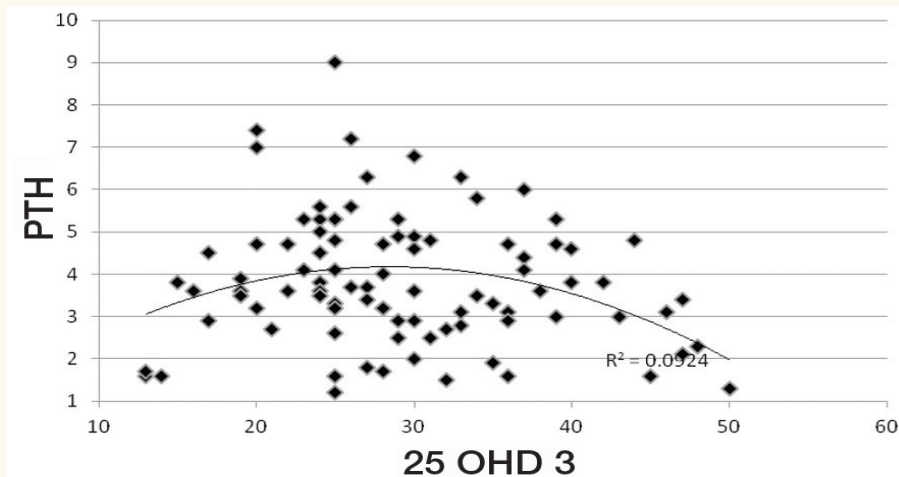


Figure 1: Relationship between PTH (normal range 1.6–9.3 pmol/L) and 25(OH)D₃ levels. There was no linear correlation between PTH and 25OHD₃ levels, but using a polynomial curve, the correlation coefficient was significant at 0.55.
Legend: PTH = parathyroid hormone; 25(OH)D₃ = vitamin D₃.

trimester of pregnancy as pregnancy and lactation are associated with profound alterations in calcium absorption and skeletal remodelling necessitating increased utilisation of vitamin D. Our findings are reported below.

Methods

Blood samples were obtained from a cohort of 103 consecutive healthy Omani patients at their first antenatal visit, usually in the first, but sometimes the second trimester. They were then assayed for serum calcium (Ca), phosphate (Phos), and serum alkaline phosphatase (ALP), which were measured by spectrophotometry, (COBAS Integra 800, Roche Diagnostics, Indianapolis, USA) on the same day. Serum samples for parathyroid hormone (PTH) were measured by immunochemiluminescence (Access 2, Beckman Coulter, Inc., CA, USA), and 25(OH)D₃ by the LB211 gamma counter (Berthold GmBH & Co. KG, Bad Wilbad, Germany), having been centrifuged and deep frozen at -40° C. PTH and 25(OH)D₃ were then measured on the same day at the end of the study.

Statistical analysis was performed to determine the relationship between the level of serum Ca, Phos, ALP and PTH versus the level of serum 25(OH)D. We used a correlation test to calculate the significance of these relationships. As this showed no significant linear correlation, a polynomial trend curve was employed. The calculations were made

for all groups of patients.

Fully informed consent was obtained from each patient to extract the blood needed for the above procedures in addition to that required for routine antenatal screening. The study was approved by the Armed Forces Hospital authorities.

Results

Serum 25OHD₃ levels were deficient (<25 nmol/L) in 34 patients, between 25 and 50 nmol/L in 67 patients (at risk) and two patients had values between 50 and 75 nmol/L. There was no significant linear correlation between 25(OH)D₃ and serum Ca, Phos or ALP levels or parity. However, a significant relationship between PTH and 25(OH)D₃ was observed which differed between the 'deficient' and the 'at risk' groups. This was confirmed using a polynomial curve, which had a significant correlation value of 0.55 [Figure 1].

Discussion

This is the first study to report vitamin D status in normal pregnant Omanis. The results are alarming: 34% of these apparently healthy women were vitamin D deficient and a further 64% 'at risk' at a time when there is a critical need for calcium metabolism to be normal. A pregnant woman must provide 25 to 30 gm of calcium to support the developing foetal skeleton. Much of this demand

occurs in the third trimester when the foetal skeleton undergoes mineralisation. This demand is compensated for by an increased absorption of calcium from the gut induced by rising levels of PTH and the active metabolite of vitamin D, 1,25 dihydroxy vitamin D (1,25(OH)2D).⁹ At this point 25(OH)D will be utilised to make more 1,25(OH)2D and those patients with low stores will be at considerable risk for the development of vitamin D deficiency and osteoporosis in old age.¹⁰

To compound this problem, many Omani women have 6 or more children and breast feed for up to 2 years. During lactation, hyperabsorption of calcium does not occur and remineralisation of the maternal skeleton only starts after weaning when PTH, and 1,25(OH)2D levels rise, calcium absorption increases and urinary calcium levels fall, a process that may persist for months.¹¹ Obviously, adequate stores of 25(OH)D are vital during this period, otherwise skeleton remineralisation will be seriously impaired and possibly result in the development of osteoporosis in old age.^{4,5}

Interestingly, none of the patients in the 25(OH)D₃ deficiency group were symptomatic and serum PTH and ALP levels were still within the normal range. However there was a significant increase of the percentage rise in PTH in the face of a declining 25(OH)D level suggesting the early stages of a biological response to vitamin D deficiency in the "at risk" group. In the deficiency group the reverse response was seen. Our 25(OH)D₃ immunoassay results have been carefully checked and are correct. It is possible therefore that an overt rise of PTH and ALP levels has been suppressed by an oral intake of calcium in excess of 1 gm daily as this will delay the development of secondary hyperparathyroidism.^{12,13} Other factors such as body mass index may also be relevant¹⁴ but this was not examined here.

In addition to its musculo-skeletal actions, vitamin D deficiency is reportedly associated with the development of certain cancers, the metabolic syndromes and infections, as well as type 1 and type 2 diabetes,^{4,5} disorders which are common in Oman.

Our results confirm that vitamin D3 stores are low even in Omanis of reproductive age. These findings are similar to those reported in Saudi Arabians more than 25 years ago² and more recently in the UAE and Qatar.^{3,12} It therefore seems

sensible to advocate vitamin D supplementation for all pregnant women in the Middle East. At the present time, there are no clear cut recommendations as to the dose, but we recommend at least 1000 IU of vitamin D3 a day which should be continued throughout lactation. Until more is known about the daily calcium intake of Omanis, it would be prudent to advocate calcium supplementation as well.¹⁵

Conclusion

This study shows that vitamin D3 scores are low in pregnant Omanis. Further studies are required to confirm these findings. Until then, we recommend supplementation with vitamin D3 (cholecalciferol) for all pregnant and lactating mothers.

CONFLICT OF INTEREST

The authors reported no conflict of interest.

References

1. Thacher TD, Fisher PR, Strand MA, Pettifor JM. Nutritional rickets around the world: causes and future directions. *Ann Tropical Paediatr* 2006; 26: 1–16.
2. Woodhouse NY, Norton W. Low vitamin d levels in Saudi Arabians. *King Faisal Spec Hosp Med J* 1982; 2:127–31.
3. Saadi HF, Dawodu A, Afandi BO, Zayed R, Benedict S, Nagelkerke N. Efficacy of daily and monthly high dose calciferol in vitamin D deficient nulliparous and lactating women. *Am J Clin Nutr* 2007; 85:1565–71.
4. Holick MF. Vitamin D: A delightful health perspective. *Nutrition Rev* 2008; 66:5182–94.
5. Pearce SHS, Cheetham TD. Diagnosis and management of vitamin D deficiency. *BMJ* 2010; 340:b5664.
6. Holick MF. Vitamin D deficiency. Review article. *N Engl J Med* 2007; 357:266–81.
7. Hyponen E, Laara E, Reunanen A, Jarvelin M-R, Vertanen SM. Intake of vitamin D and risk of type 1 diabetes. A birth cohort study. *Lancet* 2001; 358:1500–03.
8. Llewellyn DJ, Lang IA, Langa KM, Muniz-Terrera G, Phillips CL, Cherubini A, et al. Vitamin D and risk of cognitive decline in elderly persons. *Arch Intern Med* 2010; 170:1099–100.
9. Affinito P, Tommaselli GA, di Carlo C, Guida F, Nappi C. Changes in bone mineral density and calcium metabolism in breastfeeding women: A one-

- year follow-up study. *J Clin Endocrinol Metab* 1996; 81:2314–18.
10. Javaid MK, Crozier SR, Harvey NC, Gale CR, Dennison EM, Boucher BJ. Maternal vitamin D status during pregnancy and childhood mass at age 9 years: a longitudinal study. *Lancet* 2006; 367:36–43.
 11. Kalkwarf HJ, Specker BL, Heubi JE, Viera NE, Yergey AL. Intestinal calcium absorption of women during lactation and after weaning. *Am J Clin Nutr* 1996; 63:526–31.
 12. Saadi HF, Nagelkerke N, Benedict S, Qazaq HS, Zilahi E, Mohamadiyah MK, et al. Predictors and relationships of serum 25 hydroxyvitamin D concentration with bone turnover markers, bone mineral density and vitamin D receptor genotype in Emirati women. *Bone* 2006; 39: 1136–43. Epub 2006 June 30.
 13. Steingrimsdottir L, Gúmarsson O, Indridason OS, Franzson L, Sigurdsson G. Relationship between serum parathyroid hormone levels, vitamin D sufficiency and calcium intake. *JAMA* 2005; 294: 2336–41.
 14. Paik J, Curhan G, Forman J, Taylor E. Determinant of plasma parathyroid hormone levels in young women. *Calcified Tissue Int* 2010; 87:211–17.
 15. Abrahamsen B. Patient level pooled analysis of 68,500 patients from seven major vitamin D fracture trials in US and Europe. (The DIPART group) *BMJ* 2010; 340:b5463.