Risk factors precipitating exacerbations in adult asthma patients presenting at Kalafong Hospital, Pretoria

[a] **Geyser MM,** BSc, DipPEC(SA), BSc(Pharm)Honns, MPraxMed, FCEM(SA), MSc(ClinEpi)
[b] **Rheeder P,** MMed (IntMed), FCP(SA), MSc (ClinEpi), PhD

[a] School of Health Systems and Public Health, University of Pretoria, Department of Family Medicine, Kalafong Hospital
[b] Department of Internal Medicine, University of Pretoria

Correspondence to: Mimi Geyser, e-mail: mimi.geyser@up.ac.za

Abstract

Background: Research into asthma is proceeding at an unprecedented rate and yet we live with a disease that escalates in prevalence and severity, despite a greater understanding of its pathophysiology and the necessary therapy. The total prevalence of asthma is estimated to lie at 7.2% of the world's population (6% in adults, 10% in children). Data from Australia, Canada and Spain report that acute asthma accounted for 1 to 12% of all adult emergency department visits. The prevalence of asthma in South Africa lies at 5% for adults and 10% for children. Asthma is reported as taking up 1 to 2% of the total health budget in direct costs, with equally large indirect costs being incurred for time lost from work and reduced productivity. It has also been reported that approximately one-third of the direct care costs of asthma are attributable to emergency department visits and hospitalisations. In some cases, exposure may be unavoidable (for example exposures to cold air, exercise or the asthma-inducing effects of pregnancy). Many studies have been done in other countries on specific triggers, especially allergens and viral respiratory infections. However, circumstances differ in the public sector in South Africa and other factors such as compliance and under-treatment, which may be applicable, should be studied in contention.

Methods: A matched case-control study was undertaken matched on age and gender between December 2003 and May 2005. Known asthma patients with exacerbations presenting at Kalafong Hospital's emergency unit were chosen as cases. Controls were stable asthma patients recruited from the outpatient departments. A structured questionnaire was used to interview patients concerning their possible exposure to certain triggers and risk factors. Univariate and multivariate analyses with conditional logistic regression were done to determine any significant exposures. Participants were between 18 and 65 years of age.

Results: In total, 356 patients were evaluated. Fifty cases and 100 controls were enrolled. Cases were shown to be more non-compliant than controls (OR = 2.18; 95% Confidence interval (CI): 1.09 to 4.38, p = 0.03). Missing follow-up doctor's appointments for the last six months were statistically significant with an OR of 2.39 (95% CI 1.08 to 5.27) and p = 0.03.

Conclusions: Non-compliance was a strong predictor of exacerbations in adult asthma patients at Kalafong Hospital.

Ⓟ **This article has been peer reviewed. Full text available at www.safpj.co.za** **SA Fam Pract 2008;50(4):67**

Background

Research into asthma is proceeding at unprecedented rates and yet we live with a disease that is escalating in prevalence and severity, despite a greater understanding of its pathophysiology and the necessary therapy.[1–4] The total prevalence of asthma is estimated to lie at 7.2% of the world's population (6% in adults, 10% in children).[5] Data from Australia, Canada and Spain report that acute asthma accounts for 1 to 12% of all adult Emergency Department (ED) visits.[6] The prevalence of asthma in South Africa lies at 3.8% for adults[7] (3% for males and 4.4% for females)[8] and 13.3% for adolescents.[9] Green et al report that asthma takes up 1 to 2% of the total health budget in direct costs, with equally large indirect costs being incurred for time lost from work and reduced productivity.[10] Osur states that approximately one-third of the direct care costs of asthma are attributable to ED visits and hospitalisations.[2]

The reasons for rising rates of morbidity and mortality connected with asthma are unclear. Case-control studies using retrospectively collected data have suggested that excess use of short-acting ß-agonists and under-use of inhaled corticosteroids may be associated with this phenomenon, although more recent data suggest that patterns of $ß_2$-agonist use may be a marker of more severe asthma rather than a causal factor.[1]

The beneficial effects of inhaled steroids when used as maintenance therapy in chronic asthma are well known. When used regularly, inhaled steroids decrease the number of asthma exacerbations caused by most triggers, including exercise.[11] This fact has also been recognised in a Cape Town study, in which it was concluded that practitioners should increase the use of current asthma guidelines, as under-treatment is a huge problem.[12]

Patients at any level of severity – from mild intermittent to severe persistent – can have exacerbations. Each patient with asthma responds to a unique set of triggers. In some cases, exposure may be unavoidable (for example, exposures to cold air, exercise or the asthma-inducing effects of pregnancy).[13]

Many triggers can provoke asthma exacerbations. According to the literature the following are possibilities: (1) inhalant irritants such as passive smoke (cigarette) exposure[1,4,13,14] and diesel exhaust fumes;[15] (2) inhalant allergens such as house dust mites;[2,4,14] (3) adverse drugs;[13,16] (4) poor adherence/non-compliance to therapy;[13,17] (5) extremes in weather or temperatures;[13] (6) exercise;[4] (7) respiratory infections;[18–20] (8) strong emotions,[13,21] etc.

Many studies have been done in other countries on specific triggers, especially allergens and viral respiratory infections. However, circumstances differ in the public sector in South Africa, and other factors such as compliance and under-treatment, which may be applicable in this context, should be studied in contention.

Methods

The setting for this study was the emergency unit, the primary health clinic and the asthma clinics at the secondary family medicine and internal medicine outpatient departments at Kalafong Hospital, a secondary regional and teaching hospital affiliated to the University of Pretoria. The study population consisted of adult asthma patients between 18 and 65 years of age, who were representative of the communities served by Kalafong Hospital.

The study design used was a matched case-control study – matched on age and gender. Each of the cases was matched with two controls. Known asthma patients were considered cases if they had developed an acute asthma exacerbation, defined as shortness of breath, chest tightness, wheezing and a peak expiratory flow rate (PEFR) that was at least 15 to 25% less than normal, requiring an ED visit, between December 2003 and May 2005. Known asthma patients were considered controls if they had had no exacerbations requiring emergency visits during the preceding month. Controls were recruited from the primary health clinic, secondary family medicine clinic and the internal medicine outpatients department.

Inclusion criteria for study participants

Inclusion criteria for the study participants consisted of the following:

- Diagnosis of asthma according to the National Guidelines of Management of Asthma in Adults at the Primary Level: Department of Health Directorate: Chronic Diseases, Disabilities and Geriatrics.[22]
- Duration of asthma of more than one year.
- Attendance of an asthma clinic at the family medicine or internal medicine departments of Kalafong Hospital for six months or longer.

Exclusion criteria

Exclusion criteria were:

- Any history of smoking
- Self-diagnosed asthma
- Newly diagnosed asthma
- Pulmonary embolism
- Active pulmonary tuberculosis
- Chronic Obstructive Pulmonary Disease (COPD)
- Congestive heart failure
- Cough secondary to medications (e.g. angiotensin-converting enzyme inhibitors)
- Mechanical obstruction (e.g. tumour)
- Pulmonary eosinophilic infiltration
- Vocal cord dysfunction

A complete sampling of all cases that met the inclusion criteria was done. In total, 444 asthma patients were treated at the unit between December 2003 and May 2005. Of these, 356 patients were evaluated by the investigator. Fifty patients fitted the inclusion criteria and were included in the study as cases.

The investigator used a structured questionnaire as a basis for interviewing the participants, after obtaining informed consent from the participants to interview them. Information obtained from the questionnaire about exposure to possible triggers included age, gender, compliance, literacy, allergic rhinitis, infections, exercise, passive smoking, in-house coal fires, adverse drugs, stress/anxiety, exposure to household pets, premenstrual/menstrual phases, pregnancy, work-related exposures and under-treatment. Exposure to triggers was noted for the previous four weeks in both cases and controls.

Definitions of possible trigger/risk factors

The definitions of the possible trigger/risk factors are set out below.

1. **Non-compliance**
   Non-compliance was identified as a trigger/risk factor when participants missed one or more doctor's appointment in the past

six months, or missed one or more script appointment in the past six months or did not take medication as prescribed. The patients were required to describe exactly how they used their medication, and this was compared to the prescriptions in their files. The doctor and script appointments were available from each patient's file.

2. Literacy level

The following four sub-groups were included:

1. No schooling
2. Some primary schooling
3. Some high school training
4. Matriculation

A low literacy level was seen as a trigger/risk factor.

3. Severity of the chronic phase of asthma

The following four sub-groups were investigated in accordance with the Guidelines for the Management of Chronic Asthma in Adults – 2000 Update.[23]

1. Mild intermittent
2. Mild persistent
3. Moderate persistent
4. Severe persistent

A high level of severity of chronic asthma was seen as a trigger/risk factor.

4. Under-treatment

The prescribed medication of the patient was evaluated against the severity of the chronic phase of the patient's asthma as specified in the guidelines for the management of chronic asthma in adults.[23] Under-treatment was defined as the omission of corticosteroid inhalers to patients who qualified for treatment with them or the prescription of inappropriate dosages of inhaled corticosteroids. All insufficient prescriptions were seen as a trigger/risk factor.

5. Exercise/sport

Participation in any formal or informal sport activities was seen as a possible trigger/risk factor for an asthma exacerbation. This included walking distances of at least 1 km.

6. Viral infections

A viral infection was seen as a trigger/risk factor when at least three of the following five components on the questionnaire were marked positive:

1. Sore throat
2. Fever
3. Runny/blocked nose
4. Muscle aches
5. Exposure to other people with a cold

7. Household pets

This trigger/risk factor was restricted to cats or caged birds in the house or in the direct work place.

8. Passive smoking

Passive tobacco smoking indoors at home, at the work place or at any other institution was seen as a trigger/risk factor.

9. Strong emotions

The following types of strong emotion were considered as trigger/risk factors:

1. Anger

Anger was seen as a trigger/risk factor when a participant had any loss of temper.

2. Excitement

Excitement was seen as a trigger/risk factor when a participant was extremely excited or happy about something, such as gifts, sports, finances or relationships.

3. Anxiety

Anxiety was seen as a trigger/risk factor when a participant was anxious for reasons related to crime or the death of a relative, for example, or when the participant was having an anxiety attack.

10. Coal stoves

Exposure of participants to in-house wood burning or to coal stoves was seen as a trigger/risk factor.

11. Weather

Weather was seen as a trigger/risk factor for all participants experiencing rainy weather conditions during their exposure assessment period.

12. Medication

The following types of medication were considered as trigger/risk factors:

Nonsteroidal anti-inflammatory drugs (NSAIDs)

Any orally ingested, rectally inserted or injected NSAID received by participants was seen as a trigger/risk factor for acute asthma exacerbations.

β-blockers

Any β-blocker-containing medication was seen as a trigger/risk factor. This included eye drops, intravenous preparations and tablets.

13. Allergic rhinitis

Allergic rhinitis was seen as a trigger/risk factor when symptoms were present for more than one hour per day over two weeks and when at least two of the following four components on the questionnaire were marked positive:

1. Blocked nose
2. Sneezing
3. Runny nose
4. Seasonal symptoms

15. Work-related exposures

Work-related exposures were seen as a trigger/risk factor when participants were exposed to, for example, spray-painting, diisocyanate or when they were employed in the pharmaceutical, plastics or platinum industries.

16. Pregnancy, menopause, and premenstrual/menstrual phases

All female participants were evaluated regarding pregnancy, menopause or their menstrual cycles. Pregnancy was diagnosed with a positive β-human chorionic gonado trophins (β-HCG) blood test and menopause was established from a history of normal cessation of menstruation. Premenstrual/menstrual phases were seen as a possible trigger/risk factor for cases in their premenstrual or menstrual phase during an exacerbation and for controls with no amenorrhoea in the previous four weeks.

Table I: Characteristics of study participants

Character	Cases (n = 50)	Controls (n = 100)	OR matched	95% CI	p - value
	N	N			
Gender					
Male	8 (16%)	16 (16%)	N/A		
Female	42 (84%)	84 (84%)	N/A		
Age Mean ± SD	43.8 ± 11.1	44.8 ± 10.2	N/A		0.49
1. Literacy					0.07
a. NS*	6 (12%)	20 (20%)			
b. SPS†	14 (28%)	29 (29%)	1.68	0.55–5.16	0.37
c. SHT‡	13 (26%)	35 (35%)	1.36	0.42–4.46	0.61
d. M§	17 (34%)	16 (16%)	4.60	1.26–6.79	0.02
2. Severity					0.36
a. MIǁ	10 (20%)	19 (19%)			
b. MP**	18 (36%)	32 (32%)	1.14	0.43–3.02	0.79
c. Mod P††	19 (38%)	48 (48%)	0.79	0.30–2.07	0.64
d. SP‡‡	3 (6%)	1 (1%)	5.77	0.51–65.86	0.16
3. Non-compliance	32 (64%)	44 (44%)	2.18	1.09–4.38	0.03
4. Under-treatment	8 (16%)	11 (11%)	1.57	0.57–4.33	0.38
5. Exercise	22 (44%)	48 (48%)	0.80	0.36–1.79	0.59
6. Viral infections	16 (32%)	23 (23%)	1.50	0.74–3.05	0.26
7. Pets: cats	4 (8%)	10 (10%)	0.79	0.24–2.61	0.70
8. Passive smoke	18 (36%)	26 (26%)	1.66	0.77–3.58	0.19
9. Emotions:					
a. anger	21 (42%)	41 (41%)	1.05	0.51–2.13	0.90
b. excitement	15 (30%)	40 (40%)	0.64	0.31–1.33	0.24
c. anxiety	11 (22%)	23 (23%)	0.95	0.42–2.11	0.89
10. Coal stoves	4 (8%)	4 (4%)	2.00	0.50–8.00	0.33
11. Weather: rain	41 (82%)	90 (90%)	0.00	0.00–∞	1.00
12. NSAIDs	20 (40%)	34 (34%)	1.32	0.64–2.76	0.45
13. β-blockers	0 (0%)	1 (1%)	0.00	0.00–∞	1.00
14. Allergic rhinitis	4 (8%)	11 (11%)	0.70	0.21–2.35	0.56
15. Work-related	4 (8%)	2 (2%)	4.00	0.73–21.84	0.11
16. Females:					
a. pregnancy	2 (4.8%)	1 (1.2%)	4.00	0.36–44.11	0.26
b. menopause	16(38.1%)	39 (46.4%)	0.38	0.10–1.49	0.17
c. menstrual/ premenstrual	23(54.8%)	42 (50%)	1.56	0.49–4.93	0.45

* NS No schooling
† SPS Some primary schooling
‡ SHT Some high school training
§ M Matriculation
ǁ MI Mild intermittent
** MP Mild persistent
†† Mod P Moderate persistent
‡‡ SP Severe persistent

Prescribed medication

Prescribed medication was recorded from the patients' files. This included β-agonist-, ipratropium bromide, beclomethasone and budesonide inhalers, oral theophylline, long-acting β_2-agonists and daily oral steroids.

Statistical package used

Univariate statistical analysis was done to assess characteristics and risk factors of participants. The Intercooled Stata 8.1 (Intercooled for Windows; STATA Corp, College Station, Tex; 2003) statistical package was used. Student's t-test was used for continuous data. Conditional logistic regression was used for multivariate analysis.

Ethical considerations

The Ethics Committee of the Faculty of Human Health Sciences of the University of Pretoria authorised the study, which was conducted in accordance with the ethical principles of the Declaration of Helsinki and Geneva Declaration of the World Medical Association.

Results

A total of 150 patients were recruited: 50 cases with acute asthma exacerbations, from the emergency unit, and 100 controls with stable asthma, from the outpatient departments. Results (see Table I) revealed that cases were more likely than controls not to comply with treatment (OR = 2.18; 95% CI 1.09 to 4.38; p = 0.03). According to responses to the questionnaire, respiratory viral infections were present in 32% of cases and in 23% of controls. The literacy level (matriculation) was higher in cases than controls – 34% versus 16%.

Females were more likely to be included in the study, as 84% of participants were females and only 16% were males. Under-treatment was detected in less than 20% of cases and controls. Rainy weather was present in 82% of cases and also in 90% of controls. More female controls (46%) than cases (38%) were in their menopause. Although more cases than controls were exposed to passive smoke (36% versus 26%) and to non-steroid anti-inflammatory drugs (40% versus 34%), these results were not statistically significant.

The parameters used to determine non-compliance are shown in Table II. Only one of the three parameters needed to be fulfilled in order to mark a participant as not complying. "Missing follow-up appointments in the last six months" was statistically significant, with an OR of 2.39 (95% CI 1.08 to 5.27) and p = 0.03.

Table II: Exposition of compliance of study participants

Parameters	Cases (n = 50)	Controls (n = 100)	OR matched	95% CI	p - value
	N	N			
Missed follow-up appointment(s) past 6 months	16 (32%)	16 (16%)	2.39	1.08–5.27	0.03
Missed script appointment(s) past 6 months	19 (38%)	24 (24%)	2.18	0.96–4.93	0.06
Meds not taken as prescribed	20 (40%)	27 (27%)	1.78	0.87–3.62	0.11

Analysis of the case-control data was also done with conditional logistic regression to assess clinically relevant and statistically significant variables identified in the univariate analysis. The final model consisted of the dependent variable (case/control) and non-compliance. The odds ratio was found to be 2.82 with CI 1.31 to 6.10; p = 0.008.

In Table III all the medication prescribed for the cases and controls is shown. There was no difference of note between the cases and controls. Daily oral steroids were prescribed for six cases – only three of these cases had severe persistent asthma in the dataset – and for eight controls, with only one severe persistent participant. One participant received two β-agonist inhalers and another participant did not receive a budesonide inhaler from the pharmacy although it was prescribed. In total, 88% of cases and 93% of controls were on inhaled corticosteroids.

Table III: Prescribed medication of study participants

Prescribed medication	Cases (n = 50)	Controls (n = 100)	OR matched	95% CI	p - value
	N	N			
β_2-agonist inhaler	47 (94%)	97 (97%)	0.25	0.02–2.76	0.26
Ipratropium bromide inhaler	1 (2%)	2 (2%)	1	0.09–11.03	1.00
Beclomethasone inhaler	11 (22%)	29 (29%)	0.69	0.31–1.54	0.36
Budesonide inhaler	33 (66%)	64 (64%)	1.23	0.65–2.32	0.52
Oral theophylline	31 (62%)	64 (64%)	0.92	0.45–1.86	0.81
Long-acting β-agonist inhaler	1 (2%)	3 (3%)	0.67	0.07–6.41	0.73
Oral steroids	6 (12%)	8 (8%)	1.55	0.51–4.69	0.44

Discussion

This was a matched case-control study, investigating the potential triggers or risk factors causing exacerbations in known adult asthma patients in a hospital setting. A significant association was shown between non-compliance and asthma exacerbations. Compliance was determined by (1) evaluating the patients' records to decide whether they kept follow-up appointments; (2) evaluating the prescription chart for script follow-ups; and (3) interviewing each patient to assess whether they used medication as prescribed. According to the literature, poor adherence to therapy is a common phenomenon.[17] Social class might have been a potential confounding factor here, but the controls and cases were selected from the same environment and communities. This effectively matched for social class and indicated that the results are unlikely to be the result of misclassifications. Many of the patients who did not keep follow-up appointments complained about money and transport problems.

The literacy level (matriculation) was higher in cases than in controls. One can therefore speculate that education would not decrease the number of asthma exacerbations. Under-usage of inhaled corticosteroids was one of the major elements that surfaced in response to interview questions on the use of prescribed medication. This has also been found in other studies.[1,10] A study conducted by Green et al,[3] for example, found that patients did not know the difference between controller and reliever treatment.

According to some studies, 40 to 50% of asthma exacerbations are caused by viral upper respiratory infections.[2,18] A British study undertaken by Green et al10 in a large district hospital detected viruses in 26% of acute asthma and 18% of stable asthma control patients with polymerase chain reaction (PCR) assays. This study found that viral infection was noticeably less common in adults admitted to hospital with acute asthma than in children or adults having asthma exacerbations in the community.[10] In our study the odds ratio for viral infections in the exposure assessment was only 1.5 (p = 0.26). This could be ascribed to the high occurrence (23%) of viral infections in the controls. Green et al explained this phenomenon, which also occurred in their study (controls of 18%), by stating that patients with asthma are more susceptible to viral infections than patients without asthma, but that such an infection may not necessarily induce a deterioration in asthma to the point where hospital admission is required.[10] Tan et al. confirm this in their study in which viruses were recovered from asymptomatic adolescents with asthma.[18] This finding corresponds with the findings of our study.

The definitive diagnosis of respiratory viral infections is complicated by the lack of commercial availability of a rapid and cost-effective laboratory test to confirm the presence of viral respiratory infections.[18] In this study questionnaires, and not cultures of nasopharyngeal swabs and serology, were used to evaluate the presence of respiratory viral infections. According to Osur, polymerase chain reaction (PCR) is only available in the research setting. Therefore, in the evaluation of typical viral infections, clinical signs and symptoms are the clinician's only tool for establishing the diagnosis of viral respiratory infections.[2]

Although the approach of self-administered questionnaires or interviews was cost-effective, the quality of this data was variable, in part because many exposures were inherently difficult to specify and quantify, and in part because of the difficulty the participants experienced in recalling events that had occurred in the past. Some of these inaccuracies could be reduced with careful questionnaire design but even with the best design considerable exposure misclassification might be expected.

In accordance with a Canadian study,[24] our controls were chronic asthmatics with no exacerbations during the preceding four weeks, selected from the asthma clinics at Kalafong Hospital. Controls were selected longitudinally throughout the course of the study (density sampling). This did not involve a random sample of the person-time in the study base since controls were only sampled for the 'instantaneous' time periods in which cases occurred. Controls could become cases later during the study, but cases could not become controls.

Limitations

This study cannot be generalised beyond the study population, as it involved patients within the public sector and at a single centre.

Definitive diagnosis of respiratory viral infections was not done with the use of laboratory tests such as serology, culture confirmation or PCR. Questionnaires on clinical symptomatology were used instead.

Recommendations

Self-management should be an important goal for asthma patients. The key features of a self-management programme would be a written action plan, the monitoring of asthma symptoms and the scheduling of regular reviews.[17] Doctors could help patients follow their self-management programme.

A pharmacist care programme in which the pharmacist monitors symptoms, provides medication counselling, helps resolve drug-related problems and facilitates communication with the patients' doctors may be able to enhance patients' adherence to therapy and outcomes.[25]

Patients with asthma should be motivated and receive education on the proper and regular use of inhalers. Doctors should also explain to them the appropriate dosing according to the severity level of their asthma in order to promote compliance.

Conclusion

To conclude, non-compliance was a strong predictor of exacerbations in adult asthma patients at Kalafong Hospital, which forms part of a third world community. Viral infections were, however, still common in cases without inducing deterioration in asthma to the point where hospital admission was required.

References

1. Turner MO, Noertjojo K, Vedal S, Bai T, Crump S, Fitzgerald JM. Risk factors for near-fatal asthma. Am J Respir Crit Care Med 1998;157:18049.
2. Osur SL. Viral respiratory infections in association with asthma and sinusitis: A review. Ann Allergy Asthma Immunol 2002;89:55360.

3. Green RJ, Greenblatt MM, Plit M, Jones S, Adam B. Asthma management and perceptions in rural South Africa. Ann Allergy Asthma Immunol 2001;86:3437.
4. Lemanske RF, Busse WW. Asthma. J Allergy Clin Immunol 2003;111 Suppl 2:50219.
5. Merckmedicus.com [homepage on the Internet], New York: Asthma, Merck & Co. [updated 2001 March]. Available from: http://www.merckmedicus.com/pp/us/hcp/diseasemodules/asthma/default.jsp (Accessed 05/12/2005).
6. Rodrigo GJ, Rodrigo C, Hall B. Acute asthma in adults. Chest 2004;125(3):1081102.
7. Ehrlich RI, White N, Norman R, et al. Wheeze, asthma diagnosis and medication use: A national adult survey in a developing country. Thorax 2005;60:895901.
8. SA Demographic & Health Survey 2003. DOH & MRC Report. Available from: http://www.doh.gov.za/facts/sadhs2003/part2.pdf (Accessed 03/12/2007).
9. Poyser MA, Nelson H, Ehrlich RI, et al. Socioeconomic deprivation and asthma prevalence and severity in young adolescents. Eur Respir J 2002;19:8928.
10. Green RM, Custovic A, Sanderson G, Hunter J, Johnston SL, Woodcock A. Synergism between allergens and viruses and risk of hospital admission with asthma: Case-control study. BMJ 2002;324:76372.
11. Tan RA, Spector SL. Exercise-induced asthma: Diagnosis and management. Ann Allergy Asthma Immunol 2002;89:22636.
12. Ehrlich RI, Jordaan E, Du Toit D, Volmink JA, Weinberg E, Zwarenstein M. Underrecognition and undertreatment of asthma in Cape Town primary school children. S Afr Med J 1998;88:98694.
13. Reinke LF, Hoffman L. Asthma education: creating a partnership. Heart Lung 2000;29:22536.
14. Peebles RS, Hartert TV. Highlights from the annual scientific assembly: Patient-centered approaches to asthma management: strategies for treatment and management of asthma. South Med J 2002;95:7759.
15. Peden DB. Pollutants and asthma: role of air toxics. Environ Health Perspect 2002;110 Suppl 4:5658.
16. Andreoli TE, Carpenter CCJ, Plum F, Lloyd HS, eds. Cecil essentials of medicine. Philadelphia: W B Saunders Company; 1986.
17. Sawyer SM. Action plans, self-monitoring and adherence: Changing behaviour to promote better self-management. Med J Aust 2002;177 Suppl:724.
18. Johnston SL. Viruses and asthma. Allergy 1998;53(10):92232.
19. Isaacs D, Joshi P. Respiratory infections and asthma. Med J Aust 2002;177 Suppl: 501.
20. Clementsen P, Permin H, Norn S. Chlamydia pneumoniae infection and its role in asthma and chronic obstructive pulmonary disease. J Investig Allergol Clin Immunol 2002;12:739.
21. Von Leupoldt A, Dahme B. Emotions and airway resistance in asthma: Study with whole body pletysmography. Psychophysiology 2005;42(1):92.
22. National Guideline on Management of Asthma in. Adults at Primary Level 2002 December. Available from: http://www.doh.gov.za/docs/ (Accessed 03/10/2006).
23. Lalloo UG, Bateman ED, Feldman C, et al. Guidelines for the management of chronic asthma in adults 2000 update. S Afr Med J May 2000;90(5pt2):5401, 54452.
24. Tarlo SM, Broder I, Corey P, et al. A case-control study of the role of cold symptoms and other historical triggering factors in asthma exacerbations. Can Respir J 2000;7: 428.
25. Weinberger M, Murray MD, Marrero DG. Effectiveness of pharmacist care for patients with reactive airways disease. JAMA 2002;288(13):1594602.