

International Journal of Nursing and Medical Investigation

International Peer Reviewed Journal

Review article

Patients with bronchial asthma- Purview of patient condition

Priyadarsini John

Associate Professor, D Y Patil College of Nursing, Nerul, Navi Mumbai.

Abstract

Asthma is the most common chronic disease in childhood, imposing a huge burden on the patient, their family and society. It is a worldwide disease with variable expression between countries and between different populations in a country. There is evidence that its prevalence has increased considerably over the last two decades and is still increasing, despite there being some indications that the increase in prevalence may have plateau in some countries in the last few years. Better understanding of the natural course of asthma and improved asthma control can lead to a decreased burden on the patient, their family and society. The burden of asthma consists mainly of a decreased quality of life for the patient and their family, as well as high costs for society; the healthcare expenditures for asthma in developed countries are 1–2% of the total healthcare costs. Although the association between asthma and psychosocial factors has long been recognised, it is only in the last decade that the impact of coexisting asthma and depression has become the focus of considerable research interest. However, the findings so far have been confusing and often contradictory. This paper sets out a review of the literature to date, including suggestions for future research.

Some positive results were described with homeopathy in good-quality trials in rhinitis, but a number of negative studies were also found. Therefore it is not possible to provide evidence-based recommendations for homeopathy in the treatment of allergic rhinitis, and further trials are needed. A limited number of studies of herbal remedies showed some efficacy in rhinitis and asthma, but the studies were too few to make recommendations. There are also unresolved safety concerns. Therapeutic efficacy of complementary-alternative treatments for rhinitis and asthma is not supported by currently available evidence. The main findings from this review included: (a) Asthma and its impact on individual well being (b) Prevalence of asthma across the globe (c) Prevalence of asthma in India (d) Quality of Life in patients with Asthma (e) Measuring Quality of Life in Patients with Asthma (f) Measuring Asthma Control (g) Relevance of Asthma Quality of life Questionnaire in India .

Keywords: Bronchial asthma, patient condition

*Corresponding author: Mrs. Priyadarsini John Associate Professor, D Y Patil College of Nursing, Nerul, Navi Mumbai. Email: priyapearljohn@yahoo.co.in

1. Introduction

The association between asthma and psychological factors has been recognised for centuries. Asthma has long been considered a psychosomatic disease, and during the 1930s–50s, was even known as one of the 'holy seven' psychosomatic illnesses. At that time, psychoanalytic theories described the aetiology of asthma as psychological, with treatment often

primarily involving psychoanalysis and other 'talking cures'. As the asthmatic wheeze was interpreted as the child's suppressed cry for his or her mother, psychoanalysts viewed the treatment of depression as especially important for individuals with asthma.

During the early 1970s, as the understanding of the aetiology and pathophysiology of asthma improved, the emphasis on psychological issues decreased. There were, however, increases in asthma-related morbidity

@International Journal of Nursing and Medical Investigation, All rights reserved

and mortality in many first-world countries, which were eventually attributed to the inappropriate use of β-agonists without corticosteroids. This issue led to a resurrection of psychosocial research relating to nonmedical factors in asthma, involving variables such as poor family functioning, poor doctor-patient relationships, and social difficulties. In the 1980s-1990s the growing interest in psychosocial variables also led to a number of studies being conducted into the links between asthma and anxiety and variables such as 'negative affect' or 'psychological distress', and in the late 1990s the connections between asthma and depression came to the research forefront, as the potential importance of this relationship came to be recognised. Today, as a result of years of biopsychosocial research, asthma is considered a disease of the pulmonary system with genetic and allergic origins that is significantly affected by psychosocial factors.

It is well documented that individuals with asthma tend to experience reduced health-related quality of life (HRQOL), and although HRQOL tends to be lower for individuals with severe asthma, the effect on those with more mild asthma can also be considerable. Asthma of any severity may lead to reductions in each of the physical, psychological, and social domains of HRQOL, with most people with asthma reporting some restriction on their life and having poorer health status than individuals without asthma. The Medical Outcomes Study demonstrated that depression and chronic disease often have 'additive' adverse effects on wellbeing, and there is evidence to support this finding for asthma and depression. People with coexisting asthma and depression have significantly lower overall HRQOL, and also experience lower physical and mental health functioning than those with similar asthma activity but fewer depressive symptoms These findings of reduced asthma-related quality of life are similar to those found in studies of other chronic medical conditions, where a history of depression has also been associated with poorer functional health

Asthma and its impact on individual well being

Asthma is one of the most prevalent chronic health conditions among adults. The increasing mortality rates and hospitalizations related to asthma are a major cause of concern. Survey conducted amongst 126 asthmatic women by the Asthma and Bronchitis Association of India [1]; found that asthma was actually a taboo subject for women and also a major social handicap. According to Niphadkar, chest physician states that women are especially vulnerable to several social stigmas and therefore go out of their way to hide their condition. His study found that 59 per cent of the women did not get any help from their husbands in coping with their ailment. 30 per cent reported that their families publicly denied that there was an asthmatic in the family. Asthma resulted in depression

in 34% of women. Nearly a third of them claimed to have given up travel altogether. Embarrassment on being called an asthmatic made 21 per cent withdraw from attending social functions [2].

Prevalence of asthma across the globe

Worldwide, the prevalence of asthma are increasing at a rate of 50 per cent every decade, and according to the World Health Organization, by the year 2020, asthma, along with Chronic Obstructive Pulmonary Disease (COPD) will become the third leading cause of death. Each year asthma accounts for 10 million missed school days, 1.2 million emergency room visits, 15 million outpatient visits, and 500,000 hospitalizations [3].

Nearly 5 million people in the UK are currently being treated for asthma and 8 million have been diagnosed as having asthma at some point in their lives. Globally, over 180,000 people die from asthma each year. New Zealand has the world's highest incidence of asthma-32 percent, whereas the disease is virtually unknown in Papua New Guinea [4]

Prevalence of asthma in India

Finding specific data on the number of asthmatics in India is a major challenge. Different reports and unscientific studies present an inaccurate picture of the prevalence of asthma in India. India has approximately 15-20 million asthmatics; 50 per cent of the patients visiting the OPD at the Post Graduate Institute of Medical Research in Chandigarh are asthmatic. The climate of Bangalore, where the weather can change every two hours, gives it the dubious distinction of having the highest number of asthmatics in India. Though the prevalence is higher amongst men, it is women who suffer the most from asthma.

Experts estimate that the level of pollutants, especially Suspended Particulate Matter (SPM), may double during celebrations such as Diwali, due to the incidence of fire crackers and pollutants. "The sulphur dioxide and nitrogen dioxide content could go up by 30 to 40 per cent during these days since crackers are largely made of sulphur and phosphorus," says Rakesh Kumar, a scientist at the National Environmental Engineering Research Institute. While exact data is not available, it is clear that for the million-odd citizens suffering from asthma and chronic respiratory problems in Mumbai, Diwali is a time to pull out the inhalers and extra medicines. Dr Niphadkar, says there is a 30 per cent rise in the number of patients he sees during this time (Health News Letter, December -January 2002). Chowgule, chest specialist says she sees 50 per cent more patients during Diwali, they are serious and many of them had been asymptomatic. Study done by her shows that 17 per cent of Mumbaikars suffer from asthma, 27 per cent are vulnerable to developing the illness [5].

A field study conducted [6] for Asthma Epidemiology Study Group at Chandigarh, Delhi, Kanpur and Bangalore through a two stage stratified (urban/rural) sampling employed uniform methodology using a previously validated questionnaire, to estimate prevalence of bronchial asthma in different regions of India and to define risk factors influencing disease prevalence. Data from 73605 respondents (37682 men, 35923 women) were analyzed. One or more respiratory symptoms were present in 4.3-10.5% subjects. Asthma was diagnosed in 2.28%, 1.69%, 2.05% and 3.47% respondents respectively at Chandigarh, Delhi, Kanpur and Bangalore, with an overall prevalence of 2.38%. Women, advancing age, usual residence in urban area, lower socio-economic status, history suggestive of atopy, history of asthma in a first degree relative, and all forms of tobacco smoking were associated with significantly higher odds of having asthma. In a study [6] as part of the European Community Respiratory Health Survey, asthma prevalence in adults aged 20-44 years was reported to be 3.5% using 'clinician diagnosis' and 17% were using a very broad definition (which included prior physician diagnosis and/or a positive bronchoprovocation test). Prevalence was similar in men (3.8%) and women (3.4%). Thus, the study concluded that the prevalence estimates of asthma in adults, although lower than several previously reported figures, point to a high overall national burden of disease.

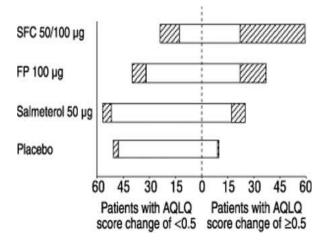


Fig. 1

Number of patients in study A (by treatment group) who achieved a clinically important change (≥0.5) in Asthma Quality of Life Questionnaire (AQLQ) score, analysed by level of control: not well controlled; L: well controlled. All doses shown were given twice daily. FP: fluticasone propionate; SFC: salmeterol/fluticasone propionate combination.

Quality of life in patients with asthma

Researchers have long recognized the value of measuring quality of life. Consequently, a fair number of adult [7], [8] and pediatric [9] asthma-specific quality-of-life questionnaires have been developed and are routinely used in studies of self-management and pharmacologic treatment of asthma [10]. Quality-oflife studies of parents or caretakers of patients with asthma have also been conducted. In addition, healthcare providers have been urged to incorporate qualityof-life measures in their care of patients with asthma. [11]. Measuring quality of life in patients with asthma may help to distinguish the severity of the disease [12] and change in reported quality of life may correlate with change in the clinical status of patients [13], [14]. Furthermore, patients with diminished quality of life are more likely to use health-care services [15]. Despite the impressive literature about asthma and quality of life, few population-based studies of the impact of asthma on quality of life have been conducted [16]. Physical functioning scores from the SF-36 of 110 adult patients with asthma were lower than were population norms in the Netherlands [17]. Among 5,580 Health Maintenance Organization (HMO) patients with asthma aged 14 to 65 years, the mean scores for eight subscales of functional status were lower than those reported by the general population in a separate survey performed 6 years earlier [18]. Furthermore, the authors found significant decreases in functional status with increasing severity of asthma. In a British study, quality of life among 60 asthmatic patients aged >/=70 years was worse than that among control patients [19]. Scores for mental health and social functioning were comparable to scores found in the general population. In a French study of participants aged 20 to 44 years, persons with asthma (21 patients with severe asthma and 77 patients with mild-to-moderate asthma) had lower scores on the SF-36 than control subjects without asthma [20]. In a study of 3,001 Australians aged >/=15 years, participants with asthma reported significantly lower scores on several SF-36 scales [21]. The authors concluded that asthma had a major negative impact on the health-related quality of life in the community and that its impact was similar to that of other chronic health conditions. Studies from New York State, Connecticut, and Los Angeles, that used the Behavioral Risk Factor Surveillance System (BRFSS) questions also showed that people with asthma experienced worse quality of life than people without asthma [22].

A study conducted [23] from a sample of 3021 Hispanics and non-Hispanic white subjects who were 65 years and older found that asthma is a common medical condition in the elderly and it significantly impacts quality of life and general health status. Results support adopting an integrated approach in identifying and controlling asthma in this population. The estimated prevalence of current asthma and

probable asthma were 6.3% (95%CI: 5.3-7.2) and 9.0% (95%CI: 7.8-10.1) respectively. The majority of subjects with current asthma (mean SF-12 score 35.8, 95%CI: 34.2-37.4) or probable asthma (35.3, 34.0-36.6) had significantly worse physical health-related quality of life as compared to subjects without asthma (42.6, 42.1–43.1). In multiple logistic regression analyses, women had a 1.64 times greater odds of current asthma (95%CI: 1.12-2.38) as compared to men. Hay fever was a strong predictor of both current and probable asthma. The odds of current asthma were 1.78 times (95%CI: 1.24-2.55) greater among past smokers; whereas the odds of probable asthma were 2.73 times (95% CI: 1.77-4.21) greater among current smokers as compared to non-smokers. Similarly fair/poor self rated health and complaints of severe pain were independently associated with current and probable asthma. The odds of current and probable asthma were almost two fold greater for obesity. When stratified by gender, the odds were significantly greater among females (p-value for interaction term = 0.038). The odds of current asthma were significantly greater for farm-related occupations (adjusted OR = 2.09, 95%CI: 1.00–4.39); whereas the odds were significantly lower among those who reported teaching as their longest held occupation (adjusted OR = 0.36, 95% CI = 0.18-0.74).

Measuring quality of life in patients with asthma

A study evaluated the measurement properties of an Asthma Quality of Life Questionnaire [14]. The Asthma Quality of Life Questionnaire was able to detect changes in patients who responded to treatment or who had natural fluctuations in their asthma (p < 0.001) and to differentiate these patients from those who remained stable (p < 0.001). The questionnaire was reproducible in patients who were stable (intra class correlation coefficient = 0.92). There were significant longitudinal and cross-sectional correlations between asthma quality of life and other measures of both clinical asthma and generic quality of life. The researchers concluded that the Asthma Quality of Life Questionnaire has good measurement properties and that it is valid as both an evaluative and a discriminative instrument. The strength of these disease-specific quality-of-life instruments generic instruments is that they focus on areas of function that are relevant to that particular condition, and as a result, they are most responsive to small but important changes.

Measuring asthma control

The concept of asthma control is evolving [24]. Emphasized that asthma control is related to the appropriateness of therapy. Subsequent reviews of the concept of asthma control have emphasized that

asthma control is a short-term evaluation of the adequacy of patient management and determines the need for clinical intervention. Thus, control is a function of underlying severity plus the adequacy of management. The primary goals of asthma treatment according to the guidelines are identical for patients regardless of disease severity. Although no specific method of asthma-control assessment is specified, the goals in current guidelines reflect asthma control: minimal or no symptoms, minimal or no use of rescue medication, no activity limitations, and (near) normal lung function with any adverse treatment effects [25]

Relevance of asthma quality of life questionnaire in INDIA

A study conducted to measure the evaluative and discriminative properties of the AQLQ (UK English version) in Indian asthmatics [26]. Thirty-eight adult patients with asthma underwent spirometry and completed the AQLQ and the Asthma Control Questionnaire (ACQ), administered by an interviewer. Standard treatment was given for four weeks during which daytime and nocturnal symptoms of asthma and use of rescue medication were recorded in diaries. The questionnaires were administered again at the end of four weeks and spirometry was repeated. The total and domain-wise scores of AQLQ improved in patients whose control of asthma improved during treatment. It had good reproducibility with no changes in scores in patients whose condition remained stable, and also high intra-class correlation coefficients for the total and domain-wise scores in these patients. Significant correlations were found between the changes in AQLQ scores and in ACQ scores confirming the longitudinal construct validity. The symptoms domain score of the AQLQ was related significantly to the patient diary recorded scores of cough, sputum and nocturnal asthma. Cross-sectional construct validity of AQLQ by established demonstrating significant correlation of the total, symptoms and emotions domain scores with the ACQ scores. The study concluded that the AQLQ (UK English version) has sufficiently acceptable evaluative and discriminatory properties in Indian asthmatics and is therefore a valid instrument for quality of life measurements in clinical and research studies in asthmatics among Indians.

Factors affecting the QOL in patients with bronchial asthma, globally

The complex nature of the disease and the difficulty of pinpointing exactly what cause asthma or triggers an attack, makes it a challenge for the medical community. Genetic factors do play an important role. But new evidence points to the ever-increasing role of the environment.

There is a growing and fascinating science of linkages between the human body and the environment. Environmental exposures and factors have been often associated with the onset of asthma, both in children and adults. Most environmental determinants of asthma are linked with changing lifestyles. Asthma also has been linked to air pollution levels, obesity, exercise, indoor smoke, exposure to Environmental Tobacco Smoke (ETS) and an affluent lifestyle [27]. Poor housing conditions such as dampness encourage the growth of moulds and house-dust mites. House-dust mite is known to be the leading cause of asthma worldwide.

An association between obesity and asthma has also been found where excess weight pressing on the lungs can cause a hyperactive response. Environmental determinants of asthma are important since many of these are modifiable and can be targeted for specific preventive measures. Though for most part they may not be the primary determinant, they do have a role to play in the worsening of the existing disease, by triggering symptoms, exacerbating airway inflammation, and by increasing the severity of the disease.

The relationship between stress and quality of life in adults with asthma has not been well studied. Stress, quantified by negative life events, may be linked to quality of life in asthma through multiple pathways, including increase in disease severity and adverse effects on socioeconomic status [28].

Years ago when a severe hurricane hit the island of Tokelau in the South Pacific, the entire indigenous population was forced to move to New Zealand. On the Tokelau Islands, asthma was virtually unknown. However, after the move, widespread incidence of asthma was noticed, especially amongst children. This suggests that environmental factors have an important role to play in causing asthma. Another anomaly is that while most lung diseases are related to poverty or air pollution, the prevalence and incidence of asthma is higher amongst the affluent (Weirmayr, 2006).Sulfur dioxide (SO2), generated from oil and coal burning, is of special concern for people with asthma. While healthy subjects exposed to SO2 show no ill effects, exposure to even low levels of SO2 alters the lung function of asthmatics [29].

A study of 171 women with adult-onset asthma requiring medication, and 137 age matched controls found a strong association between sedentary lifestyle and onset of genetically influenced asthma. , asthma is a complex disease involving multiple genes [30]. Relevant mutations in both the promoter region of the interleukin 4 (IL-4) gene or the coding regions of the IL-4 receptor has been found, some of which have been linked to loss of lung function, others to near-fatal events [31].

Evidence of a positive association between asthma and obesity in adults and in children has been found to be true. A cross sectional analysis of 18,218 children aged 4-11 years in the UK found that obesity had a role to play in the development of asthma symptoms in children. This was regardless of the ethnicity of these children. The study made an association between the

body mass index (BMI) and the prevalence of asthma attacks. The association was found to be stronger in girls than in boys. A similar study conducted by Schachter, et al (2001) found that although obesity played a role in wheeze and shortness of breath, it did not support an increase in airway hyper responsiveness. The Center for Disease Control and Prevention (CDC) places air pollution-related health costs at \$14 billion a year. The urban poor bear the brunt of air pollution because they often live in densely populated neighborhoods that use dirty household fuels, burn garbage nearby, and are close to traffic corridors or industries. They travel in open vehicles or walk, and spend much more time outdoors. Thus, the world's poor are increasingly experiencing the 'double burden' of both traditional and modern environmental health

The debate on the role that ambient air pollution has to play in the severity of asthma has been ongoing for many years. It is not yet clear how air pollution exacerbates asthma. For example, Tokyo has a much higher incidence of pollution than Wellington, New Zealand, yet the asthma incidence is at least five times higher in Wellington than in Tokyo. Similarly, though there are no pollution or dust mites in the Isle of Skye in the UK, it has the highest incidence of asthma anywhere in the UK. The global pattern of asthma prevalence provides evidence that air pollution is not a major risk factor for the development of asthma; rather, it is merely a minor trigger in some individuals. Studies conducted in some regions in China and Eastern Europe with high levels of air pollution has shown low rates of asthma prevalence.

Though air pollution is not amongst the primary causes of asthma, it significantly exacerbates the condition and contributes to increase in hospital admissions and emergency room visits. Air pollutants such as sulphur dioxide, particulate matter and ozone are known to trigger acute respiratory symptoms. Ozone has been associated with rising asthma. Exposure to even low levels of sulphur dioxide is known to alter lung function. Particulate matter has been linked with decreased lung function to absenteeism from school and work and to increase in emergency and hospital admissions due to asthma.

A recent study carried out by Ritz's team at the University of California Los Angeles (UCLA) has found that pregnant women exposed to air pollution are more likely to give birth to children with heart defects. Since children have narrower airways as compared to adults, they have been found to be more susceptible to air pollution. A study [32] followed 110 children through their teen years staying in polluted areas and compared them with those with who stayed in less polluted areas or those who moved away to other communities. His study showed that air pollution levels could have long term effects on lung health of children. The lungs which acts as a protector from

breathing dust, pollen, germs, is made to work more due to air pollution. Indoor air pollution due to secondhand smoke and poorly ventilated homes has also been strongly linked to the development of pediatric asthma. According to [33] Asthma control has been hypothesized to be inversely related to asthma severity, directly related to effective management, and also related to other definable factors, but empiric data to support this construct are few. This surmise is further strengthened by erstwhile researchers; Chhabra & Kaushik (2004) concluded in a study that in India. People who are fluent in English are generally betteroff economically. Hence, extrapolating the results gained by the validation of the AQLQ in English to all social and economic classes would be difficult. Further, given its acceptable Asthma Quality of Life discriminative and evaluative properties observed in the present study, the AQLQ needs to be studied in a wider spectrum of patients with diverse educational and economic backgrounds. A study [34] described the AQLQ as a useful indicator of health related quality of life in low income asthmatics.

Conclusion

The review of existing literature and studies carried out in the ambit of quality of life of patients affected by asthma within the Indian context is rather limited. The enormity of the studies carried out elsewhere in the world and the magnitude of this problem within the Indian subcontinent makes this an important aspect for further research and detailed understanding. It is imperative that we involve our medical community – doctors, epidemiologists, public health specialists, to deal with the challenges in achieving this mammoth task.

References

- [1] Jindal, S. K., & Gupta, D. (2004). The relationship between tobacco smoke & bronchial asthma. *Indian Journal of Medical Research*, 120(5), 443.
- [2] Herzlinger, R. E. (2004). Consumer-driven health care: implications for providers, payers, and policy-makers. John Wiley & Sons.
- [3] Vilsack, T. J., Pederson, G. S. J., & Governor, L. (2003). Iowa Asthma Surveillance Plan.
- [4] Odhiambo, J. A., Mungai, M. W., Gicheha, C. M., Nyamwaya, J. K., Karimi, F., Macklem, P. T., & Becklake, M. R. (1998). Urban-rural differences in questionnaire-derived markers of asthma in Kenyan school children. *European Respiratory Journal*, 12(5), 1105-1112.
- [5] N. G. Women Adjusting for Survival. Democracy in the Family. *Insights from India*. 2008 Mar 11;(:25.).
- [6] Aggarwal, A. N., Chaudhry, K., Chhabra, S. K., D Souza, G. A., Gupta, D., Jindal, S. K., ... & Vijayan, V. K. (2006). Prevalence and risk

- factors for bronchial asthma in Indian adults: a multicentre study. *Indian Journal of Chest Diseases and Allied Sciences*, 48(1), 13.
- [7] Jones, P. W., Quirk, F. H., & Baveystock, C. M. (1991). The St George's respiratory questionnaire. *Respiratory medicine*, 85, 25-31.
- [8] Juniper, E. F., Guyatt, G. H., Epstein, R. S., Ferrie, P. J., Jaeschke, R., & Hiller, T. K. (1992). Evaluation of impairment of health related quality of life in asthma: development of a questionnaire for use in clinical trials. *Thorax*, 47(2), 76-83..
- [9] Juniper, E. F., Guyatt, G. H., Feeny, D. H., Ferrie, P. J., Griffith, L. E., & Townsend, M. (1996). Measuring quality of life in the parents of children with asthma. *Quality of Life Research*, 5(1), 27-34.
- [10] Marquis, P., & Trudeau, E. (2001). Quality of life and patient satisfaction: two important aspects in asthma therapy. *Current opinion in pulmonary medicine*, 7, S18-20.
- [11] Blackstien-Hirsch, P., Anderson, G., Cicutto, L., McIvor, A., & Norton, P. (2000). Implementing continuing education strategies for family physicians to enhance asthma patients' quality of life. *Journal of Asthma*, 37(3), 247-257.
- [12] Gruffydd-Jones, K., Hood, C. A., & Price, D. B. (1997). A within-patient comparison of subcutaneous and oral sumatriptan in the acute treatment of migraine in general practice. *Cephalalgia*, 17(1), 31-36.
- [13] Marks, G. B., Dunn, S. M., & Woolcock, A. J. (1993). An evaluation of an asthma quality of life questionnaire as a measure of change in adults with asthma. *Journal of clinical epidemiology*, 46(10), 1103-1111.
- [14] Juniper, E. F., Guyatt, G. H., Ferrie, P. J., & Griffith, L. E. (1993). Measuring quality of life in asthma. *American Review of Respiratory Disease*, 147, 832-832.
- [15] Osman, L. M., Calder, C., Robertson, R., Friend, J. A., Legge, J. S., & Graham Douglas, J. (2000). Symptoms, quality of life, and health service contact among young adults with mild asthma. American Journal of Respiratory and Critical Care Medicine, 161(2), 498-503.
- [16] Adams, R., Wakefield, M., Wilson, D., Parsons, J., Campbell, D., Smith, B., & Ruffin, R. (2001). Quality of life in asthma: a comparison of community and hospital asthma patients. *Journal of Asthma*, 38(3), 205-214.
- [17] Van der Molen, T., Sears, M. R., De Graaff, C. S., Postma, D. S., & Meyboom-de Jong, B. F. (1998). Quality of life during formoterol treatment: comparison between asthma-specific and generic questionnaires. Canadian and the Dutch Formoterol Investigators. *European Respiratory Journal*, 12(1), 30-34.
- [18] Legorreta, A. P., Christian-Herman, J., O'connor, R. D., Hasan, M. M., Evans, R., &

- Leung, K. M. (1998). Compliance with national asthma management guidelines and specialty care: a health maintenance organization experience. *Archives of Internal Medicine*, 158(5), 457-464.
- [19] Dyer, C. A. E., Hill, S. L., Stockley, R. A., & Sinclair, A. J. (1999). Quality of life in elderly subjects with a diagnostic label of asthma from general practice registers. *European Respiratory Journal*, 14(1), 39-45.
- [20] Leynaert, B., Neukirch, C., Liard, R., Bousquet, J., & Neukirch, F. (2000). Quality of life in allergic rhinitis and asthma: a population-based study of young adults. *American journal of respiratory and critical care medicine*, 162(4), 1391-1396.
- [21] Adams, R., Wakefield, M., Wilson, D., Parsons, J., Campbell, D., Smith, B., & Ruffin, R. (2001). Quality of life in asthma: a comparison of community and hospital asthma patients. Journal of Asthma, 38(3), 205-214.
- [22] Simon P LAZZWCFJ. Health-related quality of life-Los Angeles County, California, 1999 (Reprinted from MMWR, vol 50, pg 556-559, 2001). JAMA-JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION. 2001 Sep 19; 286(;(11):1309-10.).
- [23] Arif, A. A., Rohrer, J. E., & Delclos, G. L. (2005). A population-based study of asthma, quality of life, and occupation among elderly Hispanic and non-Hispanic whites: a cross-sectional investigation. *BMC public health*, 5(1), 97.
- [24] Gauvreau, G. M. (1998). Pharmacological modulation of allergen-induced airway inflammation (Doctoral dissertation).
- [25] Wu, F., & Takaro, T. K. (2007). Childhood asthma and environmental interventions. *Environmental Health Perspectives*, 971-975.
- [26] Chhabra, S. K., & Kaushik, S. (2005). Validation of the asthma quality of life questionnaire (AQLQ-UK English version) in Indian asthmatic subjects. *Indian Journal of Chest Diseases and Allied Sciences*, 47(3), 167.
- [27] Jindal, S. K., Aggarwal, A. N., Chaudhry, K., Chhabra, S. K., D Souza, G. A., Gupta, D., ... & Vijayan, V. K. (2006). A multicentric study on epidemiology of chronic obstructive pulmonary disease and its relationship with tobacco smoking and environmental tobacco smoke exposure. *Indian Journal of Chest Diseases and Allied Sciences*, 48(1), 23.
- [28] Yen, I. H., Yelin, E. H., Katz, P., Eisner, M. D., & Blanc, P. D. (2006). Perceived neighborhood problems and quality of life, physical functioning, and depressive symptoms among adults with asthma. *American journal of public health*, 96(5), 873-879.
- [29] Kwon, H. J., Cho, S. H., Chun, Y., Lagarde, F., & Pershagen, G. (2002). Effects of the Asian

- dust events on daily mortality in Seoul, Korea. *Environmental Research*, 90(1), 1-5.
- [30] Wenzel, S. (2005). Severe asthma in adults. *American journal of respiratory and critical care medicine*, 172(2), 149-160.
- [31] Drazen, J. M., Yandava, C. N., Dubé, L., Szczerback, N., Hippensteel, R., Pillari, A., ... & Drajesk, J. (1999). Pharmacogenetic association between ALOX5 promoter genotype and the response to anti-asthma treatment. *Nature genetics*, 22(2), 168-170.
- [32] McConnell, R., Berhane, K., Gilliland, F., London, S. J., Islam, T., Gauderman, W. J. ... & Peters, J. M. (2002). Asthma in exercising children exposed to ozone: a cohort study. *The Lancet*, 359(9304), 386-391.
- [33] Schatz, M., Sorkness, C. A., Li, J. T., Marcus, P., Murray, J. J., Nathan, R. A., ... & Jhingran, P. (2006). Asthma Control Test: reliability, validity, and responsiveness in patients not previously followed by asthma specialists. *Journal of Allergy and Clinical Immunology*, 117(3), 549-556.
- [34] Leidy, N. K., & Coughlin, C. (1998). Psychometric performance of the Asthma Quality of Life Questionnaire in a US sample. *Quality of Life Research*, 7(2), 127-134.