# Chapter 5
# Depression and Anxiety in Adult Patients with Asthma

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## Introduction

Asthma is a major cause of morbidity, disability and healthcare utilization. It is estimated to affect over 300 million people [1] worldwide and has a significant impact on individual's personal, e.g. work-related activities, social interaction and quality of life. The cost of caring for moderate to severe asthma is substantial. In 2007, in the USA alone, the total cost of annual direct medical expenditure attributable to asthma treatment is estimated at approximately $37.2 billion [2].

Asthma is a multifactorial lung disease that is related to significant development of medical comorbidity. Anxiety and depression are two commonly, untreated and undiagnosed comorbidities for patients with asthma. A recent worldwide survey of 54 countries including developed and developing nations [3] reported that persistent wheezing in the past month was associated with elevated symptoms of anxiety and depression in adult patients with asthma. It also highlights the importance of addressing the 'asthma-mental health problems' as they are inadequately diagnosed and treated as a public health agenda and clinical management priorities. The prevalence of depressive and anxiety symptoms in patients with asthma are estimated to be 27 and 35% [4, 5], respectively. A recent meta-analysis [6] of 8 studies (3546 adolescents with asthma and 24, 884 controls) reported that asthmatic patients are twice more likely at risk of developing depressive symptoms and 83% more likely to exhibit anxiety symptoms compared to healthy aged-matched controls.

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In addition, panic disorder occurs at a higher rate in patients with asthma compared with the general population [7, 8]. These comorbid disorders are associated with increased physical disability, social isolation, poor treatment adherence, greater asthma symptom severity, increased healthcare utilization and premature mortality [4–8].

There is a lack of strong evidence for the management of depression and anxiety for patients with asthma. This is partly due to that current clinical practice both in primary and secondary care does not routinely screen patients diagnosed with asthma for anxiety or depression or provide specific interventions to reduce psychological distress for this patient group. In addition, there is a lack of specific guidance from current evidence-based guidelines, e.g. the Global Initiative for Asthma [9] on management of depression and anxiety in asthma.

Dyspnoea-related anxiety and exhaustion of asthma combined with the hopelessness, helplessness and depression corrode the patients' ability to adhere to their rehabilitation and other treatment regimens. Consequently, depressed asthmatic patients often continue to smoke and have frequent medical complications, increased mortality, persistent depressive symptoms and signs, disability, decreased social interactions, increased wheezing and poor quality of life [4–8]. Anxious asthmatic patients may have also difficulties in coping with the disease during exacerbations. They are most likely to access emergency healthcare services frequently and longer-hospital stay after acute exacerbations. Furthermore, poor asthma control may exacerbate the incidence of depressive symptoms [10].

Understanding comorbid diseases such as depression and anxiety in patients with asthma may help clinicians to develop appropriate prevention and treatment strategies to improve the health outcomes. Despite high prevalence and impact of anxiety and depression in patients with asthma, management of these comorbidities is often inadequate. This chapter evaluates the prevalence, management of anxiety and depression in patients with asthma. It will also outline implications for clinical practice and research.

## Impact and Mechanisms of Depression and Anxiety in Asthma

Although the exact mechanism of how depression and anxiety symptoms develop (manifest) in patients with asthma is uncertain, it is most likely to be multifactorial as listed in Table 5.1. Psychiatric comorbidities including depression and anxiety in asthmatic patients have been associated with disease severity, poor adherence to medical treatment and loss of asthma control. In a two-year longitudinal study, Katz et al. [11] investigated the incidence of depression in community-based sample [$n = 439$] of adults with asthma. Using the Center for Epidemiologic Studies Depression questionnaire (CES-D $\geq$ 23), the incidence of new onset depression was 8%. Decreased in perception of asthma control was associated with the new onset of depression (odds ratio, 7.47, 95% CI 2.15–26.01). It is worth exploring the

**Table 5.1** Risk factors associated with development of anxiety and depressive symptoms in asthma

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| Increased physical disability |
| Poor quality of life |
| Poor adherence to treatment |
| Prenatal smoking exposure |
| Low perceived control of asthma |
| Caucasian (white race) |
| Active smokers |
| Prednisone dependent |
| Severity of wheezing |
| Severity of respiratory impairment |
| Maladaptive behaviour |
| Female gender |
| Physical inactivity |
| Inadequate social support |
| Lower socio-economic status |

efficacy of asthma education in subset of asthmatic patients with poor perception. However, caution is required in interpretation of these finding as CES-D is usually considered a screening tool and not a diagnostic measure.

Lavoie et al. examined [12] the prevalence of psychiatric disorders in asthmatic patients attending an outpatient clinic [$N = 504$]. Psychiatric assessment was carried out using the Primary Care Evaluation for Mental Disorders (PRIME-MD) [13], a short questionnaire that takes about 20 min to administer. About one-third of the patients met the diagnostic criteria for one or more psychiatric disorders. Eight per cent of the patients met criteria for major depression, 12% for anxiety disorder and 11% for panic disorder. In addition, 11% of these patients had both anxiety and depressive disorders. In addition, major depression was independently associated with poor asthma control (not anxiety). This signify depression compromises individual's ability initiating and managing complex treatment regimens that require sustained effort, self-monitoring and administration. Furthermore, depression may have compromised patients' active role in the family, dependency on others for activities of daily living, lowered self-efficacy and social interaction.

In a separate study, Lavoie et al. examined [14] the influence of psychological distress and maladaptive coping styles in patients [$n = 84$] with moderate and severe patients with asthma. Patients were categorized into moderate to severe lung function impairment using the standard pulmonary function testing according to American Thoracic Society/European Respiratory guidelines [15, 16]. Their findings indicate that patients with severe asthma [$n = 42$] reported high level of psychological distress, worse cognitive dysfunction, emotional coping, future pessimism and apprehension compared to moderate asthmatics [$n = 42$]. A cross-sectional study in Spain [17] from outpatient clinic of patients with asthma ($n = 354$) reported the prevalence of anxiety was 31%, depression was 2% and anxiety plus depression was 10%. Over 77% of the asthmatic patients had poor or

partial control of their condition. In addition, patients with poor asthma control are three times more likely to exhibit the risk of developing anxiety plus depression. Elevated level of anxiety was associated with impaired quality of life in patients with asthma. In a community survey [18] of older people ($n$ = 20,888) in Norfolk, England examined the association between psychosocial factors and asthma. Out of these, 1699 (8.1%) of the participants had physicians diagnosed asthma. Major depression, adverse childhood circumstances, difficulties in adulthood and inadequate social support were associated with the chronicity of asthma. Furthermore, Bacon et al. [19] reported that asthmatic patients from the lower socio-economic status (SES) had utilized greater emergency healthcare services and worse self-asthma control compared to patients with higher SES. All these factors signify that psychosocial factors have deleterious effect on psychological well-being and impaired quality of patients with asthma.

Vazquez et al. [20] examined the influence of 'near-fatal asthma [NFA]' experience [$n$ = 44] in stable adult patients with asthma compared to patients 'without near-fatal asthma' [$n$ = 44], in their coping mechanism, self-management and psychological problems. Patients with asthma who experience a near-fatal experience had higher levels of trait anxiety (a tendency to perceive situations as threatening and consequently increase) and more difficulties describing and communicating feelings compared those who did not have a NFA. There was no difference in self-management in both groups. However, because of the cross-sectional nature of the study, it could not infer whether the association of psychological problems with NFA can be regarded as risk factors or a consequence of the experience of a NFA crisis [20]. Thus, longitudinal study is worthy of consideration to elucidate this point.

Work-related asthma (the cause of the stimuli is individual's work environment) is a common cause of adult on-onset asthma. It affects 9–15% of adult patients with asthma [21]. Lavoie et al. [22] in a prospective study ($n$ = 219) using the PRIME-MD, examined the prevalence of psychiatric disorders including mood and anxiety disorders and hypochondriasis in patients referred for the occupational asthma assessment. Thirty-four per cent of the patients with occupational asthma had psychiatric disorders. Out of these, 29% mood disorders and 24% anxiety disorders were diagnosed, respectively. Seven per cent of the patients' with occupational asthma was diagnosed with hypochondriasis. In addition, hypochondriasis is associated with increased risk of not receiving any medical diagnoses. In a large survey of ($n$ = 1267) occupational asthmatic (OA), patients who were exposed to workplace moisture and moulds had worse quality of life compared to patients without OA [23]. Furthermore, being unemployed (due to disability, retirement, job loss or other reasons) and the greater need for asthma medication were associated with poorer quality of life.

In 2010, Goodwin et al. [24] using data from the Canadian Community Health Survey Cycle 1.2 ($N$ = 36,984; age $\geq$ 15 years) examined the association between mental health disorders and asthma and the impact of asthma and mental disorder on functional impairment and mental healthcare service use among adults in the community. Their findings indicated that asthma was related to mental health

disorders such as post-traumatic stress disorder, mania and panic disorder. Thus, asthma patients with comorbid mental health disorders had elevated rates of functional impairment and use of mental health services compared with those either asthma patients or mental health disorders. Furthermore, data that were drawn [25] from the Third National Health and Nutrition Examination Survey, a representative sample of adults ($N = 6584$) in the USA, showed that current asthma was related with an increased likelihood risk of 77% suicidal ideation (odds ratio: 1.77, confidence interval: 1.11, 2.84) and suicide attempt (odds ratio: 3.26, confidence interval: 1.97, 5.39), respectively. Adult asthmatic patients are prone to a threefold increased risk of attempting to commit suicide compared to patients without asthma counterparts, although the exact cause(s) that instigate asthmatic patients for suicidal ideation are unknown. It is most likely multifactorial including psychosocial factors, hopelessness due to severity of asthma, elevated symptoms of depression and anxiety. Those asthmatic patients identified with suicidal ideation promptly referred to mental health services for treatment. Further studies are needed.

## Management of Anxiety and Depression in Asthma

### *Pulmonary Rehabilitation*

Pulmonary rehabilitation (PR) has been shown to improve exercise capacity, quality of life and improve depressive and anxiety symptoms and is now considered cornerstone in the management of chronic obstructive pulmonary disease (COPD) [26]. However, the efficacy of PR in improving outcomes in patients with asthma is unclear.

A recent study [27] examined the efficacy of an 8-week home-based PR in patients with persistent asthma. Fifty-two patients (20 men and 32 women) were recruited. The intervention comprised group exercise training program, educational sessions and respiratory physiotherapy. Three quarter of the patients completed the PR programme. A statistically significant improvement in exercise capacity using the 6-min walk test (mean increase was 33 m) was observed although this change did not reach clinically significant difference, which was 54 m [28]. There were some improvement in physiological indices, e.g. in peak oxygen uptake. Twenty-five per cent of the patients did not complete the rehabilitation programme. The dropout rate was significantly higher in younger patients who were employed. There was no statistically significant improvement in health-related quality of life using the Short Form-36 (SF-36) item Health Survey. Thus, further well-controlled studies are needed to demonstrate the efficacy of PR in larger sample.

In another mixed group of asthma ($n = 7$) and COPD (13) of 3 months, outpatient PR programme three times per week, with a high aerobic intensity exercise programme and each session for two hours, was conducted [29]. There was a statistically and clinically significant improvement in exercise capacity using the 6-min

walk test and improvement in quality of life using SF-36 were observed. However, there was no improvement in anxiety and depression scores for both groups. This might be due to small sample size and unblinded nature of the study. Further studies are needed to determine the optimal frequency and intensity of PR including psychological therapy to treat the severity of depression and anxiety in patients with asthma.

Haavee and Hyland [30] examined the efficacy of 4 weeks intensive inpatient PR program to ameliorate trait anxiety (negative emotions such as fears, worries, and anxiety in different situations) and improve quality of life in patients with asthma ($n$ = 92) and COPD ($n$ = 40) following the program and longitudinal changes in 6 months. There was significant improvement in quality of life for both groups immediately after rehabilitation but gained improvement was diminished at 6 months. There was no change in trait anxiety scores. For both groups, significant improvement was observed in quality-of-life scores in patients who were living alone compared with those who live with spouse or partner. The findings of the study may implicate that it is important to consider maintenance exercise program following PR to achieve sustain improvement in quality of life. However, because the availability of inpatient PR is very limited in most countries in the world, and access to this type of service is unlikely to be available in the foreseeable future because of higher cost to run the programme. The cost effectiveness of the programme was not examined.

A Cochrane review [31] examined of twenty-one randomized control trials which enrolled asthmatic patients aged 8 years and over (772 participants) who participated in physical exercise training or not. Physical training had to be undertaken for at least 20 min, two times a week, over a minimum period of four week. Physical training was shown to be beneficial in improving maximum oxygen uptake. However, there were no significant improvements in lung function test or other outcome measures. More recently, another systematic review [32] examined the effects of physical training on airway inflammation in asthmatic patients. The systematic review included 23 studies (16 randomized controlled and 7 prospective cohort studies) of 2635 asthmatic patients. Generally, the study sample sizes were relatively small (with median sample size = 30). Physical training was beneficial in reducing C-reactive protein, malondialdehyde, nitric oxide, sputum cell counts and Immunoglobulin E (IgE) in asthmatics compared to patients without physical training. However, the authors have observed significant variations among the studies in terms of physical training intervention type, duration, intensity, frequency, primary outcome measures, methods of assessing outcome measures and study designs. Therefore, it was difficult to provide firm conclusion about the efficacy of physical training in asthmatic patients. Further, well-controlled trials are needed.

## *Cognitive Behavioural Therapy*

Anxiety is a common reaction to extreme dyspnoea in patients with chronic respiratory diseases. However, uncontrolled excessive anxiety and high levels of panic may contribute to exacerbation of the condition (making it worse) and poor

management of asthma. Cognitive behavioural therapy (CBT) is an action-oriented treatment in which both cognitive (e.g. identification and challenging of interpretation errors) and behavioural (e.g. planned exposure to avoided sensations and situations) strategies are used to interrupt the panic and/or anxiety cycle and facilitate more adaptive responses [33].

Parry et al. [34] examined the efficacy CBT in 94 highly anxious adult patients with asthma that were randomly allocated to receive either a cognitive behavioural intervention to improve self-management of their anxiety symptoms ($n = 50$) or routine clinical care ($n = 44$). The primary outcome was to reduce asthma-specific fear at 6-, 12- and 24-week follow-up. Treatment was specifically designed to include education about asthma and anxiety using the CBT to improve self-management of asthma-specific fear. Their findings indicate that the CBT significantly reduced asthma-specific fear at the end of intervention and at 6 months compared to the control group. In addition, there was significant reduction in the depression score and improvement in quality of life in the CBT group at the end of intervention. However, there was no significant difference at 6-month follow-up in these parameters both in the CBT and control group. Furthermore, cost for the use of healthcare resources was not reduced (not cost-effective) in the CBT group. Thus, further studies are needed to determine the duration, frequency of CBT and the potential benefits of 'booster-sessions of CBT' in longer-treatment follow-up.

In another nurse led [35] 8 week evaluating CBT therapy in a group of 48 adult women with asthma with coexisting panic disorder was conducted with 6-month follow-up. Patients were randomly allocated to a CBT therapy ($n = 25$) or a waiting-list control group ($n = 23$). Sixty per cent of the CBT group and 44% of the control group completed the study. The CBT group showed significant improvement in their anxiety and panic scores at 8-week and at 24-week follow-up compared to the control group, respectively. However, the improvement that was achieved at 8 weeks in quality of life was not sustained at 24 weeks. This was a specific female gender study and generalizability of the findings to the wider asthma population is questionable.

## *Antidepressants*

There is little evidence in the literature about the use of antidepressants in the treatment of depression and anxiety in patients with asthma. Only one pilot study examined the efficacy of antidepressants. In a single blind pilot study, Brown et al. [36] investigated the efficacy of bupropion 20 mg daily over 12 weeks. Eighteen depressed asthmatic patients participated in the bupropion therapy. Depression and anxiety severity were measured using the Hamilton Rating Scale for Depression (HAM-D-17) and the Hamilton Rating Scale for Anxiety (HAM-A), respectively. In total, 27.8% of the patients responded to treatment (50% reduction in the HAM-D) and 16.7% patients remitted (no depression). There was significant

correlation between changes in percentage forced expiratory volume in one second, asthma control and changes in HAM-D scores after 12 weeks of bupropion therapy. In addition, there was a statistically significant change in anxiety score (mean change = 2.12, SD = 3.97, $p = 0.04$). This pilot study demonstrated that the benefits of antidepressant to treat anxiety and depression. However, caution is required in interpretation of these findings because of small sample size and lack of a control group. Therefore, well-controlled randomized control trials are needed to evaluate the efficacy of antidepressants especially using the selective serotonin reuptake inhibitors in patients with asthma.

## Implications for Research and Clinical Practice

Anxiety and depression are common comorbidities in adult patients with asthma and are associated with increased morbidity and healthcare utilization. Most of the existing data are based on studies, which are cross sectional, and there is a scarcity of longitudinal research. In asthmatic patients, anxiety and depression were associated with increased healthcare utilization, physical disability and impaired quality of life. Psychosocial assets, individual, interpersonal relationship and socio-economic status are all valuable in determining the patient's response to treatment and psychological well-being of patients with asthma. Thus, healthcare professionals should play an active role in the early diagnosis and adequate treatment of these comorbid conditions.

The exact mechanisms linking the physical burden of asthma to elevated depressive and anxiety symptoms may require further investigation in longitudinal studies.

Very few studies have investigated the efficacy of PR in the treatment of anxiety and depression in adult patients with asthma. Because of the fact that findings of these studies were mostly inconclusive, well-controlled studies are needed to examine the benefits of PR in long-term follow-up. In addition, a few studies [34, 35] have examined the role of CBT in reducing depressive, anxiety and panic symptoms in patients with asthma. CBT may have a role in treating these symptoms, but the available data and access to CBT services are scant but well-controlled studies are needed to evaluate this further. The efficacy of antidepressants for treating depression and anxiety in adult patients with asthma has not been evaluated, and thus caution is required for the judicious use of antidepressants especially patients with mild-to-moderate depression in patients with asthma. Further studies are required to determine which class of antidepressants, duration and dosage are effective in the treatment of comorbid depression and anxiety in patients with asthma.

A comprehensive treatment strategy such as collaborative care model (CCM) [case management] with partnership with patients and family has been shown to be effective in the treatment of depression in patients with chronic diseases [37]. Education about depression treatment and ongoing support from healthcare professionals is important in depressed patients with asthma and/or COPD given their reluctance to accept antidepressant drug therapy [38]. Therefore,

it is worthy to examine the benefits of CCM in patients with asthma who suffer from clinical depression and/or anxiety disorders.

### Clinical Tips

1. Adult asthmatic patients with recent changes in their lifestyle (e.g. loss of loved ones, divorce) with recurrent episodes of chest infections and hospital admission should be assessed for anxiety and depressive symptoms, e.g. using the Hospital and Anxiety Depression scale [37]. Those identified with the elevated symptoms of depression HAD > 11 or anxiety HAD > 11, where by mental health services are available, to be referred to a psychologist or a psychiatrist for further assessment.
2. Exercise therapy should be the first line of treatment for adult asthmatic patients with comorbid mild or moderate depressive and anxiety of symptoms. The exercise therapy should be tailored to individual's need in terms of repetition, intensity and duration.
3. In a community-based rehabilitation including gymnasium, asthmatic patients should be encouraged to engage in a group or individual exercise programs to break the cycle of negative thoughts and hopelessness that feed into anxiety and depression.
4. Counselling therapy and educational therapy should be considered for adults asthmatic patients with elevated symptoms of anxiety and depression. It is paramount as well to monitor asthmatic patients with comorbid anxiety and depressive symptoms in routine clinical visits or telephone contacts, e.g. using the HAD scale.
5. If there is no improvement after the course of counselling therapy in depression or anxiety symptoms, further treatment can be considered to high intensity psychological interventions such as one-to-one CBT or group CBT. This depends on the patient's choice and provision of psychological therapy including CBT in local setting.
6. For those asthmatic patients with high level of depressive and anxiety symptoms with suicidal ideation should be offered antidepressants drug therapy preferably selective serotonin reuptake inhibitors because of their low side effects. In addition, follow-up visits, at least every 4 weeks, especially at the early stages are paramount in order to monitor the patient's adherence to treatment and progress and adverse events.

## Conclusion

The nature of the relationship between asthma and mental health problems (whether it is bidirectional or not) is unknown. Therefore, future studies should explore the possible mechanisms, and triggering factors for the development of elevated anxiety and depressive symptoms are worthy endeavour.

Untreated comorbid anxiety and depression in adult patients with asthma may have devastating consequences, overwhelm the coping strategies of asthma patients and their caregivers and may increase healthcare utilization [39]. Future studies should examine the efficacy of PR, cognitive behavioural and antidepressants to treat anxiety and depression in well-controlled, randomized trials, with larger samples and long-term follow-up.

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