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Observational study of mental health in asthmatic women during the prenatal and postnatal periods

Abstract

Objective: We aimed to examine the prevalence and severity of psychological distress of women with asthma in both the prenatal and postnatal periods, and to determine whether asthmatic women with and without mental health problems differ in self-management, medications knowledge, and asthma symptoms.

Methods: We assessed spirometry performance and asthma symptoms in 120 women (mean age 29.8 years) before 23 weeks gestation, as part of the Breathing for Life Trial (Trial ID: ACTRN12613000202763). Prenatal depression data was obtained from medical records. At 6 weeks postpartum, we assessed general health, self-reported asthma control, depression symptoms (with the Edinburgh Postnatal Depression Scale) and adaptive functioning (with the Achenbach System of Empirically Based Assessment (ASEBA) scales).

Results: Twenty percent of our sample reported having a current mental health diagnosis, 14% reported currently receiving mental health care, while 47% reported having received mental health care in the past (and may/may not have received a diagnosis). The sample scored high on the Aggressive Behaviour, Avoidant Personality and Attention Deficit/Hyperactivity scales. Poorer self-reported postnatal asthma control was strongly correlated with elevated somatic complaints, externalising problems, antisocial personality problems and greater withdrawal. Prenatal spirometry or asthma severity and control were largely not associated with measures of psychopathology.

Conclusions: These findings indicate that pregnant women with asthma frequently report issues with psychopathology during the prenatal and postnatal periods, and that the

subjective perception of asthma control may be more related to psychopathology than objective asthma measures. However, due to sample bias, these findings are likely to be understated.

Introduction

Asthma is one of the most common medical conditions to affect women during pregnancy (1). In Australia, approximately 12% of pregnant women experience symptoms of asthma (2). The global prevalence of asthma during pregnancy ranges between 4-12% (3-5). Pregnant women with asthma are at risk of experiencing higher frequency and severity of asthma exacerbations, especially amongst more severe asthma cases (6). Furthermore, asthma and asthma exacerbations during pregnancy are linked to increased risk of adverse perinatal outcomes, including pre-eclampsia, preterm birth, low infant birth weight and small for gestational age, compared to non-asthmatic women (7-10). It is important, therefore, to minimise the occurrence of asthma exacerbations through active asthma management (7, 11, 12). However, adherence to asthma control plans may be affected by mental health, an issue particularly salient for asthmatic women in the perinatal period (13).

The risk of depression and anxiety in women increases during prenatal and postpartum periods. A recent Australian retrospective cohort study reported rates of depression antenatally at 6.2%, and postnatally at 3.3% (14). Other Australian studies have reported antenatal depression rates of 7% (15), 17% (16) and almost 30% (17), whereas rates of postnatal depression range from 6% to 12% (16, 18). In Australia, depression affects approximately 5.1% of women in any given 12 month period (19). Worldwide, estimates of postpartum depression are 6.5-12.9% (20-22).

Many studies report that poor maternal mental health perinatally can have long-term negative impacts on the infant's development. Maternal antenatal depression is associated with reduced infant growth rate and increased risk of diarrhoea (23). Postnatal depression has been associated with impaired mother-child interactions (24), less efficient parenting (25)

and less attention to infant safety (26), which in turn can lead to behavioural, cognitive, socio-emotional and health problems in the infant (27). Importantly, a recent study indicated that depressive symptoms experienced by mothers during the first 6 -7 years of their child's life are associated with increased incidence of childhood asthma, even when controlling for a history of maternal asthma (28). Taken together, these findings clearly indicate the clinical importance of understanding the nature and prevalence of perinatal psychopathology in asthmatic mothers.

Poor mental health has been associated with asthma (29). Adults with asthma have a higher risk of depression and anxiety compared to the general population (30). Asthmatic individuals who experience psychological distress often have less controlled asthma control and higher rates of hospitalisation (31-35). However, the association between asthma severity and anxiety or depression, is not robust. While one study reported that asthma severity was positively correlated with depressive problems (32), another found no difference in the incidence of reported depression between those with mild or severe asthma (36). It has been suggested that depressive symptoms such as reduced motivation, energy, and cognitive functioning may interfere with self-management behaviours, leading to poorer asthma outcomes (31, 37). A negatively reinforcing cycle may develop: depression may increase treatment non-adherence, which can exacerbate asthma symptoms, and this, in turn, may increase depressive symptom severity (38, 39).

Conversely, the associations between asthma and poor mental health may reflect the complex, bidirectional interactions between the immune and nervous systems, particularly through the signalling of G protein-coupled cell surface receptors, receptor tyrosine kinases, cytokines, growth factors and neuropeptides during inflammation (40). Thoren and

Petermann (41) noted that, in individuals with comorbid asthma and anxiety, a fear of asthma symptoms would be expected to increase motivation to effectively manage and control asthma symptoms. However, they argue that intense asthma-related anxiety may trigger asthma symptoms, which may compromise engagement in self-management behaviours and lead to reduced quality of life. The higher mortality rates amongst asthmatic adults with a comorbid diagnosis of depression (42) support this notion.

There is a paucity of research on perinatal mental health amongst women with asthma. Recent studies report that the risk for depression and anxiety in pregnant women ranges from 6.1% (43), to 28% (44) to 45% (13). Other studies suggest that the risk of depression during pregnancy may increase with greater asthma severity and associated exacerbations (45), and that anxiety may significantly increase the odds of subsequent exacerbations during pregnancy (46). This is consistent with the findings of a recent study showing that uncontrolled asthma was more common in asthmatic pregnant women who also experienced anxiety and depression (13).

On the other hand, amongst asthmatic adults the use of oral corticosteroids to treat asthma exacerbations has been associated with depressive symptoms (47), and depression was associated with longer duration of oral corticosteroid use (48) as well as higher doses of ICS (e.g. 49).

In summary, there is some evidence that pregnant women with asthma have heightened risk of depression and anxiety, which in turn, may impact asthma exacerbations during pregnancy. However, the mental health characteristics of asthmatic women in the post-partum period, which is associated with higher risk of depression and anxiety, have not been well-characterised. The current study has three primary aims: 1) to examine the prevalence

and severity of psychological distress of women with asthma in both the prenatal and postnatal periods, 2) to examine whether asthmatic women with and without mental health problems differ in self-management, medications knowledge, and asthma symptoms, and 3) to examine whether subjective and objective measures of asthma severity are related to psychological distress.

Methods

Participants

Pregnant women at 12-22 weeks gestation were recruited from the greater Newcastle, Australia area to the current study as part of the Breathing for Life Trial (BLT), a large randomised clinical trial (RCT) examining the effects of a novel asthma management strategy for pregnant women (50). The Breathing for Life Trial is registered with the Australian New Zealand Clinical Trials Registry (Trial ID: ACTRN12613000202763). Participants were included if they were aged over 18 years, had an asthma diagnosis from a physician, had symptoms of and/or treatment for asthma in the last 12 months, and reported no additional lung disease, no drug or alcohol dependence, and no requirement for oral corticosteroid use for >14 days in the past 3 months. Participants were randomised to either a control or intervention group, in a 1:1 ratio with block sizes of four or six. From June 2015 through to September 2017, 259 BLT participants were invited into the current study, of which 155 were randomised to the active intervention arm of the RCT. As this RCT is ongoing, data regarding intervention effects is not yet available. A total of 120 participants (60 from the intervention arm and 60 from the treat-as-usual arm) consented to participate in the current study (mean age = 29.8 ± 5.4

years). These participants had been recruited into the BLT study between November 2014 and March 2017.

Procedure

Consenting participants completed prenatal asthma and mental health measures (described below) and at 6 weeks postpartum (range 4-8 weeks) participants were asked to complete further ratings of mental health symptoms along with sociodemographic and medical history questionnaires. Information collected included maternal country of birth, age, marital status, current breastfeeding and/or formula feeding status, primiparity, medical conditions in addition to asthma, personal and family history of psychopathology (current and past presence of a mental health condition), annual household income (as an marker of socioeconomic status; SES), medical history, and maternal education level. Women who reported experiencing high levels of psychological distress were offered the services of a clinical psychologist.

Participants were reimbursed $20 for expenses. This study was approved by the Hunter New England Human Research Committee and the University of Newcastle Human Ethics Research Committee (HREC approval number 15/05/20/4.05).

Measures

Asthma measures

Prenatal data, including body mass index (BMI, kg/m^2), smoking status, weeks gestation, age at asthma diagnosis, as well as hospital admissions, emergency department visits and oral corticosteroid (OCS) use for asthma in the previous year were collected before participants reached 23 weeks gestation. Forced expiratory volume in 1 second (FEV_1) and forced vital

capacity (FVC) were measured prenatally using spirometry. Age-adjusted and height-adjusted % predicted FEV_1 and FVC were calculated in line with the 2012 Global Lung Function equations (51). Adherence and self-management skills were also assessed prenatally. Adherence to inhaled corticosteroids was assessed by asking participants "It can be difficult to remember all of your medicines when things get busy. How many times in the last week have you missed a dose of your preventer?" Participants who had missed more than 20% of their medication doses were considered to be non-adherent. Knowledge about preventer and reliever medication was determined by asking women direct questions about how each medication worked and when they were to use each type, and responses were scored by trained nurses/midwives. Participants were also asked whether they had a written action plan (WAP) and to demonstrate correct use of their inhaler, in accordance with the technique described in Murphy, Gibson, Talbot, Kessel, and Clifton (52). At 6 weeks postpartum, participants completed the Juniper Asthma Control Questionnaire (ACQ; 53) and women scoring above 1.5 were considered to have uncontrolled asthma (54). The list of measures completed by women who consented to participate in this study (participants) and women who only participated in the larger BLT project (non-participants) is shown in Table 1.

Table 1. Prenatal measures for participants and non-participants of the current study. For all of the chi-squared analyses, some cells had expected counts less than 5 so an exact significance test was selected for Pearson's chi square. P values are bolded if significant after FDR correction.

	Participants		Non-participants			
	N	M (±SD)	N	M (±SD)	p<.05	p<.05 after FDR correction
Prenatal EPDS	102	5.26 (±4.00)	118	6.76 (±4.72)	***p*=.013****	*p*=.091
0-9 (Low risk)	92 (91%)		85 (70%)			
10-12 (Medium risk)	3 (3.4%)		17 (16%)		***p*=.002****	***p*=.028***
13-30 (High risk)	7 (5.6%)		16 (14%)			
BMI	119	30.74 (±7.91)	139	29.83 (±8.54)	*p*=.337	*p*=.786

Age	119	29.30 (±5.29)	142	29.44 (±5.84)	*p*=.845	*p*=.845
Asthma control questionnaire[a]	60	1.46 (±1.00)	67	1.63 (±.97)	*p*=.344	*p*=.602
FEV_1FVC %	107	81.97 (±7.51)	124	81.37 (±7.14)	*p*=.534	*p*=.748
FEV_1 %	111	88.21 (±12.38)	124	89.09 (±12.32)	*p*=.588	*p*=.686
FVC %	108	90.84 (±10.98)	124	92.47 (±10.43)	*p*=.248	*p*=.868
Smoking status	N	(%)	N	(%)		
Current	13	11%	36	26%		
Ex	31	26%	43	30%	***p*=.018***	*p*=.084
Never	74	63%	61	44%		
Adherent[b] (missed <20% of ICS dose)	27	60%	27	53%	*p*=.465	*p*=.814
History (times in the past year)						
Emergency visits						
0	103	87%	120	85%	*p*=.735	*p*=.735
1 or more	16	13%	22	15%		
Hospital visits						
0	112	93%	134	93%	*p*=.539	*p*=.686
1 or more	7	6%	8	6%		
Missing	1	1%	2	1%		
Medication type						
ICS	11	9%	18	28%		
ICS/LABA	34	29%	33	51%	*p*=.488	*p*=.759
Other	4	3%	6	9%		
SABA	69	59%	8	12%		
Correct Knowledge						
Action plan	12	48%	4	16%	***p*=.013***	*p*=.091
Preventer	2	8%	6	24%	*p*=.076	*p*=.266
Reliever	11	44%	15	60%	*p*=.662	*p*=.713
Technique						
Preventer (Pressurised metered dose inhaler)						
Optimal	32	27%	22	16%	*p*=.103	*p*=.288
Adequate	7	6%	10	7%		
Inadequate	66	55%	81	58%		
Missing	14	12%	27	19%		
Turbuhaler						
Optimal	20	22%	26	18%		
Adequate	3	3%	4	3%	*p*=.630	*p*=.735
Inadequate	1	1%	5	4%		
Missing	68	74%	104	75%		
Activity limitation (days/week)						
0	78	65%	92	68%		
1 – 5	27	23%	24	18%	*p*=.510	*p*=.714
6 – 7	14	12%	20	14%		

Mornings						
0	48	40%	51	40%		
1 – 5	45	38%	38	29%	*p*=.332	*p*=.664
6 – 7	26	22%	40	31%		
Nights						
0	38	32%	34	29%		
1 – 5	54	45%	44	37%	*p*=.112	*p*=.261
6 – 7	27	23%	41	34%		
GINA Asthma severity and control classifications (during pregnancy)						
Asthma severity	N	(%)				
Mild	81	(68.1)				
Moderate	10	(8.4)				
Severe	28	(23.5)				
Asthma control						
Uncontrolled	60	(50.4)				
Partly controlled	37	(31.1)				
Well controlled	22	(18.5)				
Asthma severity and control						
Mild uncontrolled	36	(30.3)				
Mild partly controlled and controlled	45	(37.8)				
Moderate-severe uncontrolled	24	(20.2)				
Moderate-severe controlled	14	(11.8)				

Abbreviations: FDR = False discovery rate; N = sample size; M = sample mean; SD = sample standard deviation; % = percent; *p* = p-value; FEV_1FVC % = Ratio of forced expiratory volume in 1 second and forced vital capacity percentage; FEV_1 % = Forced expiratory volume in 1 second percentage; FVC % = Forced vital capacity percentage; ICS = Inhaled corticosteroid; LABA = Long acting beta agonist; SABA = Slow acting beta agonist.

*$p < 0.05$

** $p < 0.01$

[a]Intervention participants only

[b]Calculated for participants taking ICS/ICS LABA medications only

Asthma severity and control classifications

Prenatally, participants were classified as having mild, moderate or severe asthma using criteria from the Global Initiative for Asthma guidelines (GINA; 55). In brief, we used treatment step as a surrogate measure of *asthma severity*. Women using step 1 (reliever alone) or step 2 (low dose inhaled corticosteroid; ICS) therapy were considered to have mild asthma. Women using step 3 (low dose ICS/long-acting beta agonist; LABA or medium/high dose ICS) therapy were considered to have moderate asthma. Women using step 4 (medium/high dose ICS/LABA) therapy were considered to have severe asthma.

Asthma control was classified as well controlled, partly controlled or uncontrolled according to an adaptation of the GINA criteria. Asthma was well controlled if there were none of the following symptoms in the previous week: night waking, activity limitation, daytime symptoms >2 times per week, or reliever use >2 times per week. If 1-2 of these symptoms were present, asthma was considered to be partly controlled, and if 3-4 symptoms were present, was considered to be uncontrolled.

Mental health measures

Participants completed the Edinburgh Postnatal Depression Scale (EPDS; 56) at their first antenatal appointment (2nd trimester of pregnancy) as part of routine antenatal care. At the postpartum visit, participants completed both the EPDS and the Adult Self Report (ASR) from the Achenbach System of Empirically Based Assessment (ASEBA; 57).

The EPDS is a brief, 10-item self-report scale that screens for postpartum depression. Women are asked to respond in a way that best describes how they have felt in the past week.

Apart from one sleep-related item, the EPDS excludes somatic complaints such as fatigue and appetite variations that are typical experiences during the pre- and post-natal periods. Scores ≥10 are recommended for referral for diagnostic evaluation of postpartum depression. The EPDS has been validated worldwide and demonstrates high test-retest reliability and internal consistency (56, 58-61). It has also been validated for prenatal depression (62).

The ASR is a standardised self-report questionnaire designed for adults aged 18-59 years. The ASR assesses adaptive functioning across a range of domains (i.e., friends, spouse/partner, family, job; education, personal strengths). It generates age and gender normed T-scores across two composite scales (externalising/internalising and total problems) and syndrome scales (Anxious/Depressed, Withdrawn, Somatic Complaints, Thought Problems, Attention Problems, Aggressive Behaviour, Rule-breaking Behaviour, and Intrusive problems). It also produces scores for Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5; 63) oriented scales: depressive, anxiety, somatic, avoidant personality, attention deficit/hyperactivity and antisocial personality problems. Scores between the 93rd and 97th percentile are considered borderline clinical, and above the 97th percentile are in the clinical range, both signalling the need for further assessment and diagnosis.

Analysis

Data were analysed using the Statistical Package for the Social Sciences (SPSS) software for Windows, with level of significance set to $\alpha = .05$. To investigate sample bias, demographic, mental health and asthma data were compared between participants and non-participants. Total scores, percentile scores, and T-scores for DSM-5 oriented scales and syndrome scales of the ASR were derived and categorised in the normal, borderline, or clinical range for each participant. EPDS scoring uses clinical brackets: 0-9 is considered low risk, 10-12 is medium

risk, and 13-30 is high risk. Scores from the EPDS and ASR were used to characterise the nature of psychological distress. We used multidimensional χ^2 analyses, and phi (ϕ) to measure the association between variables (64). To avoid inflation of type 1 error rate as a result of multiple comparisons, we used false discovery rate (FDR) corrected p-values. FDR is a well-validated way of controlling for multiple comparisons and is less conservative than other Bonferroni-type corrections (65). As many prior studies do not correct for multiple comparisons, we report both uncorrected and FDR-corrected p-values for comparability. Further associations between asthma and psychopathology were determined by computing odds ratios for the association between high ASR scores in this sample of asthmatic women, as compared to normative ASR data. Given that prior work has found associations between oral corticosteroid use and depression, we compared total scores on the EPDS and relevant ASR scales between participants who used ICS and those that did not. Multiple regression was used to determine whether mental health explained any variance in GINA control or severity classifications. Specifically, total scores from the DSM-5 oriented scales and syndrome scales of the ASR, pre- and post-natal EPDS total scores, self-reported presence of mental illness diagnosis (binary yes/no), current psychiatric care (yes/no), past psychiatric care (yes/no), maternal age at the time of their infant's birth, and breastfeeding status were all entered into the model as predictors.

Results

Sampling bias

First, we examined whether there were any systematic differences between the 120 participants and 139 non-participants from the larger BLT study. The primary reasons for non-

participation included: loss to follow-up, too busy, not interested, or they did not attend their BLT appointment. Descriptive measures of mental health and asthma status for participants and non-participants are presented in Table 1. Participants did not significantly differ from non-participants in age, BMI, or any asthma-related measures, with the exception that participants had greater knowledge of their action plan (which was non-significant after FDR correction). Non-participants had higher rates of current smoking, but this did not remain significant after FDR correction. Information on parity, SES and GINA asthma severity and control classifications was not available for non-participants.

The groups also differed in prenatal mental health status. Prenatal EPDS scores were lower (less mental health risk) in participants than non-participants ($t(218) = 2.52$, $p=.013$) but the effect was not significant after FDR correction ($p=.091$). A significantly greater percentage of non-participants than participants scored in the medium and high-risk categories, ($\chi^2(2, N=220) = 12.50$, $p=.002$ FDR-corrected: $p=.028$). The strength of the association between EPDS category and group was moderate ($\phi = .238$) and participation status accounted for 5.66% of the variance in prenatal depression scores.

The current sample

Sociodemographic characteristics of participating women were obtained at 6 weeks post-partum. The majority were: born in Australia (95%), Caucasian (83%), well educated (81% completed at least the final year of high school), primiparous (52%), in a relationship (93%), and represented a diverse range of socio-economic status (52% reported an annual household income over $80,001 and 19% under $37,000). Of the infants, 53% were male and 49% were exclusively breastfed. Asthma status was assessed prenatally. In terms of asthma status, 35% of participants were using ICS or ICS/LABA (median dose 500µg), 9% were current

smokers, 12% had at least 1 emergency hospital visit in the last year for their asthma, 22.5% were able to demonstrate optimal technique for their inhaler, and 22.5% were adherent to their asthma medication.

Mental health results

Postnatal EPDS scores, self-reported mental illness diagnoses, psychotropic medications, past and current mental health care, and alcohol and drug use are reported in Table 2. The percentage of participants scoring in the medium-high categories of the EPDS (indicating that they should be referred for evaluation for perinatal depression) rose from 9% prenatally (n=102; Table 1) to 15.5% postnatally (n=110; Table 2). Total scores for pre- and post-natal depression did not significantly differ (t=-.691, p=.491). However, there were significant differences in the risk category proportions between pre- and post-natal depression scores $\chi^2(4, N=92) = 16.42$, p=.003. Twenty percent of the sample reported a mental health diagnosis, with 14% currently receiving mental health care, and 47% of participants having received mental health care in the past (but did not necessarily receive a diagnosis of a mental health condition; Table 2). Participants had low rates of current alcohol and drug use, with 73% reporting that they rarely or never drank alcohol, and 59% reporting that they have never used non-prescription drugs (Table 2).

Table 2. Postnatal measures for participants of the current study.

	N	M (±SD)
Asthma control questionnaire	55	.833 (±1.07)
Postnatal EPDS	110	5.44 (±4.05)
0-9 (Low risk)	93 (84.5%)	
10-12 (Medium risk)	10 (9.1%)	
13-30 (High risk)	7 (6.4%)	
	N	(%)
Mental health diagnoses	110	
Depression	6	(5%)
Anxiety	4	(4%)
Depression and anxiety	6	(5%)

Bipolar disorder	2	(2%)
Depression and Borderline Personality disorder	2	(2%)
Depression, Bipolar disorder and anxiety	1	(1%)
PTSD and anxiety	1	(1%)
Any mental health diagnosis	22	(20%)
Medicated for mental health issue[a]	16	(15%)
Mental health care[b]		
Currently in (N=118)	16	(14%)
Past (N=114)	54	(47%)
Alcohol use	117	
Rarely/never	81	(69%)
Once a month	19	(16%)
1-2 days/week or more	17	(15%)
Illicit drug use	115	
Never	68	(59%)
Past use	43	(37%)
Current use[c]	4	(4%)

Abbreviations: N = sample size; M = sample mean; SD = sample standard deviation; EPDS = Edinburgh Postnatal Depression Scale; % = percent; PTSD = Post-traumatic Stress Disorder.

[a]Included any reported psychotropic medication used for the purposes of treating a mental illness/mood disorder. Two participants were taking medication for a mental health issue but did not disclose a diagnosis.

[b]Refers to self-reported visits to a psychologist or counsellor for psychotherapy, and does not necessarily reflect a diagnosis of a mental health disorder.

[c]Painkillers were reported for current drug use

Scores from the internalising and externalising problem scales, syndrome scales and the DSM-5 oriented subscales, of the ASR are presented in Table 3. On most subscales, the percentage of women scoring in the borderline or clinical range (above the 93rd percentile) was less than the expected 7%. However, somewhat higher than expected percentages were found for the Aggressive Behaviour Syndrome scale (9.5%), as well as the Avoidant Personality and Attention Deficit Hyperactivity Problems DSM-oriented subscales (8.6% and 7.7%, respectively).

Table 3. Postnatal ASEBA subscale percentiles for participants, odds ratios and the bivariate correlation between ASEBA subscale total scores and postnatal asthma control questionnaire mean score.

					Correlation with postnatal asthma control		
Subscale	Borderline (93rd – 97th percentile) n (%)	Odds ratio	Clinical (97th – 100th percentile) n (%)	Odds ratio	R[a]	p value	FDR-corrected p value
DSM-oriented subscales							
Depressive problems	2 (1.9%)	0.41	2 (1.9%)	0.54	**.201**	.146	.166
Anxiety problems	3 (2.9%)	0.61	3 (2.9%)	0.83	**.075**	.589	.589
Somatic problems	4 (3.8%)	0.83	2 (1.9%)	0.54	***.461****	<.001	.009
Avoidant personality problems	5 (4.8%)	1.04	4 (3.8%)	1.12	**.272**	.047	.073
Attention Deficit Hyperactivity problems	2 (1.9%)	0.41	6 (5.8%)	1.70	**.282**	.039	.066
Antisocial Personality	1 (1.0%)	0.20	2 (1.9%)	0.54	***.506****	<.001	.006
Syndrome scales							
Anxious/Depressed	4 (3.9%)	0.83	1 (1%)	0.27	**.164**	.235	.250
Withdrawn	2 (1.9%)	0.41	3 (2.9%)	0.83	***.490****	<.001	.004
Somatic complaints	3 (2.9%)	0.61	3 (2.9%)	0.83	***.393****	.003	.009
Thought problems	2 (1.9%)	0.41	4 (3.8%)	1.12	**.230**	.094	.114
Attention problems	4 (3.9%)	0.83	2 (1.9%)	0.54	**.271**	.047	.067
Aggressive behaviour	6 (5.7%)	1.26	4 (3.8%)	1.12	***.407****	.002	.007
Rule-breaking behaviour	1 (1.0%)	0.20	0		**.232**	.092	.120
Intrusive	0		2 (1.9%)	0.54	***.389****	.004	.010
Internalising problems	1 (1%)	0.20	4 (3.8%)	1.12	***.324****	.017	.032
Externalising problems	1 (1%)	0.20	3 (2.9%)	0.83	***.430****	.001	.017
Total problems	3 (2.9%)	0.61	4 (3.8%)	1.12	***.329****	.015	.032

Abbreviations: DSM = Diagnostic and statistical manual of mental disorders; N = sample size; % = percent; R = Pearson correlation coefficient; FDR = False discovery rate.

*p< 0.05

** p< 0.01

[a] R values are bolded if significant after FDR correction

No odds ratios were statistically significant

Mental health and asthma results

Postnatal ACQ scores did not significantly correlate with prenatal or postnatal depression scores from the EPDS (r = .229, p = 0.14, FDR-corrected p = 1.07, r = .294, p = 0.02, FDR-corrected p = 0.38). Table 3 also shows the bivariate correlation coefficients between postnatal ACQ scores and ASR-based total scores of mental health. Postnatal asthma control was moderately correlated with many ASR DSM-5 oriented scales, syndrome scales and problem scales. However, after FDR correction for multiple comparisons, nine scales remained statistically significant. Specifically, as shown in Table 3, poorer asthma control was more strongly associated with higher level of Somatic Problems and Antisocial Personality Problems on DSM-5 oriented scales, higher scores on the Withdrawn, Somatic complaints, Aggressive behaviour and Intrusive Syndrome scales, and more Internalising, Externalising and Total Problems. The Antisocial Personality scale and Internalising, Externalising and Total Problems scales may receive contributions from similar ASR items and therefore share variance. Prenatal spirometry or treatment adherence did not correlate with either prenatal or postnatal EPDS or any ASR measures (p =.24 to p =1.32 FDR corrected). We calculated odds ratios to examine the incidence of poor mental health in asthmatic women during the postnatal period, as compared to normative healthy women. There was some indication that asthma raises the odds of having poorer postnatal mental health, particularly experiencing aggressive behaviour (OR 1.26, 95% CI: 0.35-4.60) and attention deficit/hyperactivity problems (OR 1.70, 95% CI: 0.52-6.78). However, while these odd ratios are highly clinically significant, they were not statistically significant. No significant differences were found between pre- or post-natal depression scores, or DSM-oriented or Syndrome scale scores between participants who used ICS and those that did not.

We found significant positive correlations between pre- and post-natal EPDS scores (r=.458, FDR-corrected p<.01). Additionally, modest, positive correlations were found between prenatal EPDS scores and total scores from the anxious depressed ASR scale (r=.557, p<.01 FDR), as well as the DSM-oriented depressive problems scale (r=.471, p<.01 FDR) and the anxiety problems scale (r=.462, p<.01 FDR). Strong correlations were found between postnatal EPDS scores and the anxious depressed scale (r=.657, p<.01 FDR), depressive problems (r=.662, p<.01 FDR) and anxiety problems (r=.495, p<.01 FDR) scales of the ASR.

GINA severity and control results

One-hundred and nineteen women were classified as having mild, moderate or severe prenatal asthma (Table 1). The majority of women had mild asthma (68.1%), while approximately half had uncontrolled asthma (50.4%) at their baseline pregnancy assessment. Univariate ANOVA analyses indicated that asthma severity status did not significantly influence pre- or post-natal depression scores, or total scores on the DSM-5 oriented or syndrome scales of the ASR (p =.72 to p =1.69 FDR corrected). Regression analyses revealed that psychological distress did not account for any variance in asthma severity and control groupings. Likewise, results from Chi-Square analyses indicated no differences in asthma severity or asthma control regardless of depression risk level either prenatally (severity: $\chi^2(4, N=101) = 2.4$, p=.664; control: $\chi^2(4, N=101) = 8.6$, p=.073) or postnatally (severity: $\chi^2(4, N=91) = 4.7$, p=.326; control: $\chi^2(4, N=91) = 1.8$, p=.766). Chi-squared analyses showed no significant differences in the proportion of asthma severity ($\chi2(2, N=109) = .248$, p=.883) or asthma control ($\chi2(2, N=109) = 1.364$, p=.506) between participants who reported being diagnosed with a mental health disorder and those who did not.

Discussion

The present study aimed to characterise the presence and severity of psychopathology in the prenatal and postnatal period in asthmatic women, and investigate whether there is a relationship between psychopathology and severity or control of asthma during and after pregnancy. We found moderate correlations between poorer postnatal asthma control and elevated psychopathology at 6 weeks post-partum – and especially more somatic complaints, more externalising problems and more withdrawn behaviours. Thus, women who reported poorer psychological well-being also reported poorer asthma control. In contrast, prenatal spirometry, or GINA-classified prenatal asthma severity and control were not associated with prenatal depression or postnatal psychological well-being.

These findings provide some evidence for a higher incidence of pre- or post-natal psychopathology in asthmatic women, when compared to non-asthmatic women. Twenty-two women (20.2%) reported having had a mental health diagnosis and 47% reported receiving mental health care in the past. Seventeen women (15.5%) scored medium to high levels of postnatal depression on the EPDS. These figures are within the range of recent estimates (45% (13), 28% (44), 6.1% (43) of prevalence of self-reported depression among women with asthma. However, despite elevated incidence of psychopathology in these women as compared to normative data from the ASR, odd ratios did not reach statistical significance.

It is likely that these findings underestimate the relationship between asthma and mental health concerns, as women from the BLT study who participated in the current study reported fewer mental illness symptoms than non-participants. Specifically, pre-natal depression scores were significantly lower in participants than non-participants, and 31% of non-

participants reported levels of prenatal depression that warranted further investigation. This is in line with findings from previous studies showing that women with asthma are at a somewhat elevated risk of anxiety and depression (e.g. 66), including when pregnant (13, 44). In conclusion, it is likely that if all women had participated in the follow up study, the relationship between asthma severity and control and psychological distress would have been stronger.

Previous studies report prevalence estimates of mental health among pregnant women with asthma, largely based on a self-reported clinical diagnosis. Here, we quantified the mental health diagnosis using self-report measures of adaptive and maladaptive behaviour derived from the ASR scales, as well as the EPDS. Asthma control was significantly associated with internalising problems, including withdrawn behaviours (e.g. loneliness and problems interacting with others) and somatic complaints (e.g. reports of aches, pains and experience of physical health), as well as externalising problems, including antisocial personality features (e.g. arguing, rule-breaking and irresponsible behaviour). These factors suggest a unique profile of psychopathology in asthmatic women, including avoidance and withdrawal from responsibilities during a stressful time in life, and/or a perceived lack of control over their life and asthma. Thus, a woman's subjective experience of asthma control in the early postpartum period appears to be strongly linked to level of postnatal psychopathology. While the incidence of poor mental health (specifically aggressive behaviour and attention/deficit hyperactivity problems) in the sample did not reach statistical significance, the higher limit of the odds ratios were highly clinically significant. These findings need replication in a larger sample of asthmatic women to clarify the clinical profiles.

Interestingly, in contrast to earlier findings (e.g. 47), there were no differences in psychopathology between women using ICS and those that were not, and there was no significant correlation between asthma symptoms and anxiety or depression levels. Perhaps the EPDS is not sensitive enough for characterising the distinctive profile of psychopathology in asthmatic women, as simple anxiety and depression measures were not associated with either self-report or objective measures of asthma severity or control. An asthma-specific tool may be required.

Although self-report measures of psychopathology were correlated with self-reported asthma control, they did not correlate with objective measures of asthma severity, including prenatal spirometry. There are a number of possible reasons for this. First, it could be due to the temporal delay between recording the objective measures (prior to 23 weeks gestation) and the self-reported measures of psychopathology (6 weeks post-partum). Second, asthma severity (including spirometry) does not necessarily directly impact subjective experience of asthma severity (67). Some previous studies have found a relationship between asthma severity and mental health. For instance, an early study found that in children, severe asthma was associated with more depressive symptoms (68), and another reported that more severe depressive symptoms are seen in adults with worse asthma, poorer asthma related quality of life and poorer physical health status (32). However, other studies have reported no association between objective measures of asthma severity and mental health (36, 69, 70). Yet, consistent with the present findings, studies using subjective measures (e.g., self-report measures like the ACQ as used here) have found significant associations between perceived asthma severity and depressive symptoms (71, 72). Thirdly, the majority of women in this study had mild asthma (68.1%), and therefore their spirometry was typically within the normal range. This suggests that FEV_1 may be an insensitive measure in this population. Taken

together, this suggests that the subjective perception of one's level of asthma control may more strongly impact or be impacted by one's mental health than the objective level of asthma severity. Mental health problems impact one's perception of how they are coping more generally, which may translate into how controlled they perceive their asthma to be, regardless of whether their asthma is well-controlled or not. How one perceives their asthma control in the early postnatal period may be more informative in determining their mental health postnatally. Last, it is also possible that this relationship could be due to measurement bias. Given that the source of the self-reported asthma control and the self-reported mental health is the same woman, it is possible that factors including her psychological health status and perceived life stress (e.g. 73) may be impacting both measures.

Overall the current findings, due to sample bias, are likely to underestimate the presence of mental health concerns in this population. However, the findings highlight the need to extensively examine the prevalence of psychiatric comorbidities in this vulnerable population of women. It is thought that the symptoms of depression, including low motivation, low energy and apathy may reduce health seeking behaviours, the ability to self-manage and adhere to asthma medication, which may lead to more severe asthma symptoms and exacerbations during the pregnancy. It has been found that anxiety in asthmatic women can increase the likelihood of asthma exacerbations during pregnancy (46). Future research needs to consider asthma exacerbations in more detail. The effect of depression and anxiety treatment, either antidepressants or psychotherapy, on asthma outcomes during pregnancy is yet to be studied, however, there is evidence to suggest that progressive muscle relaxation can improve lung parameters of asthma, anger and health related quality of life in asthmatic women during pregnancy (74).

Conclusion

Mental health screening of women in the perinatal period is becoming more commonplace. This research points to a need for mental health screening with asthma-sensitive tools and specialised mental health interventions designed for asthmatic women during this time, as they may be at an elevated risk of psychopathology.

References

1. Mehta N, Chen K, Hardy E, Powrie R. Respiratory disease in pregnancy. Best practice & research Clinical obstetrics & gynaecology. 2015;29(5):598-611.
2. Clifton, Engel P, Smith R, Gibson P, Brinsmead M, Giles WB. Maternal and neonatal outcomes of pregnancies complicated by asthma in an Australian population. Australian and New Zealand Journal of Obstetrics and Gynaecology. 2009;49(6):619-26.
3. Kwon HL, Belanger K, Bracken MB. Asthma prevalence among pregnant and childbearing-aged women in the United States: estimates from national health surveys. Annals of epidemiology. 2003;13(5):317-24.
4. Rey E, Boulet L-P. Asthma in pregnancy. Bmj. 2007;334(7593):582-5.
5. Lundbäck B, Backman H, Lötvall J, Rönmark E. Is asthma prevalence still increasing? Expert review of respiratory medicine. 2016;10(1):39-51.
6. Murphy VE. Asthma exacerbations during pregnancy: incidence and association with adverse pregnancy outcomes. Thorax. 2006;61(2):169-76.
7. Murphy V, Namazy J, Powell H, Schatz M, Chambers C, Attia J, et al. A meta-analysis of adverse perinatal outcomes in women with asthma. BJOG: An International Journal of Obstetrics & Gynaecology. 2011;118(11):1314-23.
8. Rejnö G, Lundholm C, Gong T, Larsson K, Saltvedt S, Almqvist C. Asthma during pregnancy in a population-based study-pregnancy complications and adverse perinatal outcomes. PLoS One. 2014;9(8):e104755.
9. Murphy VE, Jensen ME, Gibson PG, editors. Asthma during pregnancy: exacerbations, management, and health outcomes for mother and infant. Seminars in respiratory and critical care medicine; 2017: Thieme Medical Publishers.
10. Ali Z, Hansen A, Ulrik C. Exacerbations of asthma during pregnancy: Impact on pregnancy complications and outcome. Journal Of Obstetrics And Gynaecology. 2016;36(4):455-61.
11. Murphy VE, Wang G, Namazy JA, Powell H, Gibson PG, Chambers C, et al. The risk of congenital malformations, perinatal mortality and neonatal hospitalisation among pregnant women with asthma: a systematic review and meta-analysis. BJOG: An International Journal of Obstetrics & Gynaecology. 2013;120(7):812-22.
12. Bonham CA, Patterson KC, Strek ME. Asthma outcomes and management during pregnancy. Chest. 2018;153(2):515-27.
13. Grzeskowiak LE, Smith B, Roy A, Schubert KO, Baune BT, Dekker GA, et al. Impact of a history of maternal depression and anxiety on asthma control during pregnancy. Journal of Asthma. 2017;54(7):706-13.
14. Ogbo FA, Eastwood J, Hendry A, Jalaludin B, Agho KE, Barnett B, et al. Determinants of antenatal depression and postnatal depression in Australia. BMC psychiatry. 2018;18(1):49.
15. Eastwood J, Ogbo FA, Hendry A, Noble J, Page A, Group EYR. The impact of antenatal depression on perinatal outcomes in Australian women. PLoS One. 2017;12(1):e0169907.
16. Leigh B, Milgrom J. Risk factors for antenatal depression, postnatal depression and parenting stress. BMC Psychiatry. 2008;8(1).
17. Edwards B, Galletly C, Semmler-Booth T, Dekker G. Antenatal psychosocial risk factors and depression among women living in socioeconomically disadvantaged suburbs in

Adelaide, South Australia. Australian & New Zealand Journal of Psychiatry. 2008;42(1):45-50.
18. Eastwood JG, Phung H, Barnett B. Postnatal depression and socio-demographic risk: factors associated with Edinburgh Depression Scale scores in a metropolitan area of New South Wales, Australia. Australian and New Zealand Journal of Psychiatry. 2011;45(12):1040-6.
19. Slade T, Johnston A, Oakley Browne MA, Andrews G, Whiteford H. 2007 National Survey of Mental Health and Wellbeing: methods and key findings. Australian and New Zealand Journal of Psychiatry. 2009;43(7):594-605.
20. Gaynes BN, Gavin N, Meltzer-Brody S, Lohr KN, Swinson T, Gartlehner G, et al. Perinatal depression: Prevalence, screening accuracy, and screening outcomes: Summary. AHRQ evidence report summaries: Agency for Healthcare Research and Quality (US); 2005.
21. Howard LM, Molyneaux E, Dennis C-L, Rochat T, Stein A, Milgrom J. Non-psychotic mental disorders in the perinatal period. The Lancet. 2014;384(9956):1775-88.
22. Munk-Olsen T, Laursen TM, Pedersen CB, Mors O, Mortensen PB. New Parents and Mental Disorders. JAMA. 2006;296(21):2582.
23. Rahman A, Iqbal Z, Bunn J, Lovel H, Harrington R. Impact of maternal depression on infant nutritional status and illness: a cohort study. Archives of general psychiatry. 2004;61(9):946-52.
24. Lovejoy MC, Graczyk PA, O'Hare E, Neuman G. Maternal depression and parenting behavior: A meta-analytic review. Clinical psychology review. 2000;20(5):561-92.
25. Malphurs JE, Raag T, Field T, Pickens J, Pelaez-Nogueras M. Touch by intrusive and withdrawn mothers with depressive symptoms. Early Development and Parenting: An International Journal of Research and Practice. 1996;5(2):111-5.
26. McLearn KT, Minkovitz CS, Strobino DM, Marks E, Hou W. Maternal depressive symptoms at 2 to 4 months post partum and early parenting practices. Archives of pediatrics & adolescent medicine. 2006;160(3):279-84.
27. Beardselee WR, Versage EM, Giadstone TR. Children of affectively ill parents: A review of the past 10 years. Journal of the American Academy of Child & Adolescent Psychiatry. 1998;37(11):1134-41.
28. Giallo R, Bahreinian S, Brown S, Cooklin A, Kingston D, Kozyrskyj A. Maternal depressive symptoms across early childhood and asthma in school children: findings from a longitudinal Australian population based study. PLoS One. 2015;10(3):e0121459.
29. Lu Z, Chen L, Xu S, Bao Q, Ma Y, Guo L, et al. Allergic disorders and risk of depression: A systematic review and meta-analysis of 51 large-scale studies. Annals of Allergy, Asthma & Immunology. 2018;120(3):310-7. e2.
30. Scott KM, Von Korff M, Ormel J, Zhang M-y, Bruffaerts R, Alonso J, et al. Mental disorders among adults with asthma: results from the World Mental Health Survey. General Hospital Psychiatry. 2007;29(2):123-33.
31. Cluley S, Cochrane G. Psychological disorder in asthma is associated with poor control and poor adherence to inhaled steroids. Respiratory medicine. 2001;95(1):37-9.
32. Eisner MD, Katz PP, Lactao G, Iribarren C. Impact of depressive symptoms on adult asthma outcomes. Annals of Allergy, Asthma & Immunology. 2005;94(5):566-74.
33. Di Marco F, Verga M, Santus P, Giovannelli F, Busatto P, Neri M, et al. Close correlation between anxiety, depression, and asthma control. Respiratory Medicine. 2010;104(1):22-8.

34. Lavoie KL, Cartier A, Labrecque M, Bacon SL, Lemière C, Malo J-L, et al. Are psychiatric disorders associated with worse asthma control and quality of life in asthma patients? Respiratory Medicine. 2005;99(10):1249-57.
35. Pilipenko N, Karekla M, Georgiou A, Feldman J. Impact of psychiatric illness upon asthma patients' health care utilization and illness control. Are all psychiatric comorbidities created equal? Psychology, Health & Medicine. 2016;21(7):787-99.
36. Chapman K. Impact of 'mild'asthma on health outcomes: findings of a systematic search of the literature. Respiratory medicine. 2005;99(11):1350-62.
37. Barton C, Clarke D, Sulaiman N, Abramson M. Coping as a mediator of psychosocial impediments to optimal management and control of asthma. Respiratory Medicine. 2003;97(7):747-61.
38. DiMatteo MR, Lepper HS, Croghan TW. Depression is a risk factor for noncompliance with medical treatment: meta-analysis of the effects of anxiety and depression on patient adherence. Archives of internal medicine. 2000;160(14):2101-7.
39. Lehrer P, Feldman J, Giardino N, Song H-S, Schmaling K. Psychological aspects of asthma. Journal of Consulting and Clinical Psychology. 2002;70(3):691-711.
40. Foster SL, Seehus CR, Woolf CJ, Talbot S. Sense and immunity: context-dependent neuro-immune interplay. Frontiers in immunology. 2017;8:1463.
41. Thoren CT, Petermann F. Reviewing asthma and anxiety. Respiratory Medicine. 2000;94(5):409-15.
42. Walters P, Schofield P, Howard L, Ashworth M, Tylee A. The relationship between asthma and depression in primary care patients: a historical cohort and nested case control study. PLoS One. 2011;6(6):e20750.
43. Blais L, Ahmed SIS, Beauchesne M-F, Forget A, Kettani F-Z, Lavoie KL. Risk of Postpartum Depression Among Women with Asthma. The Journal of Allergy and Clinical Immunology: In Practice. 2018.
44. Zairina E, Abramson MJ, McDonald CF, Li J, Dharmasiri T, Stewart K, et al. Telehealth to improve asthma control in pregnancy: a randomized controlled trial. Respirology. 2016;21(5):867-74.
45. Tata LJ, Lewis SA, McKeever TM, Smith CJP, Doyle P, Smeeth L, et al. A Comprehensive Analysis of Adverse Obstetric and Pediatric Complications in Women with Asthma. American Journal of Respiratory and Critical Care Medicine. 2007;175(10):991-7.
46. Powell H, McCaffery K, Murphy VE, Hensley MJ, Clifton VL, Giles W, et al. Psychosocial variables are related to future exacerbation risk and perinatal outcomes in pregnant women with asthma. Journal of Asthma. 2013;50(4):383-9.
47. Price DB, Trudo F, Voorham J, Xu X, Kerkhof M, Jie JLZ, et al. Adverse outcomes from initiation of systemic corticosteroids for asthma: long-term observational study. Journal of asthma and allergy. 2018;11:193.
48. Kullowatz A, Kanniess F, Dahme B, Magnussen H, Ritz T. Association of depression and anxiety with health care use and quality of life in asthma patients. Respiratory medicine. 2007;101(3):638-44.
49. Bonala SB, Pina D, Silverman BA, Amara S, Bassett CW, Schneider AT. Asthma severity, psychiatric morbidity, and quality of life: correlation with inhaled corticosteroid dose. Journal of Asthma. 2003;40(6):691-9.
50. Murphy VE, Jensen ME, Mattes J, Hensley MJ, Giles WB, Peek MJ, et al. The Breathing for Life Trial: a randomised controlled trial of fractional exhaled nitric oxide (FENO)-based management of asthma during pregnancy and its impact on perinatal

outcomes and infant and childhood respiratory health. BMC pregnancy and childbirth. 2016;16(1):111.
51. Quanjer PH, Stanojevic S, Cole TJ, Baur X, Hall GL, Culver BH, et al. Multi-ethnic reference values for spirometry for the 3–95-yr age range: the global lung function 2012 equations. Eur Respiratory Soc; 2012.
52. Murphy VE, Gibson PG, Talbot PI, Kessell C, Clifton VL. Asthma self-management skills and the use of asthma education during pregnancy. European Respiratory Journal. 2005;26(3):435-41.
53. Juniper E, O' byrne P, Guyatt G, Ferrie P, King D. Development and validation of a questionnaire to measure asthma control. European respiratory journal. 1999;14(4):902-7.
54. Juniper EF, Bousquet J, Abetz L, Bateman ED, Committee G. Identifying 'well-controlled'and 'not well-controlled'asthma using the Asthma Control Questionnaire. Respiratory medicine. 2006;100(4):616-21.
55. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention. Global Initiative for Asthma; [cited 2018 May 07]. Available from: https://ginasthma.org/wp-content/uploads/2018/04/wms-GINA-2018-report-V1.3-002.pdf.
56. Cox JL, Holden JM, Sagovsky R. Detection of postnatal depression. Development of the 10-item Edinburgh Postnatal Depression Scale. The British Journal of Psychiatry. 1987;150(6):782-6.
57. Achenbach TM, Rescorla L. Manual for the ASEBA adult forms & profiles. Burlington, VT: University of Vermont, Research Center for Children, Youth …; 2003.
58. Bergant AM, Nguyen T, Heim K, Ulmer H, Dapunt O. Deutschsprachige Fassung und Validierung der »Edinburgh postnatal depression scale«. DMW - Deutsche Medizinische Wochenschrift. 1998;123(03):35-40.
59. Kernot J, Olds T, Lewis LK, Maher C. Test-retest reliability of the English version of the Edinburgh Postnatal Depression Scale. Archives of Women's Mental Health. 2014;18(2):255-7.
60. Teissèdre F, Chabrol H. Detecting Women at Risk for Postnatal Depression Using the Edinburgh Postnatal Depression Scale at 2 to 3 Days Postpartum. The Canadian Journal of Psychiatry. 2004;49(1):51-4.
61. Cox JL, Holden J. Perinatal psychiatry: use and misuse of the Edinburgh Postnatal Depression Scale: Gaskell; 1994.
62. Bergink V, Kooistra L, Lambregtse-van den Berg MP, Wijnen H, Bunevicius R, van Baar A, et al. Validation of the Edinburgh Depression Scale during pregnancy. Journal of psychosomatic research. 2011;70(4):385-9.
63. American Psychiatric Association. Diagnostic and statistical manual of mental disorders (DSM-5®): American Psychiatric Pub; 2013.
64. Agresti A. An introduction to categorical data analysis: Wiley; 2018.
65. Benjamini Y, Hochberg Y. Controlling the false discovery rate: a practical and powerful approach to multiple testing. Journal of the royal statistical society Series B (Methodological). 1995:289-300.
66. Scott KM, Bruffaerts R, Tsang A, Ormel J, Alonso J, Angermeyer M, et al. Depression–anxiety relationships with chronic physical conditions: results from the World Mental Health Surveys. Journal of affective disorders. 2007;103(1-3):113-20.
67. Opolski M, Wilson I. Asthma and depression: a pragmatic review of the literature and recommendations for future research. Clinical Practice and Epidemiology in Mental Health. 2005;1(1):18.

68. Mrazek D. Psychiatric complications of pediatric asthma. Annals of Allergy. 1992;69(4):285-90.
69. Afari N, Schmaling KB, Barnhart S, Buchwald D. Psychiatric comorbidity and functional status in adult patients with asthma. Journal of Clinical Psychology in Medical Settings. 2001;8(4):245-52.
70. Janson C, Björnsson E, Hetta J, Boman G. Anxiety and depression in relation to respiratory symptoms and asthma. American Journal of Respiratory and Critical Care Medicine. 1994;149(4):930-4.
71. Janson-Bjerklie S, Ferketich S, Benner P, Becker G. Clinical markers of asthma severity and risk: importance of subjective as well as objective factors. Heart & lung: the journal of critical care. 1992;21(3):265-72.
72. Kovács M, Stauder A, Szedmák S. Severity of allergic complaints. Journal of Psychosomatic Research. 2003;54(6):549-57.
73. Garrity TF, Somes GW, Marx MB. Factors influencing self-assessment of health. Social Science & Medicine Part A: Medical Psychology & Medical Sociology. 1978;12:77-81.
74. Nickel C, Lahmann C, Muehlbacher M, Gil FP, Kaplan P, Buschmann W, et al. Pregnant women with bronchial asthma benefit from progressive muscle relaxation: a randomized, prospective, controlled trial. Psychotherapy and psychosomatics. 2006;75(4):237-43.