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PII: S1876-2859(18)30800-3
DOI: <https://doi.org/10.1016/j.acap.2018.12.004>
Reference: ACAP 1286

To appear in: *Academic Pediatrics*

Received date: 2 August 2018
Accepted date: 14 December 2018

Please cite this article as: Michelle Shankar , Maria Fagnano MPH , Susan W. Blaakman PhD APRN , Hyekyun Rhee PhD RN PNP , Jill S. Halterman MD MPH , Depressive Symptoms among Urban Adolescents with Asthma: A Focus for Providers, *Academic Pediatrics* (2018), doi: <https://doi.org/10.1016/j.acap.2018.12.004>



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TITLE

Depressive Symptoms among Urban Adolescents with Asthma: A Focus for Providers

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KEYWORDS

Urban, Adolescent, Teen, Asthma, Depression

WORD COUNTS

Abstract: 250

Main text: 3046

ACKNOWLEDGEMENTS

This work was funded by a grant from the NHLBI (*R18 HL116244*) and University of Rochester CTSA (*TL1-TR002000*) of the National Institutes of Health. This work was presented in part at the Pediatric Academic Societies meeting in May 2018 (Toronto, ON). We would like to thank the teens and family participants in this study, the Rochester city school district, our community partners, and our research team at the Preventive Care Program for Urban Children with Asthma in Rochester, NY.

ABSTRACT

Objectives: Asthma is the most common chronic disease of childhood in the U.S., disproportionately affecting urban, poor, and minority children. Adolescents are at high risk for poor asthma outcomes and for depressive symptoms. The purpose of this study is to investigate associations between depressive symptoms and asthma-related clinical and functional outcomes among urban teens.

Methods: We used baseline data from a 3-arm randomized trial, School-Based Asthma Care for Teens (SB-ACT), in Rochester, NY. We used the Center for Epidemiological Studies -Depression scale with a standard cutoff score of 16 to identify subjects at risk for clinical depression. We used structured in-home surveys and validated scales to assess clinical and functional outcomes and conducted bivariate and multivariate analyses to evaluate differences between groups.

Results: We identified 277 eligible teens (ages 12-16, participation 80%, 54% Black, 34% Hispanic, 45% Female, 84% Medicaid). Overall, 28% reported depressive symptoms. Teens with depressive symptoms experienced greater asthma symptom severity and more acute healthcare utilization for asthma (all $p < .001$), however there was no difference in preventive care use between groups. Teens with depressive symptoms also reported lower asthma-related quality of life ($p < .001$), less sleep ($p < .001$), and more limitation in mild (aOR 2.60, [1.34,5.02]) and moderate (2.56, [1.41,4.61]) activity and in gym (2.33, [1.30,4.17]).

Conclusions: Depressive symptoms are prevalent among urban teens with asthma and are associated with worse asthma-related clinical outcomes, functional limitation, and quality of life. Providers should consider depression as a significant comorbidity that may impact multiple aspects of daily life for this population.

WHAT'S NEW (40 words)

Depressive symptoms are associated with significantly worse asthma-related clinical and functional outcomes among urban teens with asthma. Increased awareness and management of depressive symptoms may reduce illness burden and improve quality of life for this population.

Asthma is the most common chronic disease of childhood in the United States, affecting an estimated 6.2 million children under the age of 17 [1-2]. It is known that poor, urban, minority children suffer a disproportionate burden of disease [2-4]. Asthma can impact a number of outcomes for children and families in these communities, including ongoing symptoms, activity limitation, missed days of school and work, emergency department visits and hospitalizations, financial burden, and lower quality of life [5].

Both asthma prevalence and morbidity increase in adolescence [2,6], and it is also known that adolescents with asthma are at increased risk of depressive and anxiety symptoms and disorders compared to their non-asthmatic counterparts [7-10, 12, 15, 17-21]. Several studies have assessed the prevalence of depression and depressive symptoms among teens with asthma, however given the variety among study populations and among screening and diagnostic tools, findings vary widely [13-21].

The current body of literature regarding associations between depression and asthma-related outcomes is also limited. Some studies show that individuals with anxiety and/or depression are at increased risk for poor asthma control [11, 16], lower psychosocial functional status [13-14], and decreased quality of life [11]. Depression may be associated with increased suicidal ideation, planning, and attempt [17] as well as increased health seeking behavior and mortality among individuals with asthma [19].

Little is known about the potential impact of depression on asthma-related outcomes specifically among urban teens with asthma, a population that is at high risk for both depressive symptoms and poor asthma control. Thus, the purpose of our study is to:

1. Determine the prevalence of depressive symptoms among urban teens with asthma
2. Investigate associations between depressive symptoms and asthma-related clinical and functional outcomes among urban teens with asthma

METHODS

Setting and Participants

We used data collected from a 3-arm randomized control trial, *School-Based Asthma Care for Teens* (SB-ACT), an ongoing study being conducted in urban Rochester, NY. Data collected at baseline from the first three years of the study (2014-2017) were used.

We received information from school medical alert forms for teens with reported asthma or allergy symptoms, and we contacted their caregivers by telephone to assess for eligibility for SB-ACT. Inclusion criteria for this study were children ages 12-16 years with a physician diagnosis of asthma per caregiver report and persistent or poorly controlled asthma according to national guidelines [22-23]. Exclusion criteria included lack of access to a working phone for follow-up surveys, inability of families to complete consent and surveys in English, and significant comorbidities (i.e.: sickle cell anemia, cystic fibrosis, cerebral palsy, congenital heart disease, etc.) that may interfere with the assessment of asthma symptoms or ability to complete surveys.

Baseline Data Collection

Caregivers and teens provided consent and assent to participate in the study. Baseline data were collected through in-home surveys with the teen and caregiver, who were interviewed independently. We collected information about demographic characteristics, asthma symptoms, and a variety of asthma-related clinical and functional outcomes. The University of Rochester's Institutional Review Board approved the study protocol.

Depressive Symptoms

We measured depressive symptoms using the Center for Epidemiologic Studies - Depression (CES-D) survey, a screening tool validated for use in adults [24] and shown to be effective in adolescent populations [25-26]. The CES-D is a 20-item, 4-point Likert scale survey used to evaluate for depressive symptom recall over the past week. The sum of scores, ranging from 0-60, is calculated after the survey is completed. We used a standard cutoff score of 16 or greater to indicate those at risk for clinical depression, which we refer to as having depressive symptoms. Participants who scored lower on this scale were viewed as not having depressive symptoms [27]. We used the CES-D survey to measure depressive symptoms in both the caregiver and teen surveys.

Asthma-related clinical outcomes*Asthma symptom severity*

We evaluated teen-reported asthma symptom severity by symptom recall over the last 14 days. We asked teens to recall the total number of symptom-free days (defined as 24 hours with no symptoms of cough, wheeze, or shortness of breath), days with symptoms, nights with symptoms, and days needing to stop or slow down normal activity. We also asked teens about asthma symptom severity with validated symptom questionnaires from the National Heart Lung and Blood Institute (NHLBI) [22] and Asthma Control Test (ACT) [23]. We dichotomized asthma symptom severity into those who had moderate-to-severe persistent asthma symptom severity (NHLBI) or poor control (ACT) versus those with less severe outcomes on the two questionnaires.

Acute asthma-related healthcare visits

Information regarding healthcare visits was assessed more thoroughly in the caregiver baseline survey than the teen survey. We asked caregivers to report all acute asthma-related healthcare visits that the teen had in the last year, including urgent care visits, emergency department visits, and hospitalizations for asthma.

Preventive care use

We asked caregivers to report primary care visits that the teen had in the last year, including routine well-child visits and asthma check-ups. We asked teens to list their medications including whether they were currently prescribed a preventive asthma medication. We also asked teens to recall preventive medication adherence over the past 14 days using a 6-point Likert scale (not at all/0 days, a few days/1-3 days, several days/4-7 days, most days/8-11 days, almost every single day/12-13 days, every single day/14 days) [28]. We dichotomized 14-day medication adherence into “almost every day” or “every single day” versus the variables indicating lower adherence.

Asthma-related functional outcomes*Asthma-related Quality of Life (QOL)*

We asked teens to complete the Pediatric Asthma Quality of Life Questionnaire (PAQLQ), a 32-item, 7-point Likert scale survey that assesses asthma-related QOL recall over the past week. The PAQLQ questionnaire consists of three subscales measuring asthma-related QOL: Activity, Symptoms, and Emotions. The mean score of each subscale and overall range from 1-7, with higher scores indicating better QOL [29].

School Absenteeism

We asked teens to report the number of missed days of school for any reason and specifically for asthma in the last 14 days. We created variables to categorize teens that missed one or more days of school versus those that did not.

Sleep

We asked teens to recall the number of nights in the past week that they received enough sleep. We dichotomized the sleep variable into teens that received enough sleep (all 7 nights) versus those who did not. The questions about sleep were based on the National Survey of Children's Health (NSCH) [30].

Activity Limitation

We asked teens to recall the degree of limitation due to asthma over the last 14 days in the following activities: gym, sports, mild activity (such as walking), moderate activity (such as riding a bicycle), and strenuous activity (such as running fast). We assessed degree of limitation using a 5-point Likert scale (totally limited, very limited, limited some, limited a little, not limited). We dichotomized activity limitation into "very limited" or "totally limited" versus "limited some," "limited a little," and "not limited" in each category. The survey questions about activity limitation are based on Children's Health Survey for Asthma (CHSA) [31].

Analysis

We used SPSS v.22 (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.) for all analyses. We used Chi-square and t-test statistics to explore associations between depressive symptoms and demographics as well as asthma-related clinical and functional outcomes. We also conducted multivariate regression analyses adjusting for asthma symptom severity (symptom-free days), gender, race,

ethnicity, and caregiver education to explore associations between depressive symptoms and asthma-related functional outcomes. A 2-sided alpha of <0.05 was considered to be statistically significant.

RESULTS

Demographics

The participation rate for years 1-3 of the SB-ACT study was 80%, and we had data for 277 teens at the time of this analysis. Demographic data are shown in Table 1. Overall, 28% of our sample reported having depressive symptoms. The mean age of our sample was 13.4 years (SD 1.1). 45% were female, 54% Black or African-American, 34% Hispanic, 84% Medicaid-insured, and 32% had a caregiver with depressive symptoms. We found that 56% of teens with depressive symptoms were female compared to 40% of teens without depressive symptoms ($p=.031$); there were no other statistically significant demographic differences between the two groups.

Depressive symptoms and asthma-related clinical outcomes

We found that teens with depressive symptoms experienced significantly worse 14-day symptom severity than teens without depressive symptoms (Table 2). For example, teens with depressive symptoms reported an average of 7.3 symptom-free days over 2 weeks compared to 9.4 among teens without depressive symptoms ($p<.001$). Teens with depressive symptoms also reported experiencing more days with symptoms ($p=.004$), nights with symptoms ($p<.001$), and days needing to stop or slow down normal activity ($p=.013$) over the last 14 days.

Table 2 shows asthma-related healthcare visits for teens with and without depressive symptoms. We found that 38% of teens with depressive symptoms reported having at least one emergency department, urgent care visit, or hospitalization for asthma in the last year compared to 24% of teens without depressive symptoms ($p=.024$).

With respect to preventive care use, there were no significant differences in primary care visits between groups. Fewer teens with depressive symptoms reported being prescribed a preventive medication, and they

were less likely to report taking their preventive medications every day or almost every day, however these differences were not statistically significant. Of note, approximately 30% of the teens in our study had no routine physical in the past year and only 56% of teens reported currently being prescribed a preventive asthma medication. Additionally, only three teens with depressive symptoms reported being on an antidepressant medication (data not shown).

Depressive symptoms and asthma-related functional outcomes

Table 3 compares teens with and without depressive symptoms with respect to functional outcomes. The mean overall PAQLQ score for teens with depressive symptoms was 4.8 compared to 5.5 among teens without depressive symptoms ($p<.001$). Teens with depressive symptoms also demonstrated significantly lower QOL scores for the activity ($p<.001$), symptoms ($p<.001$), and emotional ($p<.001$) subscales. These differences remained significant in the multivariate models adjusting for asthma symptom severity (symptom-free days), race, ethnicity, gender and caregiver education.

With respect to absenteeism, more than half (52%) of teens with depressive symptoms reported having missed days of school for any reason in the prior 14 days compared to 40% of teens without depressive symptoms ($p=.058$, $p=.047$ in the adjusted analysis). While more teens with depressive symptoms missed school due to asthma (20% vs. 10%), the difference between groups was not statistically significant (Table 3).

Teens with depressive symptoms reported an average of 4.1 nights with enough sleep in the last week compared to 5.3 nights among teens without depressive symptoms ($p<.001$). Furthermore, only 28% of teens with depressive symptoms reported having enough sleep all 7 nights compared to 42% among teens without depressive symptoms ($p=.052$).

Teens with depressive symptoms also had more than 2 times greater odds of reporting limitation due to asthma in gym (aOR 2.33, [1.30, 4.17]) as well as mild (aOR 2.60 [1.34, 5.02]) and moderate activity (aOR 2.56 [1.41, 4.61]) in the last 14 days.

DISCUSSION

Urban teens with asthma experience a high burden of depressive symptoms. In our sample, depressive symptoms were common (28%) and found to be associated with significantly worse asthma symptom severity and more acute asthma-related healthcare visits. However, there were no statistically significant differences in preventive care use between groups. Depressive symptoms were also associated with significantly worse asthma-related quality of life, more school absenteeism, poor sleep, and greater activity limitation.

The current literature on the prevalence of depressive symptoms among adolescents with asthma is quite varied, suggesting that 20% to 50% of adolescents with asthma have significant depressive symptoms [32, 33]. One meta-analysis reports a depression prevalence of 27% among adolescents with asthma [33, 34] and another study found clinically significant depressive symptoms in 26% of participants [21], which are both similar to our sample prevalence of 28%. It seems that the prevalence of depressive symptoms among adolescents with asthma is much higher than that of the general population; one study reports point-in-time prevalence of depression to be 2.9% and 3.0% [35] and another study reported the prevalence of experiencing at least one depressive symptom “a lot of the time” or “most or all of the time” to range from 4-16% [36] among adolescents in general. In a national sample of subjects aged 15-54 years old, the general prevalence of current (30-day) major depression was estimated to be 4.9% [37]. It is important to consider that variation exists among previous studies with respect to the population examined and the tools used to measure prevalence.

With respect to associations between depressive symptoms and asthma-related outcomes, our results are also consistent with previous studies reporting associations between depressive symptoms and poor asthma control [11, 16] and decreased asthma-related quality of life [11]. Consistent with the literature suggesting associations between depression and increased health seeking behavior [19], our finding demonstrates that teens with depressive symptoms are more likely to have had at least one emergency department, urgent care, or hospitalization in the past year. However, we found no significant difference in preventive care use between groups. Our findings expand on the current literature by demonstrating significant associations between depressive symptoms and a broad set of both clinical and functional outcomes in this unique population.

Given the cross-sectional nature of this study and reliance on subjective self-report, it is difficult to explain why these associations might exist. For example, it is unclear whether teens with depressive symptoms experience greater asthma symptom severity or simply perceive that they have worse asthma. One review suggests that depression may be more related to subjective measures of asthma severity than objective measures [38]. Another review describes four hypotheses explaining the relationship between asthma and depressive symptoms: (1) suffering from poorly controlled asthma may contribute to depression, (2) depression may be related to poor medication adherence which results in worse asthma outcomes, (3) depression may cause physiologic changes such as inflammation which could result in worsening asthma symptoms, and (4) some individuals may have a genetic predisposition that underlies both asthma severity and depressive symptoms [39]. Regardless of the exact nature of these associations, our findings highlight that these adolescents are experiencing substantial asthma morbidity such as having more frequent asthma symptoms, decreased asthma control, and more acute healthcare utilization.

It is remarkable to find that even after controlling for asthma symptom severity, teens with depressive symptoms continue to experience a significant burden of suffering across multiple functional outcomes including asthma-related quality of life, school absenteeism, sleep, and asthma-related activity limitation. These functional outcomes are pertinent as they relate to the teens' overall well being. Further, sleep and activity are important during this developmental stage, and our results show that even after controlling for asthma severity, there is an association between depression and activity limitation due to asthma as well as sleep limitations. Continued limitation of sleep and physical activity may lead to additional long-term health consequences such as obesity, and they may also serve as barriers to academic performance and other aspects of teens' lives.

Our results also suggest that overall preventive asthma care is suboptimal for this group of teens with persistent asthma, with less than 1/3 consistently taking guideline recommended controller medications. Further, even though teens with depressive symptoms are experiencing significantly worse clinical outcomes, they do not seem to utilize more preventive care. Further, it was striking that very few teens reported taking medications for depression. This suggests that teens with depressive symptoms may be undertreated for both their asthma and mental health needs.

Limitations

Since this is a cross sectional study we cannot attribute a causal link between depressive symptoms and asthma-related outcomes among teens with asthma. Our study relies on self-reporting and thus we are unable to determine whether the increase in severity noted in the study is a result of a perceived severity secondary to their depressive symptoms and not to a real increase in their asthma severity. Furthermore, since the data are from teen and caregiver report there is always a risk of recall error and reporting bias, and data were not confirmed with medical or school records.

It is important to note that the CES-D survey is a screening tool for depressive symptoms, and teens scoring at the standard cutoff of 16 still may not fit diagnostic criteria for a depressive disorder according to the *Diagnostic and Statistical Manual of Mental Disorders* (5th ed.; DSM-5) [40]. Our study also did not include consideration of possible comorbidities of depressive symptoms, such as anxiety and obesity. Moreover, we acknowledge that the survey question regarding sleep is worded “During the past week (7 nights) on how many nights did you get enough sleep?” and does not include whether those nights reported as not receiving enough sleep were related to asthma symptoms or to other causes. Additionally, while only three teens with depressive symptoms reported using an anti-depressant medication, our surveys did not elicit detailed information about behavioral health services that teens may have been receiving.

Lastly, teens were recruited from a low-income urban community and there are many factors in this cohort that could contribute to prevalence of depressive symptoms and perceived asthma severity. While this may limit generalizability of our study to non-urban communities, this is a high-risk population that is important to better understand in order to develop appropriate interventions.

Future Research Directions

Clarifying the exact nature of associations between depressive symptoms and asthma-related clinical and functional outcomes requires further longitudinal study, ideally including both asthma-related and behavioral health intervention. Future studies should also include objective measures of asthma, such as biomarkers indicating asthma severity, as well as an assessment of comorbidities of depressive symptoms, such as anxiety

and obesity. While research among adolescents may pose challenges with recruitment and retention, it is important to recognize adolescence as a key developmental period where providers play a pivotal role in supporting the development of lifelong habits and experiences that will lead to enduring healthy lifestyles as adults.

Clinical Implications

Depressive symptoms are a prevalent comorbidity that may significantly impact both clinical and functional asthma outcomes for teens with asthma. We found significant associations between depressive symptoms and a broad range of clinical and functional outcomes. Our findings underscore the importance of addressing depressive symptoms to improve quality of life in teens with asthma. This study brings to light important gaps in preventive care in this population. All teens with persistent asthma should receive guideline-recommended preventive medication and follow-up care to improve asthma control and prevent utilization of higher tier healthcare services.

Further, while we cannot establish causality from this study, increased awareness and management of depressive symptoms may reduce the burden of illness and improve asthma-related quality of life for these teens. To that end, mental health screening for adolescent patients with asthma is critical, aligning with the recent guidelines released by the American Academy of Pediatrics which recommend universal depression screening for all children ages 12 and above [41]. Screening alone is not sufficient, and patients with positive screens can be referred for services to help support management of their mental health needs [42]. Through improved awareness, screening, and management, our hope is for teens with asthma to realize their full potential without the burdens of poor asthma control, depressive symptoms, and related outcomes that influence all aspects of their lives.

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Table 1: Demographics*

	Overall	Teens without Depressive Symptoms	Teens with Depressive Symptoms	p-value
N (%)	277	199 (72%)	78 (28%)	-
Age (Mean, SD)	13.4 (1.1)	13.4 (1.1)	13.5 (1.1)	.339
Gender: Female	124 (44%)	81 (40%)	43 (56%)	.031
Race: Black/ African-American	149 (54%)	114 (58%)	35 (44%)	.110
Ethnicity: Hispanic	93 (34%)	60 (30%)	33 (42%)	.066
Insurance: Medicaid	231 (84%)	166 (84%)	65 (84%)	1.00
Caregiver with depressive symptoms	86 (32%)	59 (30%)	27 (34%)	.564

*Subjects are from The School Based Asthma Care for Teens (SB-ACT) trial in Rochester, NY.

Table 2: Depressive Symptoms and Asthma-related Clinical Outcomes among Urban Teens with Asthma

	Teens without Depressive Symptoms	Teens with Depressive Symptoms	p-value	Adjusted p-value*
Asthma Symptom Severity in Last 14 Days – Mean (SD)				
Symptom-free Days	9.4 (4.5)	7.3 (4.6)	.001	.008
Days with Daytime Symptoms	3.4 (4.1)	5.0 (4.3)	.004	.023
Nights with Nighttime Symptoms	1.2 (2.6)	2.8 (4.1)	<.001	.001
Days Needing to Stop or Slow Down Normal Activity	2.2 (2.6)	3.3 (3.3)	.013	.070
Moderate-to-severe Persistent Asthma (NHLBI)	33 (17%)	24 (31%)	.013	.027
Poor control (ACT)	77 (39%)	50 (64%)	<.001	.002
Acute Asthma-related Healthcare Visits in Last Year – n (%)				
≥1 ED visit or Urgent care visit or Hospitalization	46 (24%)	29 (38%)	.024	.034
Preventive Care Use – n (%)				
≥1 Well-child check in last year	141 (70%)	55 (70%)	1.000	.715
≥1 Asthma check-up in last year	46 (24%)	21 (26%)	.534	.436
Currently prescribed a preventive medication	115 (58%)	40 (52%)	.184	.358
Took controller medicine every day or almost every day in last 14 days N=180	38 (29%)	10 (21%)	.343	.283

*Regression analysis controlling for race, ethnicity, gender, and caregiver education level.

Table 3: Depressive Symptoms and Asthma-related Functional Outcomes among Urban Teens with Asthma

	Teens without Depressive Symptoms	Teens with Depressive Symptoms	p-value	Adjusted p-value*
Pediatric Asthma Quality of Life Questionnaire (PAQLQ)*** Score – Mean (SD)				
Overall	5.8 (1.0)	4.8 (1.4)	<.001	<.001
Activity subscale	5.5 (1.2)	4.7 (1.4)	<.001	.002
Symptom subscale	5.7 (1.2)	4.8 (1.4)	<.001	<.001
Emotional subscale	6.2 (1.0)	4.9 (1.6)	<.001	<.001
School Absenteeism Due to Asthma in Last 14 Days – n (%)				
Missed school for any reason	78 (40%)	41 (52%)	.058	.047
Missed school due to asthma	21 (10%)	15 (20%)	.072	.066
Sleep in Last 7 days				
Nights with enough sleep, Mean (SD)	5.3 (2.0)	4.0 (2.3)	<.001	.001
Enough sleep all 7 nights, n (%)	79 (42%)	22 (28%)	.052	.203
Activity Limitation Due to Asthma in Last 14 days – n (%)				
Limitation			aOR**	95% CI
Mild Activities	27 (14%)	27 (34%)	2.60	(1.34, 5.02)
Moderate Activities	60 (30%)	46 (58%)	2.56	(1.41, 4.61)
Strenuous Activities	132 (66%)	64 (82%)	1.70	(0.86, 3.38)
Gym	66 (34%)	47 (60%)	2.33	(1.30, 4.17)
Sports	96 (48%)	49 (62%)	1.46	(0.82, 2.57)

*Regression analysis controlling for race, ethnicity, gender, and caregiver education level.

**Juniper, et al. "Measuring Quality of Life in Children with Asthma." Quality of Life Research. 1996 Feb; 5(1):35-46.