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Caregiver Depressive Symptoms and Primary Medication Nonadherence in Children with Asthma

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Abstract

Introduction: The purpose of this study was to identify risk factors for primary medication nonadherence among low-income minority children with persistent asthma.

Method: Data came from an environmental control and educational intervention for children with uncontrolled asthma who were treated in the Emergency Department for an asthma exacerbation. Presence or absence of pharmacy records for child asthma medications was the outcome of interest. A range of sociodemographic, health, and psychosocial measures were included in the binary logistic regression.

Results: Of the 222 youths (mean age=6.3 years; 93.7% Black), 25 (11.3%) lacked pharmacy records of asthma medications. For every one-point increase in caregiver depressive symptoms, the odds of the child having a pharmacy record declined by five percent (OR = 0.95; p = 0.012).

Discussion: Providers should systematically assess and monitor caregiver depressive symptoms as a potential contributing factor for primary medication nonadherence in low-income minority children with persistent, uncontrolled asthma.

Keywords

Asthma; medication adherence; caregiver; depressive symptoms

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Asthma affects nearly 6.2 million children under the age of 18, making it one of the most common chronic child health conditions in the United States (Centers for Disease Control, [CDC] 2019a). Not only is asthma more prevalent among racial minority and impoverished children, but morbidity and mortality disproportionately affect these children as well (Akinbami, 2006; Centers for Disease Control, 2019a; Coleman et al., 2019). Racial minority children, especially Black children, have higher rates of uncontrolled asthma, increased emergency health care utilization for asthma, more missed schools days due to asthma, and a higher asthma-related death rate compared to non-Hispanic, white children with asthma (Akinbami, 2006; CDC, 2019b; Hsu et al., 2016; Zahran et al., 2018).

Asthma management is multifocal and includes monitoring asthma symptoms, environmental control, patient education, and pharmacotherapy (National Asthma Education and Prevention Program [NAEPP], 2007). Medication adherence, defined as taking medication as prescribed by one's health care provider, is an essential component of proper asthma management (NAEPP, 2007; Desai and Oppenheimer, 2011). Prescription medications for persistent asthma include daily use of long-term controller medications to prevent symptoms and short-acting rescue medications, which are taken as needed for symptom relief (American Academy of Allergy, Asthma, & Immunology, n.d.). Adhering to asthma medications as prescribed, in particular daily use of long-term controller medications, is associated with improved asthma control and reduced morbidity and mortality and is therefore critical among low-income, racial minority children with persistent asthma (Schatz, 2012).

However, adherence to long-term controller medication is inconsistent in this vulnerable population. Data collected from electronic monitoring devices attached to inhalers found that daily controller medication adherence rates may be as low as 30% (Desai and Oppenheimer, 2011). Multiple risk factors for poor medication adherence among low-income, racial minority children with persistent asthma have been identified including: (1) medication cost and discontinuous insurance (Caveney et al., 2019); (2) access to specialty care (Authors, 2017a); (3) neighborhood disadvantage, particularly community violence exposure (Williams, Joseph, Peterson, Moon, et al., 2007); (4) health literacy and health beliefs, including lack of knowledge about asthma and how asthma medications work (Celano et al., 2010; Frey et al., 2016) and parent concerns about medications and their side effects (Authors, 2017b; Conn et al., 2005; Smith et al., 2008); and (5) caregiver depressive symptoms (Bartlett et al., 2004; Bauman et al., 2002; Authors, 2020a; Author, 2020b).

For children with asthma, especially young children, caregivers bear the responsibility for medication adherence (Authors, 2017b, 2018; Desai and Oppenheimer, 2011). The caregiver must obtain prescriptions from the child's health care provider, collect the medications from the pharmacy, and administer the medications correctly (Vrijens et al., 2012). While there may be barriers in all steps of adherence, less is known about primary medication nonadherence (i.e., failure to fill a new prescription) (Authors, 2018; Authors, 2013).

Factors associated with primary medication nonadherence are understudied but may include insurance/medication cost, health behaviors, and health beliefs (Authors, 2018; Hensley

et al., 2018; Williams, Joseph, Peterson, Wells, et al., 2007). Williams et al. (2007) examined predictors of primary medication nonadherence for inhaled corticosteroids (ICS) among individuals with asthma aged five to 56 years and found younger age, female gender, African-American race, and less frequent short-acting β2-agonist (SABA) use as risk factors. Specifically, among the African-American participants, outpatient visits and oral steroid fills in the past year predicted lower odds of primary medication nonadherence. In a qualitative study of 15 mothers of low-income, urban, racial minority children with persistent and uncontrolled asthma and frequent emergency department (ED) visits, participants described prevalent financial stress, including worries about paying for medications (Authors, 2018). Finally, using pharmacy data, Hensley et al. (2018) identified poverty (OR: 1.60, 95% CI: 1.52-1.69) and lack of access to a vehicle (OR: 1.77, 95% CI: 1.68-1.87) as predictors of primary medication nonadherence for children; however, primary medication nonadherence for asthma medications was not specifically examined.

Despite the importance of prescription medication in managing persistent asthma, significant gaps remain in our understanding of why some families of children with uncontrolled asthma do not fill prescriptions for asthma medications. The purpose of this study was (1) to describe the characteristics of low-income minority children with persistent and uncontrolled asthma who did not have a pharmacy record of filling prescription(s) for any asthma medications in the previous 12 month period and (2) to identify risk factors for the absence of pharmacy records of asthma medications.

Method

Participants and procedures

This secondary analysis used baseline data from a randomized clinical trial (RCT) that evaluated the efficacy of an environmental control and educational intervention for children with persistent asthma and frequent emergency department visits (Authors, 2019a). Participants were recruited from two large urban hospitals during a pediatric ED visit for treatment of an acute asthma exacerbation. Eligible children (1) were between the ages of three and 12 years; (2) had physician-diagnosed persistent and uncontrolled asthma based on the current NAEPP (2007) guidelines; (3) had ≥ 2 asthma-related ED visits or ≥ 1 hospitalization for an asthma exacerbation during the previous 12 months; and (4) lived in the metropolitan area where the study was conducted. Children with significant non-asthma respiratory condition (e.g., cystic fibrosis), who did not have a working phone, or were in foster care were ineligible. Enrollment occurred on a rolling basis between August 2013 and February 2016. Of the 554 children screened in the pediatric ED, 222 enrolled in the study and were randomized to the intervention or attention control group (Authors, 2019a).

The institutional review boards of participating medical centers approved the RCT. Each child's caregiver gave written informed consent (and children > 8 years of age gave verbal assent) prior to study participation which included permission to obtain the child's pharmacy records. At baseline, each caregiver completed a survey with key sociodemographic and health information as well as measures of psychosocial functioning.

Measures

Pharmacy record—Presence or absence of a pharmacy record for child asthma medications was the primary outcome of interest. Caregivers were asked to identify all pharmacies they had used in the past 12 months or were currently using to fill their child's asthma prescriptions. Each pharmacy identified by the caregiver was contacted by study staff via fax with a copy of the signed consent and Health Insurance Portability and Accountability Act forms requesting a complete list of all asthma medications dispensed in the prior 12 months. The study Principal Investigator contacted non-responsive pharmacies within one week to retrieve records by phone. Pharmacy records were considered complete if the pharmacies identified at baseline responded with data for the preceding 12-month period or indicated no record of prescriptions for the child during the designated time period (Authors, 2017a).

Demographic and socioeconomic characteristics—Child demographic characteristics were assessed via caregiver report and included age in years, gender ('Male' or 'Female'), and race ('Black/African American,' 'Hispanic/Latino,' 'White,' 'Asian/Pacific Islander,' 'American Indian or Alaskan Native,' or 'Other'). Socioeconomic characteristics, such as child health insurance status ('Medicaid' or 'private insurance/other') and poverty (using 2015 Federal Poverty Level [FPL] guidelines; U.S. Census Bureau, 2020), were also assessed via caregiver report and are presented in Table 1.

Asthma morbidity—Child asthma severity and control level were based on the NAEPP (2007) guidelines and determined by caregiver report of (1) number of symptom days over the past 14 days; (2) number of symptom nights over the past 30 nights; (3) SABA use over the past 14 days; (4) activity limitation over the past seven days; (5) number of oral corticosteroid courses in the past year; and (6) number of asthma ED visit or hospitalizations over the past 12 months.

Asthma health care utilization—Caregivers reported the presence or absence of (1) a routine preventive asthma care visit; (2) an unscheduled sick visit to the pediatrician for treatment of asthma symptoms; (3) an ED visit for asthma symptoms; and (4) a hospitalization for asthma in the past three months. Caregivers also reported whether their child had ever been admitted to the intensive care unit (ICU) or been on a ventilator for asthma. Lastly, caregivers reported whether the child had been seen by an asthma specialist (i.e., pulmonologist or allergist) in the past two years.

Medication behavior and health beliefs—Medication behaviors and health beliefs, such as medication borrowing and worry about medication side effects, were evaluated at baseline by caregiver report (See Table 1).

Caregiver and family context—Caregivers reported whether the child's biological mother had asthma ('yes' or 'no') as well as the total number of people in the household who had asthma. The caregiver's overall daily life stress and asthma specific caregiving stress were ascertained using a visual analog scale ranging from one ('no stress') to ten ('high level of stress').

Caregiver depressive symptoms were measured using the established Center for Epidemiological Studies Depression scale (CES-D; Radloff, 1977), a 20-item self-report instrument in which individuals rate how often over the past week they experienced symptoms of depression (e.g., feeling sad, having crying spells, poor appetite) on a 4-point Likert scale. Scores range from 0 to 60, and a score of 16 or higher suggests an individual may be at risk for clinically significant depressive symptoms (Henry et al., 2018; Radloff, 1977). The CES-D scale has been validated for use with Black women (Makambi et al., 2009) and has been used widely with caregivers of children with asthma (Kub et al., 2018).

Caregiver social support was measured by the Medical Outcomes Study Social Support Survey (MOS-SSS; Sherbourne & Stewart, 1991), a validated 19-item self-report instrument in which the respondent answers the question “How often are each of the following kinds of support available to you if you need it?” on a five-point Likert scale (Sherbourne & Stewart, 1991; Authors, 2019b). Scale scores range from 19 to 95 with higher scores indicating a higher level of social support.

Finally, the caregiver’s perception of their neighborhood was measured using the 34-item Perceived Neighborhood Scale (PNS; Martinez et al., 2002) which assesses social embeddedness, sense of community, satisfaction with neighborhood, and fear of crime on a five-point Likert scale. The PNS was developed with a sample of low-income, urban, racial minority mothers of young children and has demonstrated excellent reliability (Martinez et al., 2002; May et al., 2018).

Data analysis

Chi-square and t-tests were performed to explore group differences between children who had a pharmacy record of asthma medications and those who did not. Binary logistic regression was used to estimate the odds of having a pharmacy record based on the variables that were significant in the bivariate analysis. A p-value ≤ 0.05 was considered statistically significant. FPL was included in the multivariate analysis on the *a priori* assumption that lack of financial resources may have an impact on the caregiver’s ability to fill a prescription. Missing data were handled using list-wise deletion. FPL was missing on 34 cases total which were proportionally distributed among those with a pharmacy record and those without. Missing data were otherwise very minimal (<2%). The data were analyzed using SPSS version 21.0. (IBM Corp., 2012).

Results

The total sample was comprised of 222 children and their caregivers. As shown in Table 1, children were predominately Black (N=190; 93.7%), male (N=122; 64%), and had a mean age of 6.3 years (*SD*=2.7). Caregivers were female (N=206; 92.8%) and had a mean age of 31.4 years (*SD*=7.5). Twenty-five children (11.3%) lacked a pharmacy record of asthma medications. Bivariate analyses revealed that children without a pharmacy record differed from their peers in missed school days, routine asthma care, asthma specialty care, rescue medication use, maternal history of asthma, and caregiver depressive symptoms (Table 1).

Multivariate results

Model assumptions were first tested. Multicollinearity was not a concern as demonstrated by VIF < 2.5 (Allison, 2012) for all variables in the multivariate model, which included missed school days, routine visits, unscheduled clinic visits, daily rescue medication use, maternal history of asthma, caregiver depressive symptomology, and poverty. In the multivariate model, caregiver depressive symptomology was the only statistically significant factor associated with the presence or absence of pharmacy records (Table 2). For every one-point increase in caregiver depressive symptoms on the CES-D, the odds of the child having a pharmacy record was reduced by five percent.

Discussion

Although all participating children (N=222; 100%) had persistent and uncontrolled asthma, 25 youths (11.3%) lacked pharmacy records for asthma medications within the prior 12 months. At the same time, 88% of these 25 children (n=22) had used rescue medication in the past two weeks based on caregiver report, and 72% (n=18) had used at least one puff of a rescue medication most days during the preceding two-week period. These results suggest that most of these children did have access to and were using reliever medications on a regular basis, even though they did not have pharmacy records of asthma medications.

A major finding from this study was the significant association between caregiver depressive symptomology and primary medication nonadherence. Nearly two-thirds of the caregivers (n=15; 60%) of children without pharmacy records had clinically significant symptoms of depression (i.e., CES-D ≥ 16) compared to under a third (n=53; 27%) of caregivers of children with pharmacy records. Moreover, in the multivariate analysis, caregiver depressive symptomology was the only statistically significant factor associated with the absence of pharmacy records for asthma medications (i.e., primary medication nonadherence). These findings add to a growing body of literature documenting high prevalence rates of caregiver depressive symptoms and their relationship with impaired asthma management, particularly in the area of medication management (Bartlett et al., 2004; Bauman et al., 2002; Author, 2020b; Authors, 2020a; Wood et al., 2018).

Depressive symptoms, such as compromised memory, lack of concentration, inability to complete tasks, and fatigue, (National Institute of Mental Health, 2018) may negatively impact the necessary steps to fill pharmacy medications for the child's asthma. Consequently, when identifying and addressing primary medication nonadherence, providers of low-income minority children with asthma should regularly screen for caregiver depressive symptoms in all clinical encounters, including ED visits for asthma exacerbations. Indeed, these findings underscore the need for health care providers to understand the social context of children with asthma (Williams and Cooper, 2019) and provide appropriate psychosocial care (National Academies of Sciences, Engineering, and Medicine, 2019). Brief, reliable, and valid screening tools for depressive symptoms are widely available, including the two-item Patient Health Questionnaire (Arroll et al., 2010; El-Den et al., 2018). Once caregiver depressive symptoms are identified, providers should link caregivers to appropriate interventions, such as community resources for treatment of depression (Goeglein and Yatchmink, 2020). Stepped care approaches for identification and

management of postpartum depression in pediatric settings have been well-described in the literature and may provide a framework for addressing depressive symptoms among caregivers of children with asthma (Olin et al., 2017; Waldrop et al., 2018).

Caregivers with clinically significant symptoms of depression may need intensive, ongoing support and multidisciplinary care coordination to improve their management of the child's asthma. Caregivers may especially benefit from assistance with monitoring asthma medication quantities, requesting asthma medication refills, and collecting those medication from the pharmacy or having them sent to the home. Collaboration with community pharmacists who can provide additional patient education and logistical support may be fruitful (El-Rachidi et al., 2017).

Study findings also revealed a pattern of medication behavior and health care utilization suggestive of a reactive or acute approach to the child's asthma management, rather than preventative approaches as recommended by national guidelines (NAEPP, 2007). Nearly 90% of the caregivers (N=198) reported that their child used rescue medication daily in the past two weeks, and 69% (N=153) had sought asthma care in the ED at least once in the past three months. In contrast, preventive asthma management was infrequent as further evidenced by the low rates of preventive (N=109; 49%) and specialty (N=45; 20%) asthma care. Several studies have documented similarly low rates of specialty care among low-income, urban, racial minority children with asthma (Agnihotri et al., 2019; Flores, 2009; Okelo et al., 2007). Pediatric asthma management may differ by physician training (Aung et al., 2014) with some research indicating that asthma management is more consistent with national guidelines when provided by a specialist compared to a generalist physician (i.e. pediatrician, family/general practitioner, or internist) (Agnihotri et al., 2019; Aung et al., 2014; Okelo et al., 2007). For example, Aung et al. (2014) found that pediatric allergists were more likely to prescribe controller medication than pediatricians. Specialty care has also been associated with lower primary medication nonadherence (Authors, 2020c) and better controller medication adherence (Authors, 2017a) among low-income, racial minority children with asthma. Thus, it is critical for all providers who care for low-income minority children with asthma to assess the need for specialty care, discuss options with caregivers, and refer when appropriate. For caregivers with clinically significant depressive symptoms, additional concrete support in accessing pediatric asthma specialty care may be required beyond a referral, such as help making the appointment and reminders to attend.

Finally, it was striking to note that over half of the caregivers of children without pharmacy records reported that the child's mother had a history of asthma. Few studies have explored the influence of the mother's own asthma on any aspect of child asthma management, including asthma medication management and primary medication nonadherence (Caveney et al., 2019; Authors, 2019c). Focus group research previously revealed that the mother's own personal history of asthma influenced the child's asthma self-management knowledge, skills, and behaviors (Authors, 2019c). In many cases, the child's asthma management was guided by the mother's own personal experiences with asthma, which did not generally reflect the national asthma guidelines. For example, mothers described sharing rescue inhalers with their children (Authors, 2019c). However, given the paucity of literature in

this area, further research is needed on the relationship between maternal history of asthma and primary medication nonadherence.

This study has several limitations. Statistical power was limited due to only 25 participants in the group of youths without pharmacy records. Second, although all pharmacies identified by the caregivers ultimately responded with pharmacy data by fax or phone, it is possible that some pharmacies who indicated they had no record of prescriptions may not have wanted to take the time to access and transmit the records to the study team, resulting in misclassification of children without pharmacy records. Furthermore, pharmacy records do not account for the fact that prescribing practices differ by physician training and setting. Prior evidence indicates ED providers infrequently prescribe controller medications (Garro et al., 2011). It is possible that the children in the sample without pharmacy records had not received a prescription for asthma medications because they had most recently received asthma care in the ED, as opposed to having a regular asthma visit with a primary care provider or specialist who are more likely to prescribe asthma medications. Although pharmacy records have been shown to be reliable compared to other methods such as Medicaid claims data (Mudd et al., 2008) and physician assessment (Sherman et al., 2000), future research would be strengthened by using asthma medication data from multiple sources (i.e., prescribing physician, pharmacy records, and caregiver). Utilizing multiple reporters is especially important considering that aside from pharmacy records, data were based primarily on caregiver self-report which may be limited by recall bias (e.g., caregiver could have forgotten to identify a pharmacy) and social desirability bias (Shadish et al., 2001), particularly given the high rates of caregiver depressive symptoms (Bender and Zhang, 2008). Finally, the sample was restricted to low-income, urban, racial minority children with persistent and uncontrolled asthma who sought care at the ED and thus generalizability is limited. Predictors of primary medication nonadherence may differ among children from other sociodemographic backgrounds, those with intermittent or well controlled asthma, and those who have persistent and uncontrolled asthma but do not seek care at the ED.

In summary, the results of this study identified a sub-group of low-income, urban, racial minority children with persistent and uncontrolled asthma that lacked pharmacy records for asthma medications. In the multivariate analysis, caregiver depressive symptomology was the only factor significantly associated with the absence of a pharmacy record, highlighting the need for health care providers to assess and monitor depressive symptoms on an ongoing basis and refer at risk caregivers to evidence-based interventions to improve mental health functioning and, ultimately, reduce primary medication nonadherence among low-income minority children with asthma. Further investigation of the relationships between maternal history of asthma, caregiver depressive symptoms, lack of specialty care, and primary medication nonadherence with larger samples and longitudinal data is needed better elucidate associations among these important constructs as a means to reduce asthma health disparities in this vulnerable population.

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Table 1

Participant characteristics and bivariate relationships (N = 222)

	No pharmacy record (N =25)	Pharmacy record (N = 197)
Demographic characteristics		
Child age[a]	5.7 (2.5)	6.4 (2.7)
Male	14 (56)	128 (66)
Black[b]	24 (96)	184 (94)
Socioeconomic characteristics		
Below 2015 FPL	10 (43.5)	100 (59.2)
Received TANF past 6 mo.	6 (24)	52 (26.8)
Caregiver HS grad	19 (76)	159 (81.5)
Child has Medicaid	24 (96)	183 (93.8)
Caregiver employed	16 (64)	106 (54.4)
Paid out-of-pocket for meds in past mo.	3 (12)	17 (8.7)
Asthma morbidity		
Baseline severity		
Mild	8 (32)	48 (24.5)
Moderate	10 (40)	91 (46.4)
Persistent	7 (28)	57 (29.1)
Asthma control		
Not well controlled	11 (44)	89 (45.2)
Very poorly controlled	14 (56)	107 (54.6)
Day symptoms past 2 weeks	6.4 (4)	5.8 (4.9)
Night symptoms past 4 weeks	7.3 (8.7)	6.9 (8.7)
Missed ≥ 1 school days past 3 mo.*	12 (48)	136 (69.8)
Oral steroid in past 12 mo.	23 (92)	174 (89.7)
Specialist in past 2 years**	0 (0)	45 (23.1)
Asthma health care utilization		
Routine visit past 3 mo.*	6 (24)	103 (52.6)
ED visit past 3 mo.	15 (60)	138 (70.8)
Unscheduled clinic visit past 3 mo.*	2 (8)	59 (30.1)
Hospitalization past 3 mo.	2 (8)	22 (11.5)
ICU or ventilator	7 (28)	75 (38.5)
Specialist in past 2 years**	0 (0)	45 (23.1)
Medication behavior and health beliefs		
Worried about side effects	9 (36)	70 (35.9)
Parent perceives asthma control in past 4 weeks	18 (72)	106 (54.1)
Tried home remedy (e.g., herbal teas, vitamins, garlic, steam, etc.)	14 (56)	81 (41.3)
Child borrowed meds from other family member	8 (32)	33 (16.9)
Child received asthma medication sample	2 (8)	11 (5.6)

	No pharmacy record (N =25)	Pharmacy record (N = 197)
Uses ≥ 1 puff rescue med most days **	18 (72)	180 (92.3)
Used rescue med in past 2 weeks	22 (88)	164 (85.4)
Caregiver and family context		
Mother has asthma *	14 (56)	66 (33.8)
People in household with asthma [a]	2.1 (0.9)	1.7 (1.2)
Depressive symptoms (CES-D) [a]*	18.4 (13.1)	12.0 (10.8)
Social support (MOS-SSS) [a]	85.7 (13.8)	80.7 (18.2)
Daily stress [a]	6.7 (3.3)	6.0 (2.9)
Daily asthma stress [a]	4.2 (3.3)	4.4 (3.3)
Neighborhood (PNS) [a]	2.9 (0.7)	2.9 (0.8)

Note. FPL=federal poverty level. TANF=temporary assistance for needy families. HS=high school.

[a] M(SD)

[b] One biracial child did not have a pharmacy record; Of the 13 non-Black children with a pharmacy record, 3 were Hispanic, 3 were White, 1 was Asian, 3 were biracial, 1 was West Indian, and 1 was missing on race.

* $p \leq 0.05$

** $p \leq 0.01$

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Table 2

Predictors of pharmacy record of asthma medications

	OR	95% CI	p-value
≥ 1 day missed school past 3 mo.	1.75	0.65 – 4.72	0.271
Routine visit past 3 mo.	1.59	0.71 – 3.56	0.264
Unscheduled clinic visit past 3 mo.	3.65	0.74 – 17.9	0.111
Uses ≥ 1 puff rescue med daily	2.84	0.86 – 9.40	0.087
Mother has asthma	0.43	0.17 – 1.12	0.084
Depressive symptoms (CES-D)	0.95	0.92 – 0.99	0.012
Below 2015 FPL	2.25	0.83 – 6.13	0.111

Note. FPL = federal poverty level. Model fit statistics were as follows: Likelihood ratio, χ^2=24.22. p<0.001; Hosmer and Lemeshow, χ^2=5.034, p=0.754.