

Prevalence and risk factors for unrecognized obstructive lung disease among urban drug users

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Background: Obstructive lung disease (OLD) is frequently unrecognized and undertreated. Urban drug users are at higher risk for OLD due to race, behavioral, and socioeconomic characteristics, yet little data exist on prevalence and risk factors associated with unrecognized OLD in this population.

Objective: The objective of this study is to determine the prevalence of unrecognized OLD in an urban population and identify the characteristics associated with lack of physician-diagnosed OLD.

Design: Cross-sectional analysis from the Acquired Immunodeficiency Syndrome Linked to the Intravenous Experience (ALIVE) study, an observational study of current and former injection drug users in Baltimore, Maryland, USA.

Participants: All participants with spirometry-defined airflow obstruction were stratified by the presence or absence of physician diagnosis of OLD.

Main measures: Using cross-sectional demographic, clinical, and spirometric measurements, multivariable regression models were generated to identify factors independently associated with unrecognized OLD.

Key results: Of the 1083 participants evaluated in the ALIVE lung substudy, 176 (16.3%) met spirometric criteria for OLD. Of those, only 88 (50%) had a physician diagnosis of OLD. The prevalence of unrecognized OLD decreased as severity of airflow obstruction increased. Factors independently associated with unrecognized OLD were absence of respiratory symptoms (prevalence ratio [PR], 1.70; 95% confidence interval [CI]: 1.29–2.23; $P < 0.01$) and less severe dyspnea (PR, 0.83; 95% CI: 0.72–0.96, per point increase in dyspnea scale; $P = 0.01$). In the subset of human immunodeficiency virus (HIV)-infected participants, the use of antiretroviral therapy (ART) was independently associated with an increased prevalence of unrecognized OLD (PR, 1.93; 95% CI: 1.05–3.56; $P = 0.03$).

Conclusions: In a cohort of current and former urban drug users, OLD is substantially under-recognized and associated with lack of respiratory symptoms. Relying on the presence of respiratory symptoms as a trigger to perform spirometry may result in a substantial underdiagnosis of OLD in this population. HIV-infected individuals receiving ART are a population particularly vulnerable to unrecognized OLD.

Keywords: obstructive lung disease, human immunodeficiency virus infection, COPD, asthma, spirometry

Introduction

Obstructive lung diseases (OLDs), specifically asthma and chronic obstructive pulmonary disease (COPD), are prevalent conditions associated with substantial morbidity and mortality in the United States.^{1–3} OLD is frequently unrecognized even in smokers.^{4–6}

Several studies have identified populations at higher risk for unrecognized OLD including rural populations,⁷ the urban homeless,⁸ and medical inpatients.^{9,10} Urban populations with a history of current or former drug use represent a poorly studied group with a substantial burden of tobacco abuse and lower socioeconomic status.^{11–13} There is an increased risk of human immunodeficiency virus (HIV) infection in the urban population,^{14,15} and HIV is associated with an increased prevalence of OLD.^{16–18} Each of these factors markedly increases the susceptibility of this population to OLD.^{19–21} Characterizing the prevalence of unrecognized OLD is relevant given that unrecognized OLD is often undertreated.^{8,22} It remains unclear what patient characteristics may be associated with unrecognized OLD, especially in high-risk populations.

The AIDS Linked to the Intravenous Experience (ALIVE) study has prospectively observed a cohort of intravenous drug users (IDUs) in Baltimore, Maryland, USA since 1988.²³ This population has been previously recognized to have limited access and delayed care for HIV.²⁴ We have described the substantial prevalence of respiratory symptoms in this population previously.²⁵ Moreover, the heavy burden of smoking dependence in this cohort makes it an ideal population to examine issues related to undiagnosed OLD. Clinical and spirometric data have been collected on this cohort allowing for the determination of unrecognized OLD. In the current study, we use the cross-sectional data from the ALIVE study to determine the prevalence of unrecognized OLD in a large group of urban IDUs. We determine demographic and clinical factors associated with unrecognized OLD in this population.

Methods

Setting and participants

The methods for recruitment and data collection in the ALIVE study have been described previously.²³ Briefly, ALIVE participants were recruited if they were aged ≥ 18 years, living in inner-city Baltimore, Maryland, and injecting drugs at enrollment. As part of a lung disease substudy, ALIVE participants completed an extensive respiratory questionnaire and performed spirometry testing at a regularly scheduled ALIVE biannual visit. Cross-sectional demographic and clinical data collected at the time of the lung substudy evaluation (January 9, 2007–June 26, 2009) were included in this analysis. This study was approved by Institutional Review Board of the Johns Hopkins Bloomberg School of Public Health and Johns Hopkins University School of Medicine

(Protocol NA_00020295). All participants provided written informed consent.

For this analysis, all individuals with spirometry-defined obstruction (as defined below) were selected. An individual was defined as having recognized OLD if spirometric obstruction was present and the individual reported a physician diagnosis of asthma, chronic bronchitis, or emphysema. An individual was defined as having unrecognized OLD if spirometric obstruction was present and the individual reported no physician diagnosis of asthma, chronic bronchitis, or emphysema.

Measurements

Participants completed a modified version of the American Thoracic Society respiratory questionnaire.²⁶ The questionnaire collected information regarding presence, frequency and timing of respiratory symptoms (cough, phlegm, and wheezing), and dyspnea. Absence of respiratory symptoms was defined as answering in the negative to usually having cough, usually bringing up phlegm, and ever wheezing. Dyspnea was assessed using the modified Medical Research Council (MRC) questionnaire with a validated 0–4 scale, with a higher score indicating worse dyspnea.^{27,28} Smoking status and duration, injection drug use in the last 6 months, and antiretroviral use were determined by self-report. Participants were asked if they had ever received a physician diagnosis of asthma, chronic bronchitis, or emphysema.

OLD was defined as a prebronchodilator ratio of forced expiratory volume in one second (FEV_1) with forced vital capacity (FVC) of < 0.70 . Severity of spirometric obstruction was defined by using the Global Initiative for Obstructive Lung Disease criteria: mild ($FEV_1 \geq 80\%$ predicted), moderate ($FEV_1 = 50\%–79\%$ predicted), severe ($FEV_1 = 30\%–49\%$ predicted), and very severe ($FEV_1 < 30\%$ predicted).¹ Percent predicted values and lower limit of normal (LLN) criteria were calculated using standard formulas.²⁹ Spirometry was performed using a KOKO® (Pulmonary Data Services, Inc, Louisville, CO) pneumotach in accordance with American Thoracic Society guidelines.³⁰

Statistical analysis

Clinical and demographic characteristics between groups were presented as mean (standard deviation), median (interquartile range [IQR]), or n (%). Continuous variables were compared using t -test for normally distributed data and Wilcoxon–Mann–Whitney test for skewed data. Categorical variables were compared with Pearson's χ^2 test. Because odds

ratios can overestimate the magnitude of association between covariates and the outcome of interest in cross-sectional studies when the prevalence of the outcome exceeds 20%,^{31–33} univariate and adjusted prevalence ratios (PR) with 95% confidence intervals (95% CI) were generated using Poisson regression models with robust variance.^{34,35} Covariates were evaluated based upon biological plausibility and inspection of exploratory data analyses. Prevalence of unrecognized obstruction stratified by disease severity was compared using Pearson's χ^2 test. Stata software (version 10.0; Stata Corp, College Station, TX) was used for statistical analysis.

Results

Prevalence and correlates of unrecognized OLD

Of the 1083 participants evaluated in the ALIVE lung substudy, 176 (16.3%) participants met criteria for spirometric obstruction. Only 88 (50%) participants with OLD had a physician diagnosis of OLD. Among participants with recognized OLD, 51 (58%) had a physician diagnosis of asthma only, 13 (15%) COPD only, and 24 (27%) reported both asthma and COPD. As a comparison, of the 907 participants with normal pulmonary function, 213 (23%) reported a physician diagnosis of OLD. Of these, 120 (56%) had a physician diagnosis of asthma only, 60 (28%) COPD only, and 33 (16%) reported both asthma and COPD. The mean age of participants with spirometric obstruction was 50 years,

nearly 70% were male and 85% were black (Table 1). A total of 155 (88%) participants were current smokers with a median pack-years of 22. Approximately 40% reported injection drug use in the previous 6 months. Nearly 30% were HIV-positive, with a median CD4 count of 331 cells/mm³. Of HIV-infected subjects, 51% had been using antiretrovirals in the last 6 months. The prevalence of OLD did not differ by HIV status (16.5% HIV-infected vs 16.2% HIV-uninfected individuals; $P = 0.89$) or current injection drug use status (15.7% current users vs 16.6% prior users; $P = 0.70$). Participants with unrecognized OLD were more frequently male when compared to those with recognized OLD (80% vs 55%; $P < 0.01$). The prevalence of unrecognized OLD did not differ by pack-years smoking history. Aside from gender, demographic and clinical characteristics were similar between those with recognized and unrecognized OLD.

Respiratory symptoms were common in the cohort, with 74% reporting cough, wheeze, or phlegm (Table 2). Respiratory symptoms were less frequent in individuals with unrecognized OLD. A total of 50 (57%) participants with unrecognized OLD reported any respiratory symptoms compared with 81 (92%) participants with recognized OLD ($P < 0.01$). The frequencies of individual symptoms of cough, wheeze, and phlegm were all lower in individuals with unrecognized OLD. Less severe dyspnea, represented by lower MRC scores, was present in participants with unrecognized OLD.

Table 1 Demographic and clinical characteristics of study participants

	Overall	Recognized OLD	Unrecognized OLD	P value ^a
N	176	88	88	
Age (years)	49.6 (8.9)	49.9 (8.47)	49.4 (9.31)	0.74
Male, n (%)	118 (67.1)	48 (54.6)	70 (79.6)	<0.01
Black race/ethnicity, n (%)	149 (84.7)	74 (84.1)	75 (85.2)	0.83
BMI (kg/m ²)	23.9 (21.5–28.1)	23.8 (21.5–28.8)	24.1 (21.6–28.0)	0.77
Completed high school education, n (%)	68 (38.6)	36 (40.9)	32 (36.4)	0.54
Smoking status, n (%)				
Current	155 (88.1)	78 (88.6)	77 (87.5)	
Former	15 (8.5)	7 (8.0)	8 (9.1)	
Never	6 (3.4)	3 (3.4)	3 (3.4)	0.96
Smoking, pack-years	22 (14–39)	23.5 (13.5–41.0)	21.5 (14.5–38.0)	0.69
IDU, n (%) ^b	71 (40.3)	37 (42.1)	34 (38.6)	0.65
HIV-infected, n (%)	51 (29.0)	28 (31.8)	23 (26.2)	0.41
CD4 count (cells/mm ³) ^c	331 (168–491)	298 (174–489)	380 (161–574)	0.56
Viral load undetectable, n (%) ^c	25 (49.0)	13 (46.4)	12 (52.2)	0.68
Viral load (log ₁₀) ^d	4.23 (3.18–5.33)	2.85 (2.60–4.42)	2.60 (2.60–4.02)	0.60
Antiretroviral use, n (%) ^b	26 (51.0)	11 (39.9)	15 (65.2)	0.07

Notes: ^aP value comparing recognized to unrecognized OLD categories; ^bIn prior 6 months; ^cMean (SD) or n (%) of HIV-infected participants only; ^dAmong HIV-infected individuals with detectable viral load.

Abbreviations: OLD, obstructive lung disease; BMI, body mass index; IDU, injection drug use; HIV, human immunodeficiency virus.

Table 2 Respiratory symptoms and dyspnea measures of study participants

	Overall	Recognized OLD	Unrecognized OLD	P value ^a
N	176	88	88	
Respiratory symptoms				
Any ^b	131 (74.4)	81 (92.1)	50 (56.8)	<0.01
Usually have cough	82 (46.6)	53 (60.2)	29 (33.0)	<0.01
Ever wheeze	105 (59.7)	72 (81.8)	33 (37.5)	<0.01
Usually have phlegm	85 (48.2)	55 (62.5)	30 (34.1)	<0.01
MRC score				
0	108 (61.4)	41 (46.6)	67 (76.1)	
1	14 (8.0)	6 (6.8)	8 (9.1)	
2	10 (5.7)	7 (8.0)	3 (3.4)	
3	19 (10.8)	12 (13.6)	7 (8.0)	
4	25 (14.2)	22 (25.0)	3 (3.4)	<0.01

Notes: ^aP value comparing recognized to unrecognized OLD categories; ^bAny respiratory symptoms include any report of usually having cough, usually bring up phlegm, or ever wheezing.

Abbreviations: OLD, obstructive lung disease; MRC, Medical Research Council.

Effect of disease severity on OLD recognition

The median FEV₁/FVC ratio of the study sample was 0.65 (IQR: 0.60–0.68) with a mean FEV₁% predicted of 71.7% ± 18.8%. Overall, 65 (37%) had mild obstruction, 90 (51%) had moderate obstruction, 17 (10%) had severe obstruction, and 4 (2%) had very severe obstruction. The mean FEV₁% predicted was higher in participants with unrecognized OLD when compared to recognized OLD (77.9 ± 19 vs 65.5 ± 20; *P* = 0.04). To determine if the prevalence of unrecognized OLD differed by categories of disease severity, the 176 participants were stratified by FEV₁ into four groups: mild (*n* = 65), moderate (*n* = 90), severe (*n* = 17), and very severe (*n* = 4). The prevalence of unrecognized OLD decreased as severity of airflow obstruction increased (Figure 1). Of the 65 subjects with mild OLD, 44 (68%) had unrecognized OLD, whereas 40 (44%) of the 90 participants with moderate obstruction were unrecognized. Of the 17 subjects with severe obstruction, 4 (24%) were unrecognized. None of the subjects with very severe obstruction were unrecognized.

Factors independently associated with unrecognized OLD

Univariate and multivariate Poisson regression analyses were performed to explore relationships between demographic and clinical factors and unrecognized OLD (Table 3). After accounting for relevant demographic and clinical characteristics, lack of respiratory symptoms and milder dyspnea were independently associated with an increase in the prevalence of unrecognized OLD. The absence of any respiratory symptoms was independently associated with a 70% increase in the prevalence

of unrecognized OLD (PR, 1.70; 95% CI: 1.29–2.23; *P* < 0.01). Each point increase in the MRC score (indicating worse dyspnea) was associated with ~20% reduction in the prevalence of unrecognized OLD (PR, 0.83; 95% CI: 0.72–0.96; *P* = 0.01). These findings persisted after adjusting for HIV infection, current employment, and high school education.

To explore the potential association between treatment for HIV and recognition of OLD, the subset of 51 HIV-infected individuals with OLD were analyzed separately. After adjusting for baseline characteristics, respiratory symptoms, and MRC scores in this subset, the use of ART in the last 6 months was associated with an increased prevalence of unrecognized OLD (PR, 1.94; 95% CI: 1.05–3.56; *P* = 0.03). This

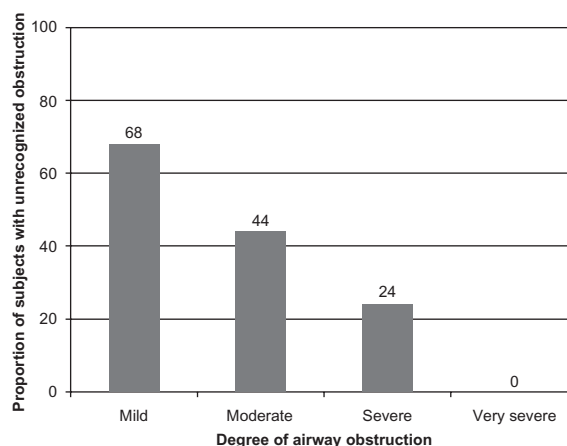


Figure 1 Prevalence of unrecognized OLD based on severity of airway obstruction. The 176 subjects were stratified by FEV₁ into four groups: mild (≥80% predicted; *n* = 65), moderate (50%–79% predicted; *n* = 90), severe (30%–49% predicted; *n* = 17), and very severe (<30% predicted; *n* = 4). Height of bar and data labels represents proportion of subjects in that stratum of OLD severity.

Abbreviations: FEV₁, forced expiratory volume in the one second; OLD, obstructive lung disease.

Table 3 Factors associated with unrecognized obstructive lung disease (n = 176)

Predictors	Unadjusted prevalence ratio (95% CI)	P value	Adjusted prevalence ratio ^a (95% CI)	P value
Age (per 10 years)	0.98 (0.82–1.15)	0.73	0.88 (0.74–1.08)	0.24
Male gender	1.91 (1.26–2.89)	<0.01	1.47 (0.97–2.22)	0.07
Race (black vs nonblack)	1.05 (0.68–1.60)	0.84	1.34 (0.90–2.00)	0.15
High school education	0.91 (0.66–1.24)	0.54	0.85 (0.64–1.12)	0.25
Pack-years (per 10 pack-years) ^b	0.96 (0.88–1.04)	0.33	1.00 (0.92–1.09)	0.94
HIV infection	0.87 (0.61–1.23)	0.42	0.88 (0.64–1.20)	0.42
FEV ₁ (per 10% predicted)	1.21 (1.11–1.32)	<0.01	1.07 (0.97–1.18)	0.15
No respiratory symptoms	2.21 (1.72–2.85)	<0.01	1.70 (1.29–2.23)	<0.01
MRC score (per point increase)	0.74 (0.64–0.86)	<0.01	0.83 (0.72–0.96)	0.01

Notes: ^aPrevalence ratio adjusted for other predictors in table; ^bPack-years calculated as number of packs per day × number of years smoking.

Abbreviations: HIV, human immunodeficiency virus; FEV₁, forced expiratory volume in the one second; MRC, Medical Research Council.

association was attenuated when incorporating % predicted FEV₁ into the adjusted model (PR, 1.79; 95% CI: 0.99–3.26; *P* = 0.055).

Discussion

In this study of OLD in an urban cohort of former and current IDUs, we have found that the prevalence of unrecognized OLD is very high, with half of participants with spirometric obstruction lacking a physician diagnosis. The prevalence of unrecognized OLD was highest among participants with milder degrees of airway obstruction. Lack of respiratory symptoms and less severe dyspnea were independently associated with unrecognized OLD in this population after accounting for severity of airway obstruction. The use of antiretroviral therapy (ART) in HIV-infected participants was associated with an increased prevalence of unrecognized OLD.

Our observation of a substantial underrecognition of OLD in this cohort identifies the urban IDU population as a group particularly susceptible to undiagnosed OLD. We observed a 50% prevalence of unrecognized OLD, higher than that observed in rural, medical inpatient, and Spanish community-based populations.^{7,9,36} Based on our findings, prevalence estimates of disease burden from OLD are likely to be significantly underestimated in the urban IDU population.

Because use of a fixed ratio to define OLD may result in overdiagnosis of disease in a younger population, we also evaluated this cohort using a LLN criteria²⁹ to define OLD. Although an additional nine participants were defined as having OLD using LLN criteria, the prevalence of unrecognized OLD did not differ (50%).

Several reasons may exist for the high prevalence of unrecognized OLD in this population. Urban populations may have fewer primary health care encounters,³⁷ the time

at which spirometric testing is most likely to occur.^{38,39} Primary care providers who care for such individuals may attend to more overt symptoms and diseases at a particular health care encounter, thereby leaving OLD unrecognized.⁴⁰ Our observation that ART use is associated with a higher prevalence of unrecognized OLD in HIV-infected participants suggests that physicians may focus on HIV-related illnesses, deferring non-HIV-related diagnoses such as OLD for subsequent encounters. Alternatively, individuals with more severe OLD (and therefore more frequently recognized OLD) may represent a cohort less likely to access HIV care. The prevalence of unrecognized OLD is similar to that observed in an analysis of the general population.⁴¹ However, unlike the general population, the urban population is exposed to increased risk factors for OLD and the difficulty in access to care. Therefore, aggressive spirometric screening programs for at-risk individuals may allow for earlier detection and subsequent lifestyle modification and treatment of OLD in the urban population.

In our analysis, lack of symptoms was a strong independent factor associated with unrecognized OLD. Several studies have explored the long-term outcomes of individuals with asymptomatic OLD, reaching conflicting results. Bridevaux and colleagues demonstrated that individuals with mild COPD who lack respiratory symptoms have long-term decline in FEV₁ and health care utilization similar to symptom-free individuals without OLD.⁴² However, in a young community-based cohort, Mannino and colleagues have shown that individuals with symptom-free moderate OLD have a 60% increase in the risk of death (hazard ratio [HR], 1.6; 95% CI: 1.3–2.1) when compared to healthy individuals.⁴³ The risk of death in moderate COPD further increases when symptoms are present (HR, 2.1; 95% CI: 1.7–2.6). These data suggest that the one-quarter of our participants with

unrecognized moderate OLD represent a group at increased risk of death, regardless of the presence of symptoms. Relying strictly on presence of respiratory symptoms as a trigger to perform spirometry in at-risk individuals may result in a substantial underdiagnosis of OLD and a missed opportunity to intervene with smoking cessation programs and pharmacological treatments in a group with increased mortality. Tobacco use has been shown to be a distal predictor of mortality among long-term narcotic addicts.^{44,45} Studies suggest that awareness of airflow obstruction among smokers enhances smoking cessation rates.^{46,47} Thus, decreasing the prevalence of unrecognized OLD may enhance smoking cessation and survival in this population.

Although the presence of OLD does not mandate pharmacological interventions, especially in the case of mild disease with few symptoms, lifestyle modifications to prevent progression of disease are of benefit.¹ Although current data do not suggest that inhaled pharmacotherapies substantially alter the decline of FEV₁ or mortality, these agents are effective at controlling symptoms and exacerbations associated with OLD.¹ Given the substantial proportion of participants with unrecognized OLD reporting symptoms of cough, wheeze, or phlegm, there exists a potential improvement in quality of life with making the diagnosis and treatment of OLD in an urban population of IDUs.

Our study has some limitations. We do not have data on pre- and postbronchodilator reversibility to allow for distinction between reversible and fixed airways obstruction. However, the use of consistent, standardized spirometry measurements allows us to make valid classification of the presence of OLD. Additionally, we did not collect data on other lung diseases (eg, bronchiectasis) which may impact the diagnosis of OLD. Although our findings are valid for an urban population of IDUs, they may not be generalizable to the urban population at large or other communities. Despite these limitations, the standardized and extensive data collection used for this analysis allows us to make valid conclusions regarding unrecognized OLD in a high-risk population.

In summary, we have observed a high prevalence of unrecognized OLD in an urban population of former and current IDUs. Lack of respiratory symptoms and milder dyspnea were independently associated with unrecognized OLD. HIV-infected individuals receiving ART are a population particularly vulnerable to unrecognized OLD. These findings emphasize the marked underrecognition of a chronic yet treatable condition in a particularly vulnerable population.

Individual practitioners and health care policy groups should use this information to help develop OLD detection, prevention, and treatment strategies for individuals in urban centers.

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Disclosure

The authors report no conflicts of interest in this work.

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