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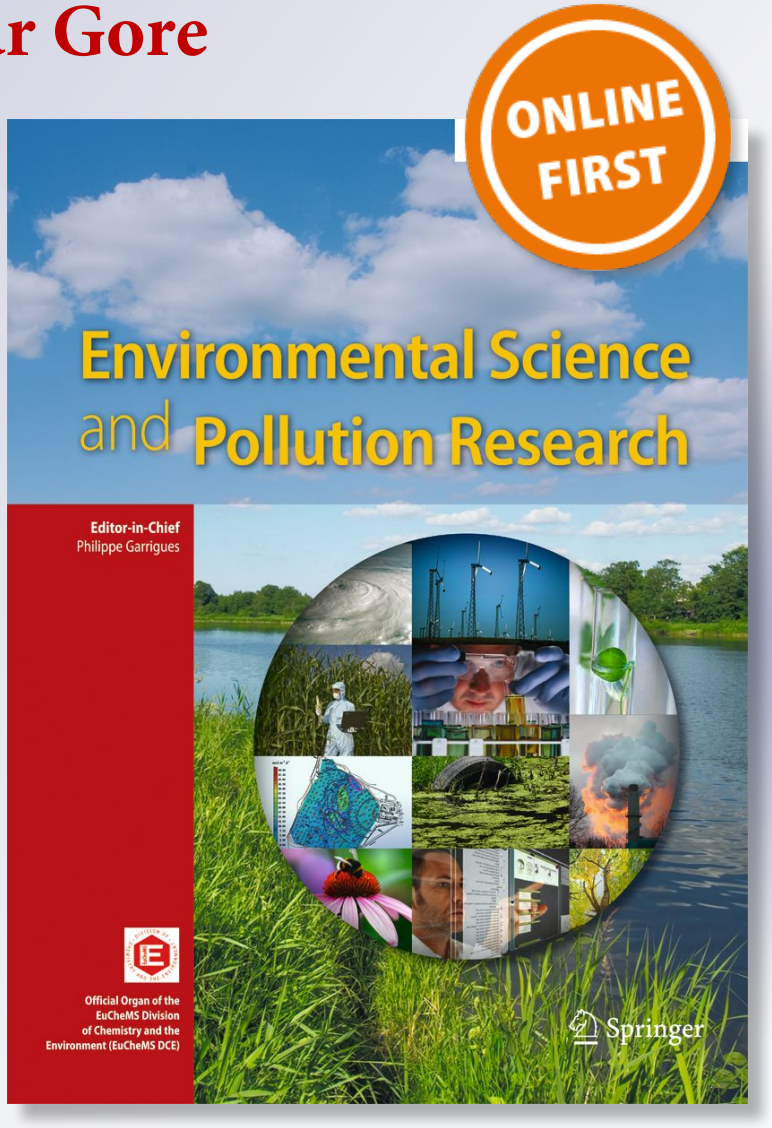

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RESEARCH ARTICLE

Air pollution and respiratory health among diabetic and non-diabetic subjects in Pune, India—results from the Wellcome Trust Genetic Study

Morteza Abdullatif Khafaie[1,2,3] · Sundeep Santosh Salvi[4] · Chittaranjan Sakerlal Yajnik[5] · Ajay Ojha[6] · Behzad Khafaie[7] · Sharad Damodar Gore[8]

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Abstract Diabetics may be more vulnerable to the harmful effects of ambient air pollutants than healthy individuals. But, the risk factors that lead to susceptibility to air pollution in diabetics have not yet been identified. We examined the effect of exposure to ambient PM_{10} on chronic symptoms and the pulmonary function tests (PFT) in diabetic and non-diabetic subjects. Also, to investigate possible determinants of susceptibility, we recruited 400 type 2 diabetic and 465 healthy subjects who were investigated for chronic respiratory symptoms (CRSs) and then underwent measurement of forced vital capacity (FVC) and forced expiratory volume 1 (FEV1) according to standard protocol. Percent predicted FEV1 and FVC (FEV1% and FVC%, respectively) for each subject were calculated. Particulate matter (PM_{10}) concentrations at residence place of subjects were estimated using AERMOD dispersion model. The association between PM_{10} and CRSs was explored using logistic regression. We also used linear regression models controlling for potential confounders to study the association between chronic exposure to PM_{10} and FEV1% and FVC%. Prevalence of current wheezing, allergy symptom, chest tightness, FEV1/FVC <70%, and physician-diagnosed asthma and COPD was significantly higher among diabetic subjects than non-diabetics. There was no significant difference between percent predicted value of PFT among diabetic and non-diabetic subjects ($P < 0.05$). We estimated that 1 SD increase in PM_{10} concentration was associated with a greater risk of having dyspnea by 1.50-fold (95% CI, 1.12–2.01). Higher exposure to PM_{10} concentration was also significantly associated with lower FVC%. The size of effect for 1 SD $\mu g/m^3$ (=98.38) increase in PM_{10} concentration was 3.71% (95% CI, 0.48–4.99) decrease in FVC%. In addition, we indicated that strength of these associations was higher in overweight, smoker, and aged persons. We demonstrated a possible contribution of air pollution to reduced lung function independent of diabetes status. This study suggests that decline in exposure may significantly reduce disease manifestation as dyspnea and impaired lung function. We conduct that higher BMI, smoking, and older age were associated with higher levels of air pollution effects.

Keywords Air pollution · PM_{10} · Chronic respiratory symptom · Lung function · Type 2 diabetes mellitus

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Introduction

Diabetes and chronic obstructive pulmonary disease (COPD) contribute heavily to worldwide morbidity and mortality (Ghanavati et al. 2012; Gregg et al. 2016; Lancet 2016; López-Campos et al. 2014). It is also suggested that both the diseases are strongly interlinked in terms of their pathophysiology (Glaser et al. 2015; Rogliani et al. 2015). Air pollution contributes to 6.6 million premature deaths every year, in rapidly developing countries (van der Wall 2015) and plays a significant role in the causality and worsening of both the diseases (Berend 2016; Nicole 2015; Weinmayr et al. 2016). Literature published from Europe and North America suggests that patients having diabetes, which is associated with a pre-existing systemic inflammation, may be more vulnerable to ambient air pollutants than healthy individuals (O'Neill et al. 2005). Moreover, the risk factors that lead to susceptibility to air pollution in these diseases have not yet been identified (Morteza Abdullatif Khafaie et al. 2016).

One hypothesis about how air pollution may exert its effects is that ambient air contains a range of pollutants that are free radicals or have the ability to drive excess free radicals. Oxidative stress, resulting from exposure to air pollution, oxidizes cell components in the lungs (Li et al. 2002), leading to tissue injury and increased numbers of activated inflammatory cells at the sites of injury with further generation and release of free radicals (Happo et al. 2010). In the absence of antioxidant defense, these free radicals attack the local tissues and components and cause cell injury in the lungs, leading to the development of histological pulmonary inflammatory foci (Gomez-Mejiba et al. 2009). Further increased oxidative stress production and development of inflammation in the lungs may stimulate the blood and lead to the systemic inflammation (Sinden and Stockley 2010). The exaggerated systemic inflammation in obese (exist in most of diabetes patients) may enhance the effects of air pollution through enhancing leukocyte recruitment, cytokine production, microvascular permeability, and edema, which could potentially increase airway obstruction (Chung 2001; Sinden and Stockley 2010). Previous Normative Aging Study demonstrated that obesity and high neutrophil were important factors that aggravated the effects of air pollution, suggesting that individuals with those disorder condition, often associated with chronic inflammation, may be more vulnerable to the harmful effects of air pollution (Alexeeff et al. 2007).

Most information in the field is generated from Europe and North America while the nature of air pollution, amount of exposures, and its effect on health in Indian people have not been well investigated. Previously, we reported that urban residents in Pune had significantly higher concentrations of C-reactive protein (CRP) compared with those living in a rural setting (Yajnik et al. 2008) and also that daily fluctuation in air pollution could produce inflammatory responses (Morteza Abdullatif; Khafaie et al. 2013). Therefore, we investigated long-term pulmonary effects of air pollution in an area like Pune in India in which the typical concentrations of PM_{10} in the ambient air are above100 $\mu g/m^3$. Measures of lung function are reliable indicators of premature cardiorespiratory mortality which are strongly associated with ambient air pollution (Ebi-Kryston et al. 1989). Therefore, lung function is an important link in the investigation of chronic effects of ambient air pollution. We hypothesized that obesity predisposes to increased susceptibility to the harmful effects of air pollution on the lungs through release of harmful adipocytokines.

Methods

Study population and design

Type 2 diabetes mellitus (DM) patients who attended the Diabetes Outpatient Department (OPD) of King Edward (KEM) Hospital, between March and December 2011, and agreed to participate were enrolled. A questionnaire was designed (provided as Supplemental questionnaire 1) to obtain detailed information such as age, gender, period of residence in current home and workplace, diet (non/vegetarian), occupation, tobacco and alcohol usage, physical activity (IPAQ-short form, available at www.ipaq.ki.se), and medical history including treatment, data on possible sources of indoor air pollution, and chronic respiratory symptoms (CRSs), including *chronic cough* (cough or phlegm apart from common cold that has been accruing for at least 3 months of the year for the last 2 years), *dyspnea* also known as shortness of breath (any attack of shortness of breath with wheeze, apart from common colds in the last 12 months), wheezing (a wheeze for at least 6 months of the year, apart from common colds), *chest tightness* (feeling of tightness in the last 12 months in their chest), and allergy (symptoms such as hay fever or any other condition making the nose runny or stuffy, apart from common colds, associated with redness of eyes, itching, burning, and eczema present in most days of the week). We used a standard questionnaire developed by Chest Research Foundation (CRF/22/OT) that has been validated in the Indian community (Brashier et al. 2012). Lung function test was then performed using an ultrasonic spirometer (ndd, Switzerland). The same procedures were conducted in an equal number of willing non-diabetic subjects (NDM) from KEM Hospital staff, matched for gender. All participants were living in their corresponding address for at least 12 months. We have investigated the cross-sectional association between background exposure to PM_{10} and respiratory parameters. The ethics committees at KEM Hospital Research Center approved the study.

Clinical parameters, tools, and procedures

Measurements of height, weight, waist, hip, and chest circumference were collected as per standard protocols. We used NDD Switzerland Diagnostic Easy One spirometry to measure lung function parameters including forced vital capacity (FVC), forced expiratory volume in 1 s (FEV_1), and FEV_1/FVC. The spirometry was performed by a well-trained and certified person using the American Thoracic Society/European Respiratory Society 2005 guideline (Pellegrino et al. 2005). The equipment's calibration was checked on a daily basis.

Reference value and interpretation

We used 90% of European Community for Steel and Coal (ECSC (Quanjer et al. 1993)) value as a reference and adjusted value for gender, age, and height through following equations:

Male

$$FEV_1 = 0.90 \times (-2.490 - 0.0290 \times A + 0.0430 \times H)$$
$$FVC = 0.90 \times (-4.344 - 0.026 \times A + 0.0576 \times H)$$

Female

$$FEV_1 = 0.90 \times (-2.600 - 0.0250 \times A + 0.0395 \times H)$$
$$FVC = 0.90 \times (-2.600 - 0.0250 \times A + 0.0395 \times H)$$

Exposure assessment

Following the Pune Regional Emissions Inventory Study (PREIS), the Ministry of Environment and Forests (MoEF) and the Central Pollution Control Board (CPCB) of India carried out a particulate pollution source apportionment study in Delhi, Kanpur, Chennai, Mumbai, Bangalore, and Pune. As part of the study, an emission inventory was also developed and published in January 2011 (CPCB 2011). The meteorological parameters for the city of Pune during the period of the study were obtained from the National Data Center, Meteorological Department. The location of air pollutant monitors, meteorological department, and KEM Hospital and distribution of diabetic patients in Pune have been published as a supplementary online material elsewhere (Morteza Abdullatif; Khafaie et al. 2013). We used the atmospheric dispersion model, AERMOD (Cimorelli et al. 1998), to estimate background PM_{10} concentration at subject's home and work (PM_{10} at home × time stay at home/24) + (PM_{10} at workplace × time stay at work/24). The emission data were added to the AERMOD along with the on-site meteorological data. Geo-position information (latitude and longitude) on the home location of subjects were obtained online during the examination session with help of subjects, using Google Earth (≈100 m accuracy). This allowed us an estimation of a year exposure to background PM_{10} concentration for the year 2010. The input data files and detail procedure have been explained elsewhere (CPCB 2011; Gaffneya et al. 2007; Morteza Abdullatif; Khafaie et al. 2017; Ojha et al. 2006).

Sample size

We carried out a pilot study and accordingly estimated the minimum sample size required for the current study. Based on the pilot study results correlating subject percent predicted forced vital capacity (observed/predicted value for correspondent age, sex, and height × 100) and ambient PM_{10} concentration ($\mu g/m^3$) at home address, we expected correlation coefficient of $r = -0.10$. With a type I error probability of 5% (alpha = 0.05) and a power of 0.80, a sample of 617 subjects to demonstrate the possible effect is needed. We scheduled 1000 appointments with DM patients visiting the Diabetes Unit, and KEM Hospital's staff, out of which 865 (465 DM and 400 NDM) participated and provided lung function test data. Quality assurance of lung function data showed valid measurement in 762 subjects (n for DM = 347 and NDM = 386). Some subjects (n = 66) also were residing outside Pune, where we could not estimate exposure to PM_{10}. The study eventually included 649 subjects.

Statistical analysis

The data are presented as frequency (%) and mean (±SD). PM_{10} extreme values ($94.08 < PM_{10} < 344.07$) and subjects who resided at their current address for less than 1 year were excluded from the analysis.

We used logistic regression models (logit) to describe the association between residential exposure to air pollution and chronic respiratory symptoms (i.e., chronic cough, dyspnea, wheezing, and tightness) and disease (i.e., COPD and asthma). The results are expressed as exponential of estimated coefficients multiplied with 1 SD = 98.38 $\mu g/m^3$ of PM_{10} concentration (OR = expo [coef. × 98.38]).

We also used multiple linear regression to investigate the association between PM_{10} and lung function parameters. Results of linear association are presented as absolute change in percent predicted PFT for 1 SD $\mu g/m^3$ increment in PM_{10} (absolute change = coef. × 98.38) where coef. = coefficients of association between PM_{10} and measures of lung function.

All models were adjusted for age, gender, body mass index (BMI), diabetes status (presence vs. absence), smoking, and temperature on the day of the blood sample collection (Morteza Abdullatif Khafaie et al. 2016).

To investigate possible effect modification for the association between PM_{10} and percent predicted FVC, conditions such as age (below and above 46 years), gender, BMI (below and above 25), and smoking status, we added an interaction term of indicator variable (above group) and exposure value (i.e., PM_{10}) simultaneously with the main effect terms in main model. The significance threshold of $P = 0.05$ was used in all analyses. All statistical analyses were performed using

STATA version 14.0 software (STATA Corporation, College Station, TX).

Results

Characteristics of the study population

Descriptive characteristics of study population are depicted in Table 1. Of the 865 (n = 465 DM and n = 400 NMD) who agreed to participate, valid lung functions were available for 762 (n = 347 DM and n = 386 NDM). There were no significant differences between the 762 for whom lung function was available and the remaining in terms of age, gender, and BMI.

Diabetic subjects were significantly older than non-diabetic subjects and they had higher BMI and bigger waist-hip ratio (WHR). We also observed that respiratory symptoms (i.e., chronic cough, dyspnea, wheezing, and tightness) and disease (i.e., COPD and asthma) were more prevalent in diabetic subjects than non-diabetic subjects. More than half of the diabetic subject patients were on at least one anti-inflammatory agent such aspirin, statin, or thiazolidinediones (TZD).

Outcome variables

Prevalence of CRSs in the previous 12 months including cough, attacks of shortness of breath, wheezing, allergy

Table 1 Descriptive characteristics of study population

	Diabetic subjects	Non-diabetic subjects	Total
Male	268 (58.00)	241 (60.00)	509 (59.00)
Age (years)*	54.58 (11.11)	36.1 (9.87)	46.03 (14.01)
BMI (kg/m^2)*	26.71 (4.08)	23.17 (4.20)	25.08 (4.49)
Waist-hip ratio*	0.96 (0.10)	0.94 (0.11)	0.97 (0.09)
Sitting height (cm)	146.57 (9.08)	145.61 (13.21)	146.97 (4.66)
FVC (l)*	2.49 (0.52)	2.90 (0.48)	2.69 (0.54)
FEV_1 (l)*	2.02 (0.44)	2.46 (0.41)	2.23 (0.48)
% FEV_1/FVC*	82.03 (6.83)	85.31 (6.51)	83.70 (6.86)
% predicted FVC	85.88 (13.53)	86.79 (13.82)	86.34 (13.68)
% predicted FEV_1	85.87 (14.06)	86.35 (11.92)	86.12 (13.01)
Smoking	34 (7)	39 (10)	73 (8.44)
Tobacco	97 (21)	89 (22)	186 (21.50)
Alcohol	76 (16)	72 (18)	148 (17.21)
Non-vegetarian*	295 (63)	344 (86)	639 (73.87)
Occupation status			
Retired*	155 (39)	0 (0)	155 (20)
Sedentary*	145 (36)	47 (14)	192 (25)
Non-sedentary*	101 (25)	310 (86)	411 (54)
Fuel type			
Natural gas	378 (99)	301 (84)	679 (91)
Kerosene stoves*	51 (13)	111 (31)	162 (21)
Chulha	12 (3)	6 (2)	18 (2)
Wood coal	2 (0)	0 (0)	2 (0)
Pesticide	112 (29)	75 (21)	187 (25)
Carpet*	243 (63)	104 (29)	347 (47)
Dryer	50 (13)	35 (10)	85 (11)
Chronic cough*	51 (11.00)	11 (2.70)	62 (7.17)
Dyspnea*	145 (31.00)	52 (13.00)	197(22.77)
Wheezing*	40 (8.60)	7 (1.70)	47 (5.43)
Tightness*	39 (8.40)	9 (2.20)	48 (5.55)
Allergy symptom	81 (17.40)	31 (7.75)	112 (12.95)
COPD history			
Self*	10 (2.40)	0 (0.00)	10 (1.16)
Family	6 (1.50)	4 (1.00)	10 (1.15)
Asthma history			
Self*	17 (4.20)	3 (0.75)	20 (2.31)
Family*	66 (16.20)	44 (11.00)	110 (12.72)
FPG (mg/dl)	143.73 (53.25)	–	–
2_hPPG (mg/dl)	217.43 (71.29)	–	–
HbA1c (%)	8.85 (2.17)	–	–

Data is shown as n (%) and mean (SD). The difference between groups was tested by t test and chi-squared, as appropriate. The test adjusted for age, gender, and BMI as appropriate. FPG = fasting plasma glucose; 2_hPG = 2 h post meal plasma glucose; HbA1c = hemoglobin A1c; Fuel = types of fuel use for cooking; Pesticide = recent pesticide application; Carpet = floor covered with carpet; Dryer = keeping cloth dryer inside

*Indicates $P < 0.05$

symptoms, and asthma or COPD varied between 3 to 20%. Explanatory variable and CRSs are depicted in Table 1.

Being a diabetic, smoker (both active and passive), woman, having a family history of asthma, consumption of alcohol, exposure to pesticide, and using dryer inside home increased the risk of having chronic respiratory symptoms from 2 to over 38% (Table 2). In addition, age and BMI were also directly and significantly associated with presence of chronic respiratory symptoms. These chronic conditions (i.e., CRSs) in subjects who are physically active or non-sedentary were less prevalent.

Lung function parameters were higher in non-diabetic subjects compared to diabetic patients, even after adjusting for age, gender, and BMI (P value < 0.01). In addition, we found an association between height and lung function; therefore, we additionally adjusted for height for further analysis. In general, better lung functions were found among younger, taller, male subjects and those who had absence of respiratory disease.

The mean percentage predicted value of lung function (PFT%) was similar among diabetic and non-diabetic subjects (P value > 0.05). Overall, 30% had FEV_1 <80, 29% had FVC <80%, and 3% FEV_1/FVC ratio <70% qualifying for "lower than normal." According to ECSC criteria, 1.75% had an obstructive pattern and 28.5% had restrictive pattern of lung function. The percent predicted values were directly associated with sitting height and inversely with air temperature. For instance, we estimated that 10 cm increase in sitting height was associated with about 5% increase in FVC%. In our study, all of those with obstructive lung (n = 12) were diabetic patients. By contrast, restrictive pattern was not predicted by any of factors we investigated.

Association between PM_{10} and chronic respiratory symptoms

Annual mean concentration of PM_{10} at resident place (work and home) of study subjects during year 2010 was 300.48 ± 98.38. Exposure to PM_{10} at residence place (home and work) was associated with presence of chronic cough and dyspnea (Table 3). However, association with cough become non-significant, after excluding subjects residing in area with extreme PM_{10} concentration ($94.08 < PM_{10} < 344.07$).

Association between PM_{10} and lung function

We found that exposure to PM_{10} (at individual home and work location) was inversely associated with FVC% (see Fig. 1). For instance, 1 SD $\mu g/m^3$ increase in PM_{10} exposure was associated with a 3.71% (95% CI, 0.65–6.77) lower FVC%. We did not find any association between PM_{10} and FEV_1% nor with FEV_1/FVC.

Table 2 Determinants of chronic respiratory symptoms in the study population

	Cough n = 62 (7.17%)	Dyspnea n = 197 (22.77%)	Wheeze n = 47 (5.43%)	Allergy sym. n = 112 (12.95)	Tightness n = 48 (5.55%)	Asthma/COPD n = 26 (3.01%)
Female	0.83 (0.52–1.52)	*1.90 (1.51–2.94)*	1.36 (0.75–2.48)	1.09 (0.73–1.64)	0.91 (0.49–1.66)	1.55 (0.70–3.41)
Age	*1.04 (1.01–1.02)*	*1.04 (1.02–1.05)*	*1.04 (1.01–1.06)*	*1.02 (1.01–1.04)*	*1.04 (1.01–1.06)*	*1.04 (1.01–1.07)*
BMI	*1.09 (1.02–1.16)*	*1.10 (1.06–1.14)*	*1.13 (1.06–1.21)*	1.03 (0.98–1.08)	*1.12 (1.05–1.20)*	*1.10 (1.01–1.20)*
Sitting height	1.08 (0.99–1.17)	1.02 (0.97–1.08)	*1.05 (0.95–1.16)*	*1.06 (0.99–1.13)*	*1.01 (0.92–1.11)*	*1.13 (1.01–1.27)*
Diabetes	*3.92 (1.75–8.76)*	*2.36 (1.50–3.73)*	*4.93 (1.88–12.90)*	*2.55 (1.46–4.47)*	*3.41 (1.39–8.35)*	*5.74 (1.43–23.04)*
Cig. smoke exp.	*3.55 (1.77–7.12)*	*2.16 (1.24–3.74)*	2.35 (0.98–5.63)	1.11 (0.54–2.26)	0.71 (0.21–2.38)	0.51 (0.7–3.88)
Tobacco	0.54 (0.26–1.16)	1.47 (0.97–2.23)	0.90 (0.42–1.96)	*0.42 (0.23–0.78)*	0.90 (0.43–1.89)	0.68 (0.22–2.06)
Alcohol	*1.96 (1.01–3.81)*	*1.65 (1.02–2.66)*	2.10 (0.95–4.65)	1.18 (0.99–2.91)	1.59 (0.74–3.41)	2.14 (0.75–6.07)
Non-veg diet	0.97 (0.54–1.75)	0.87 (0.60–1.26)	1.55 (0.75–3.18)	1.47 (0.90–2.42)	1.19 (0.60–2.37)	0.50 (0.22–1.14)
Phys. activity	0.75 (0.41–1.36)	*0.56 (0.39–0.81)*	*0.41 (0.21–0.80)*	1.18 (0.76–1.85)	0.57 (0.30–1.08)	0.82 (0.34–1.99)
Pesticide	*2.84 (1.63–4.94)*	1.09 (0.75–1.61)	1.43 (0.74–2.77)	1.36 (0.87–2.13)	*2.07 (1.11–3.84)*	2.06 (0.91–4.70)
Painting	1.21 (0.89–3.24)	0.83 (0.53–1.35)	1.05 (0.53–2.63)	1.11 (0.85–2.34)	1.22 (0.57–2.61)	1.10 (0.48–3.64)
Air freshener	*8.15 (2.75–24.16)*	1.83 (0.62–5.42)	*8.38 (2.66–26.37)*	2.90 (0.96–8.74)	3.62 (0.97–13.48)	4.32 (0.90–20.69)
Dryer	1.69 (0.82–3.52)	*1.85 (1.14–3.02)*	2.09 (0.96–4.54)	0.84 (0.43–1.64)	1.95 (0.90–4.23)	1.02 (0.30–3.52)
Non-sedentary job	*0.38 (0.17–0.84)*	0.62 (0.38–1.00)	0.58 (0.24–1.44)	*0.49 (0.27–0.92)*	*0.25 (0.10–0.63)*	1.35 (0.39–4.76)
Asthma history	*1.44 (1.10–1.88)*	*1.60 (1.30–1.97)*	1.27 (0.91–1.80)	*1.39 (1.12–1.73)*	*1.55 (1.18–2.04)*	*1.97 (1.46–2.67)*

Cig. smoke exp. = current smoking (occasional and habitual) and passive; Tobacco = current tobacco usage; Alcohol = current alcohol consumption; Non-veg = consuming non-vegetarian food; Phys. activity = those who are physically active; Pesticide = there had been any forms of pesticide application at home; Painting = house painting during the last 12 months; Air freshener = using any forms of air freshener at home; Dryer = keeping clothes dryer inside of home; Asthma history = family history of asthma. All variables are odds ratio (95% CI) and adjusted for age and gender. Italic "OR" are significant at P value < 0.05

Table 3 Association between air pollution (PM_{10}) and chronic respiratory health (i.e., cough and dyspnea). Results are OR for presence of symptoms for 1 SD μg/m^3 increment in PM_{10}

	Cough OR (95% CI)	Dyspnea OR (95% CI)
Model 1	*1.33 (1.02–1.74)*	*1.50 (1.12–2.01)*
Model 2	1.56 (0.95–2.56)	*1.45 (1.07–1.96)*

Model 1 = adjusted for age, gender, BMI, diabetes status, and smoking; excluding subjects residing <11 months in current address. Model 2 = adjusted for age, gender, BMI, diabetes status, and smoking; excluding subjects residing <11 months in current address and 94.08 < PM_{10} < 344.07. All variables are odds ratio (95% CI) and adjusted for age and gender. Italic "OR" are significant at *P* value < 0.05

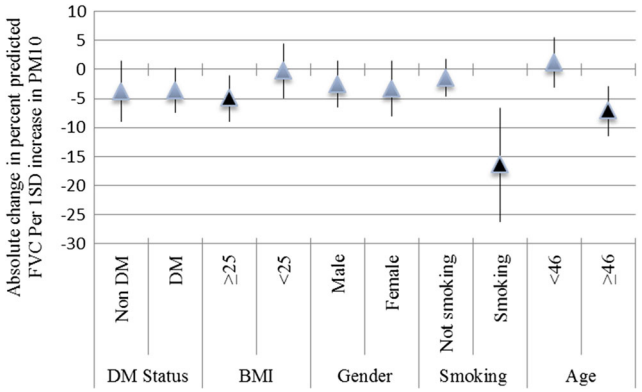

Fig. 2 Modification effects of diabetes status, BMI, gender, smoking, and age on the association between PM_{10} and FVC%. *Error bars* indicate 95% CI. *Black triangles* indicate that associations are significant

Modification effect

We observed enhanced associations between PM_{10} and FVC% among subjects with BMI ≥25, smoker, and subject age ≥46 (see Fig. 2). The interaction terms were also significant. For instance, we observed a 10% greater response to exposure to PM_{10} among smokers as compared to non-smoker subjects.

Discussions

Our study shows that living in an area with high concentration of air pollution, as assessed by the dispersion model, is associated with chronic respiratory problems, evaluated through both subjective (questionnaire) and objective (lung function) methods. In particular, a SD μg/m^3 increment in PM_{10} was associated with about 35 and 50% greater risk for having chronic cough and dyspnea, respectively. Furthermore, we showed that concentration of outdoor PM_{10} was negatively associated with FVC%. The size of the effect on population mean FVC%, expressed for 1 SD (=98.38 μg/m^3) increase in PM_{10}, was about 3.71% (0.65 to 6.77), which is equivalent to ≈108 ml. It is noteworthy to mention that the associations were stronger among older people, current or passive smokers, and those with a BMI ≥25. We did not find any associations between PM_{10} and FEV_1% (nor with FEV_1 /FVC).

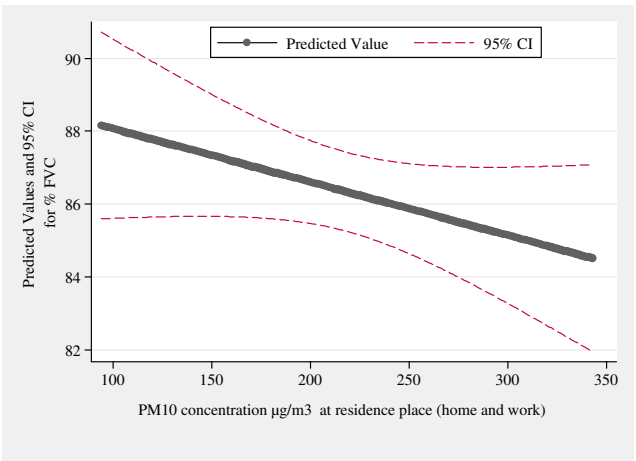

Fig. 1 Association between PM_{10} concentration at residence place during year 2010 and percent predicted FVC (FVC%) among diabetic and non-diabetic subjects in Pune, India

Only a few studies, mainly from developed countries, have investigated the impact of air pollution on lung function in diabetic and non-diabetic adults (Abbey et al. 1998; Ackermann-Liebrich et al. 1997; Chestnut et al. 1991; Forbes et al. 2009; Götschi et al. 2008; Leuenberger 1995; T. Schikowski et al. 2005). In Table 4, we have shown important cross-sectional studies investigating the association between air pollution and lung function (Ackermann-Liebrich et al. 1997; Chestnut et al. 1991; Forbes et al. 2009; Kesavachandran et al. 2013; Leuenberger 1995; Tamara Schikowski et al. 2005).

Our results are consistent with the reported inverse association between air pollution and lung function (Ackermann-Liebrich et al. 1997; Chestnut et al. 1991; Leuenberger 1995; Tamara Schikowski et al. 2005). A national-level US study revealed lower FVC in areas with higher total suspended particles (TSP). This study reported that a 1-SD (=34 μg/m^3) increase in TSP was associated with 2.25% lower FVC. The SAPALDIA study (n = 9651) in Germany (Leuenberger 1995) and Switzerland (Ackermann-Liebrich et al. 1997) reported similar finding of 3.4% decrease in FVC and a 1.6% decrease in FEV_1 per 10 μg/m^3 increment in PM_{10}. The SALIA study (n = 2593 women, mean age = 54.5 years) across seven communities showed that 10 mg/m^3 increment in PM_{10} was associated with 3.4% decrease in FVC.

Our null findings for cross-sectional effects of air pollution on FEV_1 stand in contrast to findings of other studies from Europe and North America (Abbey et al. 1998; Forbes et al. 2009; Tamara Schikowski et al. 2005). The largest cross-sectional study in adults in Europe includes four English surveys conducted between the years 1995 and 2001 (n = 41,329

Table 4 Important cross-sectional studies reported association between long-term exposure to PM_{10} and lung function in adult

Authors-year [ref.]	Place/population	Exposure	Results of exposure
Leuenberger 1995	German/SAPALDIA, n = 9651	Central monitor	CRSs , p) = " : 1 :: *pdgts*11747914811356 − 017 − 9148 − 5*Flba.eps*" Disease , p) = " : 1 :: *pdgts*11747914811356 − 017 − 9148 − 5*Flbb.eps*" FVC , p) = " : 1 :: *pdgts*11747914811356 − 017 − 9148 − 5*Flbc.eps*"
Ackermann-Liebrich et al. 1997	Switzerland/SAPALDIA, n = 9651	Dispersion model	FVC , p) = " : 1 :: *pdgts*11747914811356 − 017 − 9148 − 5*Flbd.eps*"
Chestnut et al. 1991	USA/NHANES I, n ~5000	Central monitors	FVC , p) = " : 1 :: *pdgts*11747914811356 − 017 − 9148 − 5*Flbe.eps*" FEV_1 , p) = " : 1 :: *pdgts*11747914811356 − 017 − 9148 − 5*Flbf.eps*"
Schikowski et al. 2005	Germany/women, n = 4757	Distance from main road	FVC , p) = " : 1 :: *pdgts*11747914811356 − 017 − 9148 − 5*Flbg.eps*" FEV_1 , p) = " : 1 :: *pdgts*11747914811356 − 017 − 9148 − 5*Flbh.eps*" COPD , p) = " : 1 :: *pdgts*11747914811356 − 017 − 9148 − 5*Flbi.eps*"
Forbes et al. 2009	UK, n = 41,329	Dispersion model	FEV_1 , p) = " : 1 :: *pdgts*11747914811356 − 017 − 9148 − 5*Flbj.eps*"
Kesavachandran et al. 2013	India, n = 757	Central monitors	FEV_1 , p) = " : 1 :: *pdgts*11747914811356 − 017 − 9148 − 5*Flbk.eps*" PEFR , p) = " : 1 :: *pdgts*11747914811356 − 017 − 9148 − 5*Flbl.eps*"

subjects >16 years) (Forbes et al. 2009) and showed that a 10 mg/m^3 increase in PM_{10} and NO_2 was associated with a decrease of about 3 and 0.7% in FEV_1, respectively.

A few studies from India have shown relationships between exposure to particulate matter (PM) air pollution, measured at central site, and chronic chough, dyspnea (Kamat and Doshi 1987), and reduced lung function (Kesavachandran et al. 2013; Sharma et al. 2004; Siddique et al. 2010). The Indian studies focused on the association between daily PM concentration and lung function (Kesavachandran et al. 2013; Sharma et al. 2004), and only one study (Siddique et al. 2010) compared lung function parameters in urban and rural school-age children (n = 815, 9–17 years). None of these studies focused on diabetic patients nor used dispersion model as an exposure criterion.

For the first time, we have investigated the long-term effect of background concentration of air pollution on the respiratory health of Indian diabetic and non-diabetic subjects. In our study, we used average concentration of air pollution at subject's location (home and work) as a proxy for environmental exposure. Previous similar studies did not account for subjects' exposure at workplace. In our study, the effect of estimated PM_{10} at home and work address (as an exposure) on FVC% was greater than that of PM_{10} at home alone (Supplemental Figure1). Further, more than 20% of our study population were mainly home-based, suggesting that exposure at workplace has significant effects.

Personal exposure to ambient pollution is influenced by many different factors related to lifestyle habits (i.e., time activity, physical activity, and smoking) and exposure to other air pollution sources (indoor air pollutants). We therefore included the effects of these confounding factors in our analyses (see Supplemental Table 1).

The main strengths of this study are the standard protocols, which already had passed the quality control, and the multifaceted aspects of exposure and outcome collected by means of the questionnaire.

We used recent developments in spatial analysis technology (geographic information systems, modeling capacities, etc.) to derive individual exposure estimates of spatially heterogeneous pollutants, such as traffic exhaust. We selected our subjects from the same area to minimize the effects of environmental confounding. This may explain the discrepancy between our results and those of ECRHS (Götschi et al. 2008). Our study compared across far more homogenous populations than is the case for ECRHS. Our health data could therefore offer the unique inputs to investigate prospective long-term effects of air pollution, as well as the modifying role of local or regional factors across India.

Like any cross-sectional study, residual confounding is still possible (Pirabbasi et al. 2012). However, we adjusted for known and potential confounding factors. We selected our non-diabetic population from hospital staff. This group

showed a stronger association between lung function and air pollution and this may be due to the fact that their location was mainly based in the city center of Pune which has higher levels of air pollution. They were also younger and could therefore possibly spend a greater proportion of their time outdoors. From public health perspective, there is a need to extend follow-up studies in order to quantify the magnitude of the effect of air pollution in lung function decline and to assess the population impact of air pollution and the potential consequences of its reduction.

The dispersion modeling tool, namely AERMOD, was useful to determine the association between air pollution and respiratory health outcomes. Our study suggests that long-term exposure to air pollution was found to be related to pulmonary function and CRSs. However, what exactly drives this association has to be clarified in prospective studies.

Our aim was to investigate possible impact of long-term exposure to air pollution on respiratory parameters (subjective and objective). Our analysis showed that exposure to higher PM_{10} concentration was related with increased risk of chronic cough, dyspnea, and lower FVC% on lung function testing.

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Author contributions M.A.K., S.S.S., and C.S.Y. researched, wrote, discussed, and edited the manuscript. A.A.A and A.O. contributed to the discussion and edited the manuscript. B.K. and S.D.G. contributed to the data analyses and edited the manuscript.

Compliance with ethical standards The ethics committees at KEM Hospital Research Center approved the study.

Conflict of interest The authors declare that they have no conflict of interest.

References

Abbey DE, Burchette RJ, Knutsen SF, McDonnell WF, Lebowitz MD, Enright PL (1998) Long-term particulate and other air pollutants and lung function in nonsmokers. Am J Respir Crit Care Med 158(1): 289–298

Ackermann-Liebrich U, Leuenberger P, Schwartz J, Schindler C, Monn C, Bolognini G et al (1997) Lung function and long term exposure to air pollutants in Switzerland. Study on Air Pollution and Lung Diseases in Adults (SAPALDIA) Team. Am J Respir Crit Care Med 155(1):122–129. doi:10.1164/ajrccm.155.1.9001300

Alexeeff SE, Litonjua AA, Suh H, Sparrow D, Vokonas PS, Schwartz J (2007) Ozone exposure and lung function: effect modified by obesity and airways hyperresponsiveness in the VA normative aging study. Chest 132(6):1890–1897. doi:10.1378/chest.07-1126

Berend N (2016) Contribution of air pollution to COPD and small airway dysfunction. Respirology 21(2):237–244. doi:10.1111/resp.12644

Brashier B, Londhe J, Madas S, Vincent V, Salvi S (2012) Prevalence of self-reported respiratory symptoms, asthma and chronic bronchitis in slum area of a rapidly developing Indian city. Open J Respir Dis 2(03):73

Chestnut LG, Schwartz J, Savitz DA, Burchfiel CM (1991) Pulmonary function and ambient particulate matter: epidemiological evidence from NHANES I. Arch Environ Health 46(3):135–144. doi:10.1080/00039896.1991.9937440

Chung KF (2001) Cytokines in chronic obstructive pulmonary disease. Eur Respir J 18(34 suppl):50s–59s. doi:10.1183/09031936.01.00229701

Cimorelli, A. J., Perry, S. G., Venkatram, A., Weil, J. C., Paine, R. J., & Peters, W. D. (1998). AERMOD–description of model formulation.

CPCB (2011) Air quality monitoring, emission inventory and source apportionment studies for Indian cities. Retrieved Jan 2011 from http://cpcb.nic.in/Source_Apportionment_Studies.php

Ebi-Kryston KL, Hawthorne VM, Rose G, Shipley MJ, Gillis CR, Hole DJ et al (1989) Breathlessness, chronic bronchitis and reduced pulmonary function as predictors of cardiovascular disease mortality among men in England, Scotland and the United States. Int J Epidemiol 18(1):84–88

Forbes LJ, Kapetanakis V, Rudnicka AR, Cook DG, Bush T, Stedman JR et al (2009) Chronic exposure to outdoor air pollution and lung function in adults. Thorax 64(8):657–663. doi:10.1136/thx.2008.109389

Gaffneya P, MacDonaldb T, Benjaminc M, Cored J, & Ojhae A (2007) India PM10 emission inventory training and capacity building programs: EPA efforts for developing a sustainable foundation. California: Envirnonment Protection Agency.

Ghanavati T, Shaterzadeh Yazdi MJ, Goharpey S, Arastoo AA (2012) Functional balance in elderly with diabetic neuropathy. Diabetes Res Clin Pract 96(1):24–28. doi:10.1016/j.diabres.2011.10.041

Glaser S, Kruger S, Merkel M, Bramlage P, Herth FJ (2015) Chronic obstructive pulmonary disease and diabetes mellitus: a systematic review of the literature. Respiration 89(3):253–264. doi:10.1159/000369863

Gomez-Mejiba SE, Zhai Z, Akram H, Pye QN, Hensley K, Kurien BT et al (2009) Inhalation of environmental stressors & chronic inflammation: autoimmunity and neurodegeneration. Mutat Res 674(1–2): 62–72. doi:10.1016/j.mrgentox.2008.09.016

Götschi T, Sunyer J, Chinn S, de Marco R, Forsberg B, Gauderman JW et al (2008) Air pollution and lung function in the European Community Respiratory Health Survey. Int J Epidemiol 37(6): 1349–1358

Gregg EW, Sattar N, Ali MK (2016) The changing face of diabetes complications. Lancet Diabetes Endocrinol 4(6):537–547. doi:10.1016/S2213-8587(16)30010-9

Happo MS, Salonen RO, Halinen AI, Jalava PI, Pennanen AS, Dormans JA et al (2010) Inflammation and tissue damage in mouse lung by single and repeated dosing of urban air coarse and fine particles collected from six European cities. Inhal Toxicol 22(5):402–416. doi:10.3109/08958370903527908

Kamat S, Doshi V (1987) Sequential health effect study in relation to air pollution in Bombay, India. Eur J Epidemiol 3(3):265–277

Kesavachandran C, Pangtey B, Bihari V, Fareed M, Pathak M, Srivastava A, Mathur N (2013) Particulate matter concentration in ambient air and its effects on lung functions among residents in the National Capital Region, India. Environ Monit Assess 185(2):1265–1272

Khafaie MA, Salvi SS, Ojha A, Khafaie B, Gore SD, Yajnik CS (2013) Systemic inflammation (C-reactive protein) in type 2 diabetic patients is associated with ambient air pollution in Pune City, India. Diabetes Care 36(3):625–630. doi:10.2337/dc12-0388

Khafaie MA, Yajnik C, Mojadam M, Khafaie B, Salvi SS, Ojha A, Gore SS (2016) Association between ambient temperature and blood

biomarker of systemic inflammation in (C-reactive protien) in diabetes patients. Arch Med 8:3

Khafaie MA, Yajnik CS, Salvi SS, Ojha A, Khafaie B, & Gore SD (2017) Particulate matter and markers of glycemic control, insulin resistance and β-cell function in type 2 diabetic patients: result from Wellcome Trust Genetic study. Manuscript submitted for publication.

Lancet (2016) Beat diabetes: an urgent call for global action. Lancet 387(10027):1483. doi:10.1016/S0140-6736(16)30185-4

Leuenberger P (1995) Air pollution in Switzerland and respiratory diseases in adults. Results of a preliminary study of the cross-sectional part of the Sapaldia study. Praxis (Bern 1994) 84(40):1096–1100

Li N, Wang M, Oberley TD, Sempf JM, Nel AE (2002) Comparison of the pro-oxidative and proinflammatory effects of organic diesel exhaust particle chemicals in bronchial epithelial cells and macrophages. J Immunol 169(8):4531–4541

López-Campos JL, Ruiz-Ramos M, Soriano JB (2014) Mortality trends in chronic obstructive pulmonary disease in Europe, 1994–2010: a joinpoint regression analysis. Lancet Respir Med 2(1):54–62 doi: http://dx.doi.org/10.1016/S2213-2600(13)70232-7

Nicole W (2015) Air pollution and diabetes risk: assessing the evidence to date. Environ Health Perspect 123(5):A134. doi:10.1289/ehp.123-A134

Ojha A, Kumar R, Boralkar D, Gargava P, Gaffeney P, Benjamin M, & Mukkannawar U (2006) Continual improvement of emission estimates–the Pune experience (2004 to 2006). Paper presented at the Better Air Quality 2006, Yogyakarta, Indonesia.

O'Neill MS, Veves A, Zanobetti A, Sarnat JA, Gold DR, Economides PA et al (2005) Diabetes enhances vulnerability to particulate air pollution-associated impairment in vascular reactivity and endothelial function. Circulation 111(22):2913–2920. doi:10.1161/circulationaha.104.517110

Pellegrino R, Viegi G, Brusasco V, Crapo RO, Burgos F, Casaburi R et al (2005) Interpretative strategies for lung function tests. Eur Respir J 26(5):948–968. doi:10.1183/09031936.05.00035205

Pirabbasi E, Najafiyan M, Cheraghi M, Shahar S, Abdul Manaf Z, Rajab N, Abdul Manap R (2012) What are the antioxidant status predictors' factors among male chronic obstructive pulmonary disease (COPD) patients? Glob J Health Sci 5(1):70–78. doi:10.5539/gjhs.v5n1p70

Quanjer PH, Tammeling GJ, Cotes JE, Pedersen OF, Peslin R, Yernault JC (1993) Lung volumes and forced ventilatory flows. Report Working Party Standardization of Lung Function Tests, European Community for Steel and Coal. Official Statement of the European Respiratory Society. Eur Respir J Suppl 16:5–40

Rogliani P, Lucà G, Lauro D (2015) Chronic obstructive pulmonary disease and diabetes. COPD Res Pract 1(1):1–9. doi:10.1186/s40749-015-0005-y

Schikowski T, Sugiri D, Ranft U, Gehring U, Heinrich J, Wichmann HE, Kramer U (2005) Long-term air pollution exposure and living close to busy roads are associated with COPD in women. Respir Res 6:152. doi:10.1186/1465-9921-6-152

Sharma M, Kumar VN, Katiyar SK, Sharma R, Shukla BP, Sengupta B (2004) Effects of particulate air pollution on the respiratory health of subjects who live in three areas in Kanpur, India. Arch Environ Health: An Int J 59(7):348–358

Siddique S, Banerjee M, Ray MR, Lahiri T (2010) Air pollution and its impact on lung function of children in Delhi, the capital city of India. Water Air Soil Pollut 212(1–4):89–100

Sinden NJ, Stockley RA (2010) Systemic inflammation and comorbidity in COPD: a result of 'overspill' of inflammatory mediators from the lungs? Review of the evidence. Thorax 65(10):930–936. doi:10.1136/thx.2009.130260

van der Wall EE (2015) Air pollution: 6.6 million premature deaths in 2050! Neth Heart J 23(12):557–558. doi:10.1007/s12471-015-0763-9

Weinmayr G, Hennig F, Fuks K, Nonnemacher M, Jakobs H, Mohlenkamp S et al (2016) Erratum to: Long-term exposure to fine particulate matter and incidence of type 2 diabetes mellitus in a cohort study: effects of total and traffic-specific air pollution. Environ Health 15:45. doi:10.1186/s12940-016-0128-x

Yajnik CS, Joglekar CV, Lubree HG, Rege SS, Naik SS, Bhat DS et al (2008) Adiposity, inflammation and hyperglycaemia in rural and urban Indian men: Coronary Risk of Insulin Sensitivity in Indian Subjects (CRISIS) Study. Diabetologia 51(1):39–46. doi:10.1007/s00125-007-0847-1