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Air Pollution and Incidence of Hypertension and Diabetes in African American Women Living in Los Angeles

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Abstract

Background—Evidence suggests that longer-term exposure to air pollutants over years confers higher risks of cardiovascular morbidity and mortality than shorter term exposure. One explanation is that cumulative adverse effects that develop over longer durations lead to the genesis of chronic disease. Preliminary epidemiological and clinical evidence suggest that air pollution may contribute to the development hypertension and type 2 diabetes.

Methods and Results—We used Cox proportional hazards models to assess incidence rate ratios (IRRs) and 95% confidence intervals (CI) for incident hypertension and diabetes associated with exposure to fine particulate matter ($PM_{2.5}$) and nitrogen oxides (NOx) in a cohort of African American women living in Los Angeles. Pollutant levels were estimated at participant residential addresses with land use regression models (NOx) and interpolation from monitoring station measurements ($PM_{2.5}$). Over follow-up from 1995-2005, 531 incident cases of hypertension and 183 incident cases of diabetes occurred. When pollutants were analyzed separately, the IRR for hypertension for a 10 $\mu g/m^3$ increase in $PM_{2.5}$ was 1.48 (95% CI 0.95-2.31) and the IRR for the interquartile range (12.4 parts per billion) of NOx was 1.14 (95% CI 1.03-1.25). The corresponding IRRs for diabetes were 1.63 (95% CI 0.78-3.44) and 1.25 (95% CI 1.07-1.46). When both pollutants were included in the same model, the IRRs for $PM_{2.5}$ were attenuated and the IRRs for NOx were essentially unchanged for both outcomes.

Conclusions—Our results suggest that exposure to air pollutants, especially traffic-related pollutants, may increase the risk of type 2 diabetes and possibly of hypertension.

Keywords

air pollution; epidemiology; diabetes mellitus; hypertension

Hundreds of epidemiological studies have established associations between exposure to air pollutants and increased risks of acute cardiovascular events, including fatal and nonfatal

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heart attack and stroke.[1-3] The overall evidence also suggests that longer-term exposure over years confers higher risks than does shorter-term exposure.[2] One explanation is that there are cumulative adverse health effects during longer durations that lead to the genesis of chronic diseases. In particular, given the potential for air pollutants to promote inflammation, oxidative stress, and endothelial dysfunction, it has been suggested that air pollution may contribute to two chronic conditions that are major risk factors for acute cardiovascular events, hypertension and diabetes.[2]Preliminary evidence supports the plausibility of this hypothesis. Animal[4, 5] and human[6, 7] studies have shown that air pollutant exposure is associated with another chronic condition, atherosclerosis, and both particulate matter and NO_2 have been shown to elevate blood pressure[8-11] and to increase fasting glucose levels.[12]

Associations between air pollutants and hypertension[13] and diabetes[14] prevalence have been reported in cross-sectional studies. Only two studies have assessed diabetes incidence.[15,16] In a German study, the risk of incident diabetes over 16 years of follow-up increased from15 to 42% per interquartile range of long-term traffic-related exposures including particulate matter and NO_2.[15]In the Nurses' Health Study, incident diabetes had little association with particulate matter, but living within 50 meters of a major road was associated with an 11% increase in incidence.[16]

Even a modest effect of air pollutants on the risks of hypertension and diabetes will have significant public health impact due to their high incidence and the ubiquity of exposure.[17-19]This issue is of particular importance for African American women because the incidence of both hypertension and diabetes is almost twice as high in African American women as in white women[20, 21] and African Americans experience higher levels of air pollution than do white Americans.[22]We assessed the risks of incident hypertension and diabetes associated with exposure to fine particulate matter with aerodynamic diameter of ≤2.5 μm in diameter ($PM_{2.5}$) and to nitrogen oxides (NOx), a marker of traffic-related air pollution, in a cohort of African American women living in Los Angeles.

Methods

Study population

The women included in the present analyses are participants in the Black Women's Health Study (BWHS), a prospective cohort study of black women. The BWHS was established in 1995 when approximately 59,000 African-American women aged 21 through 69 years were recruited mainly from subscribers to Essence magazine. The baseline questionnaire elicited information on demographic and lifestyle factors, reproductive history, dietary intake, and medical conditions. The cohort is followed biennially by mailed questionnaire and follow-up has averaged over 80% of the original cohort through seven questionnaire cycles. The study protocol was approved by the Institutional Review Board of Boston University. Participants indicate informed consent by completing the questionnaires.

The analytic cohorts for the present analyses were derived from 10 years of follow-up (1995-2005) of 4204 women who lived in Los Angeles at baseline in 1995. The hypertension cohort included 3236 women who were free of hypertension at baseline in 1995; the diabetes cohort included 3992 women who were free of diabetes at baseline. Mean follow-up time in both cohorts was 10 years.

Case ascertainment

Hypertension—We defined an incident case of hypertension as self-report of doctor-diagnosed hypertension during follow-up through 2005 and concurrent use of

antihypertensive medications. We assessed the accuracy of self-reported hypertension among 139 participants who met these criteria for whom we were able to obtain medical records or physician checklists; hypertension was confirmed in 99%, with all systolic pressures being 140 mmHg or higher and diastolic pressures being 90 mm Hg or higher. [23]

Diabetes—We defined an incident case of type 2 diabetes as self-report of doctor-diagnosed diabetes at age 30 or older during follow-up through 2005. Among 227 participants who met the definition of diabetes and whose physicians provided data from their medical records, the diagnosis of type 2 diabetes was confirmed in 96%.

Environmental Exposure Assessment—*$PM_{2.5}$*.To estimate $PM_{2.5}$ exposure, we interpolated from 23 state and local district monitoring stations in the Los Angeles basin for the year 2000 with a kriging model. We used a universal kriging algorithm that allowed for the assignment of long-term mean ambient $PM_{2.5}$concentrations to the ZIP code area of each participant's residential address. Further detail is given elsewhere.[7, 24] Comparison of $PM_{2.5}$ values estimated from the model with monitored concentrations for the Los Angeles region showed that >50% of the area had estimated values within 15% of monitored concentrations and 67% were within 20%.[7]

NOx. We used a land use regression model to estimate mean annual NOx (parts per billion (ppb)) levels at participant residential addresses. Methods are described in detail elsewhere.[25]In brief, the model was based on field measurements at 183 locations in Los Angeles. The measurements were obtained in both the summer and winter seasons for two-week periods closest to the seasonal mean. These measurements were averaged to represent the annual mean for 2006.The measurements then were used as the dependent variable in a spatial land use regression model with traffic, land use, population and physical geography as predictors of pollution levels. The model was highly predictive; the R^2 between the field measured and predicted pollutant level was 85%.[25]Sixteen measurements were chosen at random to use as cross-validation sites, leaving 167 for the analysis. Cross-validation with the 16 sites not used in model calibration indicated excellent model performance with R^2 ~ 92%.

Noise—Noise levels were estimated at participant addresses using the Federal Highway Adminstration's Traffic Noise Model, which has been validated against field measurements in San Francisco.[26] The model computes hourly noise levels based on traffic volumes and noise emissions rates for various classes of vehicles and then compiles the measures into a 24-hour weighted measure in units of decibels (dB). We modeled noise as a binary measure (<70 dB, ≥70 dB), since 70 dB is the level at which annoyance from traffic noise is considerable.[27]This level is also consistent with significant adverse effects on blood pressure and ischemic heart disease.[28]

Covariate Assessment—Height and weight were obtained at baseline in 1995 and weight was updated on each follow-up questionnaire. Smoking and alcohol consumption were obtained at baseline and also updated biennially. Information on household income and family size supported by that income were obtained in 2003. Educational attainment was obtained at baseline. Residential addresses from 1995 to 2003 were linked to 2000 US Census data at the block group level. Using principal components analysis, we created a neighborhood socioeconomic status (SES) score that included six census variables (median household income; median housing value; percent of households receiving interest, dividend or net rental income; percent of adults aged ≥25 years that have completed college; percent of employed persons aged ≥16 years in managerial, executive, or professional occupations; and percent of families with children not headed by a single female). Regression coefficients

from the factor analysis were used to weight the variables for a combined neighborhood score, with higher scores indicating higher neighborhood SES.

Statistical Analyses—We used Cox proportional hazards models to estimate incidence rate ratios (IRRs) and 95% confidence intervals (CI) associated with the interquartile range (IQR) of NOx and with a 10 $\mu g/m^3$ increase in $PM_{2.5}$. The IQR of NOx and 10 unit increase in $PM_{2.5}$ were chosen to capture the greatest variation in the pollutants' respective distributions. Person-time was calculated from the start of follow-up in 1995 until the occurrence of hypertension or diabetes, loss to follow-up, moving from the study area, death, or end of follow-up, whichever happened first.

IRRs for both hypertension and diabetes were adjusted for age, body mass index (weight in $kg/height^2$ in m), years of education, household income, number of people supported by the household income, smoking status, alcohol consumption, hours per week of vigorous exercise, and neighborhood SES score. IRRs for hypertension were additionally adjusted for neighborhood noise level (<70, ≥70 dB) and IRRs for diabetes were additionally adjusted for family history of diabetes. Air pollutant exposures and all covariates with the exception of education, household income, and number of people supported by the income, were time-varying.

We analyzed the pollutants separately and also included them in models together. We tested for interaction between the two pollutants for both outcomes, and for the interaction of noise with both pollutants in the hypertension analysis, by including interaction terms in the models. All analyses were conducted using the statistical analysis program R version 2.9.2.

Results

The mean annual average of $PM_{2.5}$in the study area was 20.7 $\mu g/m^3$ (SD, 2.10); the 25^{th}, 50^{th}, and 75^{th} percentiles were 20.3, 21.1, and 21.6 $\mu g/m^3$, respectively. The mean annual average of NOxwas 43.3 ppb (SD 11.0), and the 25^{th}, 50^{th}, and 75^{th} percentiles were 36.9, 41.6, and 49.2 ppb. The correlation coefficient for the two air pollutants was 0.27 ($p<.0001$).

Table 1 shows the distribution of baseline participant characteristics in the highest and lowest quartiles of the pollutant measures. Higher levels of pollutants were associated with lower levels of education, household income, neighborhood SES, and vigorous exercise. Higher levels were also positively associated with body mass index and smoking.

Over the 10 year follow-up period, 531 incident cases of hypertension and 183 cases of diabetes occurred among women at risk in 1995. Inmodels that considered the pollutants separately, the IRR was 1.48 (95% CI 0.95-2.31)for hypertension associated with a 10 unit increase in $PM_{2.5}$ and 1.14 (95% CI 1.03-1.25) for the IQR of NOx (12.4 ppb) (Table 2). When the two pollutants were modeled together, the IRR for $PM_{2.5}$ was attenuated and the IRR for NO_X did not materially change (Table 2). In single pollutant models, the IRR was 1.63 (95% CI 0.78-3.44) for diabetes associated with $PM_{2.5}$ and 1.25 (95% CI 1.07-1.46) for NOx. When the pollutants were considered together, the IRR for $PM_{2.5}$ was much diminished, and the IRR for NOx was essentially unchanged.

There was no evidence of statistical interaction between the two pollutants for either outcome. In the hypertension analysis, there was no evidence of interaction of the pollutants with noise.

Discussion

In this population of African American women in Los Angeles, exposure to NOx was associated with a statistically significant increased incidence of type 2diabetes both before and after control for effects of $PM_{2.5}$. NOx exposure also significantly increased the incidence of hypertension, although the association became marginally significant after control for $PM_{2.5}$. On the other hand, $PM_{2.5}$ was associated with nonsignificant increases in incident hypertension and diabetes before control for NOx and the associations became weaker after control for NOx. Two previous studies have assessed associations of incident type 2diabetes with air pollutants. Results from the first, the German SALIA study, were consistent with the present results in that stronger associations were found with an indicator of traffic-related pollutants, NO_2, than with particulate matter.[15] The study, conducted in the highly polluted Ruhr district, identified 87 self-reported cases of diabetes among 1775 women aged 54-55 from 1990 to 2006.Results varied according to the method used to estimate the pollutants. The highest IRR (1.42, 95% CI 1.16-1.73) was observed for the IQR of NO_2 (15 $\mu g/m^3$or about 30 ppb) estimated from a land use regression model, similar to the model used in the present study. The IRR per IQR of $PM_{2.5}$ absorbance (soot) estimated with the land use regression model was 1.27 (95% CI 1.09-1.48). The estimates were adjusted for age, body mass index, education, smoking, and indicators of indoor pollutant exposures. In the Ruhr district, NO_2 is primarily from traffic whereas soot reflects both traffic and industrial sources. Thus the results suggest that traffic-related pollutants may be the exposure responsible for the increased diabetes incidence.[15]

The second study of type 2 diabetes incidence assessed associations with several metrics of particulate matter in 23 years of follow-up in the Nurses' Health Study (3794 cases) and the Health Professionals Follow-up Study (688 cases).[16]Relative risks were adjusted for several diabetes risk factors including body mass index, physical activity, and diet. There was little evidence of an association with $PM_{2.5}$ or two other classes of particulate matter, with relative risks from ranging 1.00 to 1.07 per IQR (4 $\mu g/m^3$). The associations were stronger when analyses were restricted to the final 2 years of follow-up: the relative risk per IQR of $PM_{2.5}$ was 1.21 (95% CI 1.00-1.46) in the Nurses' Health Study and 1.52 (95% CI 0.93-2.47) in the Health Professionals Follow-up Study. For a simpler exposure metric, living within 50 meters of a major road compared to 200 or more meters away, the IRR in the Nurses' Health Study was 1.14 (95% CI 1.03-1.27). The SALIA study also found an increased IRR for women living within 100 meters of a major roadway, but only for those with a low level of education.[15]

Two studies have shown associations between diabetes prevalence and NO_2.[29, 30] In addition, two studies have shown effects of air pollutants on indicators of insulin resistance in humans.[12, 31]Ina Taiwanese study of older adults, fasting glucose and glycosylated hemoglobin (HbA1c) increased significantly per IQR increases in $PM_{2.5}$ and NO_2.[12] In a study of Iranian children aged 10-18 years, levels of PM_{10} were positively associated with insulin resistance but NO_2 was not.[31]

There have been no previous studies of air pollution and incident hypertension. The SALIA study reported that the “adjusted association” with prevalent hypertension was1.09 (95% CI 0.93-1.27) per IQR of NO_2 but no details of the analysis were given.[15]In cross-sectional analyses of National Health Interview Survey data, the odds ratios for self-reported prevalent hypertension associated with a 10 $\mu g/m^3$ increase in $PM_{2.5}$ were 1.05 (95% CI 1.04-1.17) among white and 0.90 (95% CI 0.79-1.03) among black participants.[13] Many observational studies[2] and controlled experiments[32-36] demonstrate that present-day levels of particulate matter are capable of elevating blood pressure. For example, the most recent study, from Taiwan, found significant increases of ~30 mm Hg in both systolic and diastolic

blood pressure associated with the IQR of one year averaged $PM_{2.5}$ (IQR=20.4 μg/m3) and of ~12 mm Hg with the IQR of NO_2 (IQR=12.8 ppb).[12] Other data show blood pressure increases of smaller magnitude associated with $PM_{2.5}$ averaged over shorter time periods (2-120 days).[8, 10, 37]Several studies have also reported that traffic-related pollutants including $NO_2$are capable of elevating blood pressure.[9, 38, 39]

There are plausible mechanisms by which particulate matter could contribute to the development of hypertension and diabetes, include the production of systemic inflammation, oxidative stress, and the triggering of autonomic nervous system imbalance.[40] Oxidative stress, which plays an important role in the genesis of insulin resistance,[41] has been induced in animals and humans by $PM_{2.5}$ exposure.[42] In a rodent model, $PM_{2.5}$ exposure led to insulin resistance, alterations in adipokines, and systemic inflammation.[43] In addition, particulate matter is a well-known trigger of autonomic nervous system imbalance which can promotevasoconstriction.[1] Vasoconstriction, which has been demonstrated after concentrated particulate matter exposure in humans,[44] contributes to hypertension and can reduce insulin sensitivity.[45, 46] The endothelial dysfunction that can occur after particulate matter exposure[47] can also promote arterial vasoconstriction. Other pathways are theoretically possible, including a systemic stress response, increased levels and/or bioactivity of other circulating vaso-active mediators,[48] and the translocation of soluble particle constituents into the systemic circulation.[40]

Though a direct effect of NO_2, a major constituent of NOx, cannot be ruled out, it is most plausible that the association with diabetes and hypertension is due to the fact that NOx is a marker of traffic-related air pollution exposure. Recent studies do not support a direct adverse vascular effect of gaseous NOx,[49] but rather suggest that diesel exhaust-related adverse cardiovascular effects are likely mediated by the high numbers of fine and ultrafine particulate matter.[35]

Our study contributes the first data on the relation of air pollution to incident hypertension, and is the first study of incident diabetes in a large population of African American women. We adjusted for a number of potentially confounding variables at the individual and neighborhood level. Although diabetes and hypertension were self-reported, validation studies demonstrated a high degree of accuracy of reporting. A limitation of the study is that it was not feasible to identify undiagnosed cases of hypertension and diabetes in the cohort. However, more than 90% of BWHS participants report having health insurance and having seen a physician in the previous two years which would be expected to minimize undiagnosed hypertension and diabetes. To estimate the effect of undiagnosed hypertension on the incidence rate ratios, we conducted sensitivity analyses using simulation methods under assumptions of nondifferential and differential misclassification. Under the scenario that 15% of the cohort had undiagnosed hypertension, the IRR estimates for $PM_{2.5}$ and NOx were changed by less than 10% for both types of misclassification. Since the rate of undiagnosed diabetes is far lower than that of hypertension (at most, 5%), effects on the IRRs for diabetes would be even less.[50]

With respect to the measurement of pollution exposure, we had excellent exposure assessment, based on nearly 200 monitoring sites. The very high R^2 (85%) between the NOx values estimated from the land use models and the monitored measurements indicates a higher power of prediction than the majority of previously developed land use models.[25]$PM_{2.5}$ models had data support from 23 government monitoring stations, and the kriging methods of interpolation may have oversmoothed the pollution surface and introduced relatively more exposure error than in the NOx model. The significant results for NOx may reflect the higher precision of the NOx estimates compared to the $PM_{2.5}$ estimates. A limitation is that pollutant exposures were assessed for only one year (2000 for

$PM_{2.5}$ and 2006 for NOx) and assigned to all years of follow-up. We expect this to introduce minimal measurement error because studies have shown that the spatial pattern of air pollution levels has remained stable over time.[24] Another limitation was that pollutant exposures were assigned to residential addresses only, not work addresses. Time activity studies show that Americans spend on average approximately 68% of their time at home.[51]On the other hand, we had addresses at each two year questionnaire cycle so that air pollution exposure changed to reflect the change of address of women who moved within the study area during follow-up.

In conclusion, our results suggest that exposure to air pollutants, especially traffic-related pollutants, may increase the risk of type 2 diabetes. The results for hypertension were weaker but may signal an association with the pollutants. Increased risks of diabetes and possibly hypertension could be a mechanism by which air pollution increases the risks of acute cardiovascular effects.

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Table 1

Baseline characteristics of study population in highest and lowest quartiles of PM2.5 and NOx

	Quartile of $PM_{2.5}$		Quartile of NOx	
	Lowest	**Highest**	**Lowest**	**Highest**
Mean of characteristic (SD)				
Age	38.5 (10.5)	40.2 (10.9)	41.1 (11.0)	39.0 (10.9)
Body mass index	26.9 (6.2)	28.0 (6.9)	26.7 (6.1)	27.8 (6.9)
Noise (dB)	62.7 (4.4)	62.8 (4.3)	61.1 (3.7)	64.6 (4.4)
% with characteristic				
Highest quartile neighborhood SES score	25.9	17.1	48.3	11.7
College graduate	44.2	37.9	55.8	38.0
Income >$100,000 in 2003	22.4	17.0	27.4	17.8
Current drinker	28.7	28.1	30.3	28.0
Current smoker	12.7	15.0	10.7	15.3
≥3 hrs/day vigorous exercise	33.1	28.8	31.9	28.8

Table 2

IRRs for hypertension and diabetes associated with 10 unit increase in PM2.5 and interquartile range increase of NOx

	IRR (95% CI) Pollutants modeled separately	IRR (95% CI) Pollutants modeled together
HYPERTENSION*		
$PM_{2.5}$	1.48 (0.95-2.31)	1.32 (0.84-2.05)
NOx	1.14 (1.03-1.25)	1.11 (1.00-1.23)
DIABETES†		
$PM_{2.5}$	1.63 (0.78-3.44)	1.15 (0.51-2.58)
NOx	1.25 (1.07-1.46)	1.24 (1.05-1.45)

IRRs adjusted for age (continuous), body mass index (weight in kg/height in m2) (<25, 25-29, 30+), years of education (≤12, 13-15, 16+), income (<$25,000, $25,001- $50,000, $50,001-$100,000, >$100,000), number of people in the household (1,2,3,4,5+), smoking (nonsmoker, <25/day, 25+/day), drinks per week (<1, 1-6, 7-13, 14+), hours per week of vigorous physical activity (<1, 1-4, 5+), and neighborhood SES score in quintiles. Hypertension additionally adjusted for neighborhood noise (<70dB, ≥70 dB). Diabetes additionally adjusted for family history of diabetes.

* 531 cases/25,318 person-years

† 183 cases/33,657 person-years