AMBient AIR POLLUTION AND DAILY EMERGENCY DEPARTMENT VISITS FOR ISCHEMIC STROKE IN EDMONTON, CANADA

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Abstract
Objectives: In this report, we examine the associations between emergency department (ED) visits for acute ischemic stroke and environmental conditions. Materials and Methods: The study concerned 10,881 ED visits for acute ischemic stroke (ICD-9: 434, 436) recorded at Edmonton hospitals between 1992 and 2002. Generalized linear mixed models technique was applied to build the statistical models. The logarithm of daily counts of ED visits for stroke was regressed on the levels of air pollutants (CO, NO$_2$, SO$_2$, and O$_3$) and two meteorological variables. The analyses were performed by (a) age: two age groups were distinguished: 20–64 years (n = 2873) and 65–100 years (n = 8008); (b) season (all seasons: January–December, warm: April–September, cold: October–March); and (c) gender (both, male, female). Results: The results are reported as an excess risk in relation to an increase in the interquartile range (IQR) of the pollutants. In the age group 65–100 years, the excess risk for particular pollutants was as follows: for NO$_2$ — 8.2% (95% CI: 0.4–16.7) for both genders, in the warm season; for SO$_2$ — 9.1% (95% CI: 2.2–16.4), for males, in the warm season: for a 1-day lagged SO$_2$ — 6.0% (95% CI: 0.5–11.8), for females, in the cold season. Among the patients aged 20–64 years, the excess risk for NO$_2$ was 6.3% (95% CI: 0.2–12.8), for both genders, and all seasons; and 13.8% (95% CI: 2.1–26.7), for females, in the cold season; for a 1-day lagged O$_3$ — 17.8% (95% CI: 2.2–35.6), for males, in the warm season; for a 1-day lagged SO$_2$ — 10.3% (95% CI: 0.7–20.9) for females, in the cold season. Conclusions: The findings provide evidence that exposure to air pollutants is significantly associated with ED visits for acute ischemic stroke.

Key words: Air pollution, Emergency department visit, Acute ischemic stroke, Risk, Temperature, Relative humidity

INTRODUCTION
Stroke is characterized by a sudden disruption in blood supply to the brain. Stroke is the third leading cause of death in the developed countries. It is also a common cause of hospitalization. Although stroke is often considered a disease of the elderly persons, 25% of strokes occur in persons below 65 years of age. About 25% of sufferers die as a result of the stroke or its complications, and almost 50% have moderate to severe health impairments and long-term disabilities. Only 26% recover most or all normal health and life functions. In Canada, the public health burden associated with stroke is considerable and about 16,000 Canadians are estimated to die from stroke every year [1]. Ischemic stroke occurs when an artery leading to or within the brain is blocked. It results from the formation of a clot (thrombus) and an impaired blood supply to the brain tissue. Ischemic stroke is by far the most common kind of stroke, accounting for approximately 88% of all strokes. Stroke can affect persons of all ages, including children. As the risk of this condition increases with age, many persons experience ischemic stroke at the age of about 65 years or more. Stroke is generally more common in men than women. Usually, the persons with stroke have other problems or conditions that still increase their risk for stroke,
these including high blood pressure (hypertension), heart disease, inappropriate diet, smoking, diabetes, obesity, lipid disease, and lack of or insufficient physical exercise [1,2]. The non-modifiable risk factors are increasing age, male sex, heredity and ethnicity.

Clarifying the role that air pollution plays in stroke etiology is an important undertaking [3]. There are several biological arguments that link exposure to air pollution to the stroke. According to one of them, air pollution may provoke alveolar inflammation and, consequently, increase blood coagulation and plasma viscosity, or alter the heart rate. Unlike most of the risk factors for stroke, ambient air pollution belongs to the potentially modifiable factors. In the last decade, the literature has provided compelling evidence on the association of ambient air pollution with stroke mortality [4,5]. The published reports have also evaluated associations between air pollution and hospitalization for stroke [6–11] or emergency department (ED) visits for stroke [12]. This study is based on 10 years’ daily summarized counts of ED visits for acute ischemic stroke. Such parameters as exposure to air pollutants and meteorological factors were considered. ED data were linked to the concentrations of ambient air pollutants and weather variables. We constructed models for CO, NO₂, SO₂, and O₃. Particulate matter data were only available from 1998 onwards. We did not include the results (all negative) for airborne particulates. The purpose of this study was to verify a hypothesis that exposure to ambient air pollutants may be associated with ED visits for acute ischemic stroke.

MATERIALS AND METHODS

Study population
In our study, we used ED data recorded at Edmonton hospitals, Canada. Data on ED visits were supplied by the Capital Health academic system for all the five Edmonton area hospitals. The data covered the period between April 1, 1992 and March 31, 2002. The study population consisted of the patients serviced at these emergency departments. Emergency department visits were identified based on a discharge diagnosis of acute ischemic stroke using the International Classification for Diseases, 9th Revision (ICD-9), rubric 434 and 436 [13]. In total, the analysis was based on 10 881 ED visits for ischemic stroke over a span of 3 652 days. The ED visits for stroke made up approx. 0.4% of all the recorded and diagnosed ED visits to these hospitals (n = 2 951 878) over the study period.

Environmental data
Environment Canada supplied hourly data for selected weather variables: relative humidity, temperature (dry bulb) and atmospheric pressure (sea level). In our study, we created a daily average of 24 measurements for these variables. Relative humidity and temperature were included as confounders in the statistical models.

The hourly air pollution data, also supplied by Environment Canada, were obtained from the fixed monitoring stations in Edmonton. They include data for gaseous substances: carbon monoxide (CO), nitrogen oxide (NO₂), sulphur dioxide (SO₂), and ground level ozone (O₃). For every ambient air pollutant, we recorded 24 measurements provided by a monitoring station at hourly intervals. The daily value for a given station represented an average of 24 concentration levels. In Edmonton, three monitoring stations were in operation during the study period. The daily average population exposures were expressed as the mean values across the monitoring stations. We have assumed that these values are good estimates of the concentration levels of ambient air pollutants for the whole area (catchment area for Edmonton hospitals) considered in the present study.

Statistical method
To investigate an association of the short-term effects of air pollution and weather factors with the number of daily ED visits for ischemic stroke, we applied a generalized linear mixed models (GLMM) methodology [14]. At first, we defined the clusters based on the following triplet: (year, month, day of the week). Our clusters could have 4 or 5 observations (days). The clusters have a hierarchical structure: days are nested in days of the week, which are nested in months, and months are nested in years. The
days of the same day of the week, in the same month and in the same year are grouped in one cluster. We applied a Poisson model to the clustered counts. We assumed a fixed slope and random intercept on the constructed clusters. From the available software that makes use of the GLMM technique, we have chosen the glmmPQL function from the R statistical package [15].

Relative risks (RR) of ED visits for stroke and their 95% confidence intervals (95% CI) were estimated in relation to an increase in the interquartile range (IQR) for each pollutant. RRs were adjusted for the effects of temperature and relative humidity. The percentage changes in daily visits associated with a given pollutant were calculated as \( \%RR = (RR-1)^*100\% \).

RESULTS

The results are presented in the form of three tables and two figures. Table 1 contains the number of ED visits for acute ischemic stroke by age and sex. All patients: of the 10,930 total ED visits for stroke, 52.0% (n = 5,680) concerned the male patients. Between 1992 and 2002, the percentage of ED visits for stroke, by month, ranged from 7.5% in February to 9.2% in August. The percentage of total visits by day of the week changed from 13.2% on Saturdays to 15.1% on Tuesdays (15.1% on Mondays). Patients aged 20–64 years: of the 2,873 visits for stroke, 58.4% (n = 1,679) applied to male patients. Between 1992 and 2002, the percentage of ED visits for stroke, by month, ranged from 7.4% in January to 9.3% in August (9.3% in July). The percentage of total visits by day of the week changed from 13.1% on Sundays to 15.5% on Tuesdays (15.3% on Mondays). Patients aged 65–100 years: of the 8,008 visits for stroke, 50.0% (n = 3,985) referred to males. Between 1992 and 2002, the percentage of ED visits for stroke, by month, ranged from 7.2% in February to 9.2% in August (9.0% in November). The percentage of total visits by day of the week changed from 13.1% on Saturdays to 15.0% on Tuesdays (15.0% on Mondays).

Statistical models were constructed separately for the two defined age groups. Thus, we finally analyzed 10,881 ED visits for acute ischemic stroke.

<table>
<thead>
<tr>
<th>Age group</th>
<th>ED Visits</th>
<th>%</th>
<th>Female</th>
<th>Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–19</td>
<td>43</td>
<td>0.4</td>
<td>27</td>
<td>16</td>
</tr>
<tr>
<td>20–29</td>
<td>61</td>
<td>0.6</td>
<td>40</td>
<td>21</td>
</tr>
<tr>
<td>30–39</td>
<td>177</td>
<td>1.6</td>
<td>104</td>
<td>73</td>
</tr>
<tr>
<td>40–49</td>
<td>503</td>
<td>4.6</td>
<td>231</td>
<td>272</td>
</tr>
<tr>
<td>50–59</td>
<td>1,213</td>
<td>11.1</td>
<td>464</td>
<td>749</td>
</tr>
<tr>
<td>60–69</td>
<td>2,299</td>
<td>21.0</td>
<td>863</td>
<td>1,436</td>
</tr>
<tr>
<td>70–79</td>
<td>3,618</td>
<td>33.1</td>
<td>1,678</td>
<td>1,940</td>
</tr>
<tr>
<td>80–100</td>
<td>3,016</td>
<td>27.6</td>
<td>1,843</td>
<td>1,173</td>
</tr>
<tr>
<td>Total</td>
<td>10,930</td>
<td>100.0</td>
<td>5,250</td>
<td>5,680</td>
</tr>
<tr>
<td>20–64</td>
<td>2,873</td>
<td>26.3</td>
<td>1,194</td>
<td>1,679</td>
</tr>
<tr>
<td>65–100</td>
<td>8,008</td>
<td>73.3</td>
<td>4,023</td>
<td>3,985</td>
</tr>
<tr>
<td>Others</td>
<td>49</td>
<td>0.5</td>
<td>33</td>
<td>16</td>
</tr>
</tbody>
</table>

Relative humidity (%) 3,652 66.0 13.6 66.1 18.5

Table 2 demonstrates a summary of data for ambient air pollutants and weather components which describe the environmental characteristics in Edmonton during the study period. The table shows the number of days for which the values were available. In the present study, the GLMM technique was used to construct the models with a single pollutant and two weather factors: temperature and relative humidity (Stroke ~ Pollutant + Temperature + Humidity) [16].
Our study summarizes the relationships we noted between air pollution and ED visits for acute ischemic stroke in Edmonton. We found positive and statistically significant associations between exposure to NO$_2$, CO, O$_3$ and SO$_2$ and ED visits for stroke. The figures present a detailed pattern of these associations by gender, season and a given pollutant. We observed differences in the findings for the male and female patients, with stronger associations found for the females. This could be explained by the fact that females generally have a smaller number of red blood cells than men, which makes them more susceptible to the health effects of exposure to environmental pollutants [17].

This study also examined the age-related differences in the risk for stroke associated with ambient air pollution. The results showed that for the age group 20–64 years, the associations between air pollution and stroke had a different pattern than for the older persons.

Table 3 presents a special section of the results shown in Figs. 1 and 2 which are positive and statistically significant. The criterion of including the results in Table 3 was the p-value for the estimated slope related to a given pollutant. It could be no greater than 0.1

% RR calculated as (RR-1)*100%, where RR is the estimated relative risk.

**DISCUSSION AND CONCLUSIONS**

Our study summarizes the relationships we noted between air pollution and ED visits for acute ischemic stroke in Edmonton. We found positive and statistically significant associations between exposure to NO$_2$, CO, O$_3$ and SO$_2$ and ED visits for stroke. The figures present a detailed pattern of these associations by gender, season and a given pollutant. We observed differences in the findings for the male and female patients, with stronger associations found for the females. This could be explained by the fact that females generally have a smaller number of red blood cells than men, which makes them more susceptible to the health effects of exposure to environmental pollutants [17].

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The findings from the recent study of air pollution and hospitalization for stroke in nine US cities demonstrated that an increase in the IQR value of CO, NO$_2$, PM$_{10}$...
and SO₂ was associated with 2.83, 2.94, 2.33, and 1.35% increase, respectively, in the number of hospital admissions for ischemic stroke [8]. In the study on ED data analyzed by the different types of stroke [12], the authors reported elevated ratios between the levels of air pollutants and the risk of acute ischemic stroke: during the warm season (April–September), the odds ratios (OR) associated with an increase in the IQR of the 3-day average for CO and NO₂ were 1.32 (95% CI: 1.09–1.60) and 1.26 (95% CI: 1.09–1.46), respectively.

The limitations of this study are typical for this type of research. They include the model used and the impact of measurement error on the assessment of exposure to air pollutants and the outcome variables. Fixed-site monitors provide data on daily exposures to ambient air pollution and are applied to represent the shared population exposure. Edmonton is a large city and the population exposures vary. On the other hand, the reported study is based on a well-accepted methodology that has a long positive history. The postulate to use the GLMM technique to study the data based on the triplet {year, month, day of week} has already been presented [16]. As a sensitivity analysis we recalculated all the results presented in Table 3, using a time-stratified case-crossover approach, with every three days in the same month as the matched controls and the quadratic function for temperature and relative humidity [18–19]. We obtained the same pattern of results as shown in Table 3. In addition, we performed an analysis for airborne particulates (PM₁₀ and PM₂·₅) using the case-crossover technique. No positive and statistically significant results were found for either of the age groups.

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REFERENCES


