SHORT REPORT

Environmental exposures and hospitalisation for respiratory conditions in children: a five year follow up study in Rome, Italy

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Exposure to environmental factors has been extensively studied in relation to the occurrence of respiratory diseases among children and adults. The effects of air pollution have been evaluated, and several studies indicate that respiratory symptoms may be exacerbated by living along busy roads.^{1,2} Tobacco smoke is an important cause of indoor air pollution, and children exposed to passive smoking have reduced lung function, increased risk of lower respiratory tract illnesses, and acute exacerbation of asthma resulting in hospitalisation.³ Moreover, the excessive moisture found in some homes promotes mould growth and is associated with an increased frequency of irritation, allergy, and infection.^{4,5}

Most of the evidence on the role of chronic exposure to environmental factors in the respiratory health of school-children derives from cross-sectional studies. However, there are problems in the interpretation of prevalence studies, especially when information on the exposure variables is collected in the same investigations.^{6,7} We used a longitudinal approach to evaluate whether indoor and outdoor environmental exposures at baseline are associated with the risk of subsequent hospitalisation for respiratory conditions during a five year follow up of a cohort of children.

METHODS

The cohort was made up of a representative sample of children, who lived in Rome and participated in SIDRIA (Italian Studies on Respiratory Diseases and Environment) within the ISAAC phase I study,⁸ conducted from November 1994 to February 1995. Baseline data of the cohort members (6–7 years, $n = 4027$ from 46 elementary schools) included information on environmental risk factors, and were provided by parents through a self-administered questionnaire. Length of father's education in years was taken as a proxy of socioeconomic status. The following environmental

exposures were considered: current parental smoking at the time of the interview (maternal and paternal), presence of mould or humidity in the child's room at the time of the interview (no, yes), amount of traffic in the area of residence (no, light, moderate, high), and daily truck transit along the street of residence (never or seldom (this category also included houses with no windows that faced the street), sometimes, often). Nitrogen dioxide (NO_2) concentrations were measured simultaneously with passive dosimeters at the main entrances of 34 of the 46 schools studied. Three Palmes tubes per school measured outdoor pollution over three seven-day periods (June 1995, November 1995, March 1996). The values for the three dosimeters in each period were averaged and then the school mean NO_2 concentrations over the entire period were computed (mean $\text{NO}_2 = 46.9 \mu\text{g}/\text{m}^3$; $\text{SD} = 10.2$, interquartile range (IQR) = 17, $\text{min} = 24$, $\text{max} = 66 \mu\text{g}/\text{m}^3$). The NO_2 exposure level measured at each school was assigned to the corresponding children. A five year follow up (until 31 December 1999) was conducted with the Municipal Registry of Rome. Of the original 4027 children, 3659 subjects were traced and were considered in this analysis (2947 subjects for the NO_2 analysis). During the study period, 122 children moved out of the city of Rome and two children died. Hospital admissions (1995–99) were found by linking the records of the cohort members with the regional hospital discharge database (which cover 96% of all hospital admissions to public and private hospitals in the region).

The outcome measure of interest was the incidence of hospitalisation for all respiratory conditions (ICD-9: 381.0–382.9; 460–466.1; 480–493.9), acute upper respiratory tract (URT) infections (ICD-9: 380.1–382.9; 460–465.9), and lower respiratory tract (LRT) conditions including asthma (ICD-9: 466; 480–493.9). The number of children hospitalised for asthma was too low for a meaningful analysis as a separate

Figure 1 Functional form of the association between exposure to NO_2 (at school) and subsequent risk of hospitalisation for respiratory conditions. The graphs were obtained using a generalised additive model while adjusting for gender, paternal education, and current paternal smoking. The dotted curves indicate 95% CI for the smoothed hazard.

Table 1 Association between hospitalisation and indoor/outdoor environmental exposures

Variables	n	Person-years	All respiratory conditions			Acute URT infections			Acute LRT infections and asthma		
			Incidence density per 1000	HR*	95% CI	Incidence density per 1000	HR*	95% CI	Incidence density per 1000	HR*	95% CI
All subjects	3659	18274	3.61			1.48			2.24		
Sex											
Males	1894	9464	3.38	1.00		1.37	1.00		2.21	1.00	
Females	1765	8809	3.86	1.15	0.71–1.86	1.58	1.14	0.54–2.43	2.26	1.04	0.56–1.92
Paternal education											
<9 years	1591	7939	4.03	1.97	0.82–4.74	2.13	6.50	0.86–49.24	2.01	1.13	0.41–3.12
9–13 years	1346	6726	4.16	2.15	0.89–5.21	1.33	4.23	0.53–33.45	2.96	1.80	0.67–4.82
>13 years	659	3288	1.83	1.00		0.30	1.00		1.52	1.00	
p trend				0.266			0.036			0.772	
Paternal smoking											
No	1959	9798	2.65	1.00		1.12	1.00		1.53	1.00	
Yes	1700	8475	4.72	1.66	1.01–2.73	1.88	1.42	0.65–3.08	3.06	1.99	1.05–3.78
Maternal smoking											
No	2218	11034	3.63	1.00		1.71	1.00		2.08	1.00	
Yes	1441	7240	3.59	0.80	0.47–1.34	1.10	0.49	0.21–1.16	2.48	0.96	0.50–1.85
Presence of mould or humidity in the child's room											
No	3437	17191	3.49	1.00		1.40	1.00		2.23	1.00	
Yes	168	813	4.92	1.35	0.49–3.72	3.69	2.38	0.71–7.96	2.12	0.55	0.07–3.99
Traffic in the area of residence											
No	850	4238	3.78	1.00		1.41	1.00		2.35	1.00	
Light	1172	5858	3.58	0.99	0.52–1.91	0.68	0.53	0.15–1.88	2.90	1.26	0.57–2.75
Moderate	1061	5306	3.39	0.96	0.49–1.90	1.69	1.45	0.51–4.11	1.88	0.80	0.33–1.94
High	538	2679	3.73	1.03	0.46–2.29	2.98	2.66	0.91–7.79	1.11	0.44	0.12–1.62
p trend				0.984			0.030			0.153	
Daily truck transit											
Never or seldom	2761	13785	3.92	1.00		1.37	1.00		2.53	1.00	
Sometimes	608	3064	0.65	0.16	0.04–0.68	0.65	0.47	0.11–2.04	0.00	–	
Often	214	1043	7.67	1.87	0.89–3.94	5.72	3.79	1.51–9.54	3.80	1.50	0.53–4.22
p trend				0.858			0.054			0.354	
NO₂ recorded at the school†											
Effect per 10 µg/m ³ NO ₂ increase	2947			1.28	0.98–1.68		1.56	0.96–2.56		1.10	0.80–1.51
1st quartile (24–35 µg/m ³)	842	4242	2.83	1.00		1.39	1.00		1.74	1.00	
2nd quartile (35–47 µg/m ³)	841	4209	2.85	1.06	0.45–2.53	0.37	0.55	0.08–3.61	2.21	1.34	0.51–3.21
3rd quartile (47–52 µg/m ³)	615	3088	4.21	1.57	0.59–4.13	1.62	1.25	0.25–6.24	2.59	1.58	0.35–4.10
4th quartile (52–66 µg/m ³)	649	3250	4.31	1.95	0.81–4.71	2.77	3.04	0.67–13.79	1.85	1.24	0.64–3.08
p trend				0.096			0.159			0.535	

*HR have been adjusted for sex, current paternal smoking, and paternal education.

†HR have been estimated using a model for clustered data to take into account the intra-cluster correlation among children of the same school.

HR, hazard ratio; LRT, lower respiratory tract; URT, upper respiratory tract.

entity. We considered only one hospitalisation per subject for a specific condition.

Cox regression models were employed to estimate the hazard ratios (HR) and 95% confidence intervals (CI) of the association between various environmental factors and incidence of respiratory hospitalisation, acute URT infections, and LRT conditions. Children who moved or died during the follow up were considered as censored at the time of the last residence in Rome. We adjusted for gender, paternal education (less than 9 years, 9–13 years, more than 13 years) and paternal smoking. In evaluating the effect of NO₂, a model for clustered data was used to take into account the intra-cluster correlation among children of the same school. The effect of NO₂ levels was evaluated by quartile and as a continuous variable. A generalised additive model was used to illustrate the relationship between exposure to NO₂ as a continuous variable and subsequent hospitalisation. An additional analysis was conducted for children who live in the same house.

An association was considered as significant when the *p* value was equal to or lower than 0.05. The Wald test was used to test the linear trend across ordered variables. All statistical analyses were performed with STATA 8.0.

RESULTS

A total of 66 children were hospitalised for all respiratory diseases (27 for URT infections and 41 for LRT conditions) among the 3659 cohort members during the five year follow up. The incidence of hospitalisation for all respiratory conditions was 3.61 per 1000 person-years. Two children were hospitalised for a URT infection and one for an LRT condition; they were then considered in the all respiratory condition analysis only once. Table 1 illustrates the main results.

No main gender differences were seen. Some differences in hospitalisation rates were found for parental education. There was a higher probability of hospitalisation for acute URT infections for children of fathers with lower education than children with well educated fathers (*p* trend = 0.036). Paternal smoking at baseline was associated with hospitalisation for all respiratory conditions (HR = 1.66; 95% CI 1.01–2.73) and LRT conditions (HR = 1.99; 95% CI 1.05–3.78). No effect of maternal smoking was detected. Mould/humidity exposure was related to an increased risk of all respiratory hospitalisations and URT infections, although the confidence intervals included unity.

Hospitalisation for all respiratory conditions was not related to reported traffic in the area of residence, but the risk for acute URT infections was higher in the areas with more heavy traffic (*p* value trend = 0.030). Frequent truck transit was significantly associated with acute URT infections (HR = 3.79). The risk of hospitalisation associated with NO₂ was higher for all respiratory conditions and for respiratory URT infections (fig 1). The estimated effects per 10 µg/m³ NO₂ increase approached statistical significance.

When we considered only the children who lived in the same house from birth to the end of the follow up (2016 subjects), all estimated effects of traffic and of NO₂ were strengthened: frequent truck transit on acute URT infections, HR = 4.08, 95% CI 1.31–12.66; linear effect of NO₂ per 10 µg/m³ increase = 1.85, 95% CI 1.07–3.19. Moreover, a significant effect of mould/humidity in the child's room on URT infections was found (HR = 5.95, 95% CI 1.64–21.5).

DISCUSSION

This is one of the few prospective cohort studies in environmental epidemiology to investigate whether chronic exposures to outdoor and indoor pollutants are risk factors for severe respiratory events requiring hospitalisation in

children. Our study reveals that children exposed to outdoor pollution (high levels of NO₂, living in a busy traffic area, or along a street with high truck traffic) have a higher probability to be hospitalised than non-exposed children. The stronger results observed when the analysis is limited to long term residents reinforce the findings. Of the indoor exposures investigated, parental smoking was found as a strong risk factor while presence of mould/humidity emerged as a strong risk factor when the analysis was restricted to long term residents.

The present results are coherent with the large amount of data available on the acute effects of air pollution on the respiratory health of children.^{1,2} Our study, however, also evaluated the effect of chronic exposure. Similar results were also indicated by Ciccone *et al*,⁷ in which study information on vicinity to a busy street was investigated but hospitalisations were reported in the questionnaire at the same time exposure was assessed. Increased incidence of URT infections in the first two years of life in association with long term exposure to PM_{2.5} and NO₂ has been reported in the Netherlands.⁹

There are limitations of this study that should be noted. Exposures were self-reported and we did not have air pollution data at the individual level; also, NO₂ was measured at the area level, i.e. the school, thus causing a possible random misclassification. The school, however, may well represent the average level of exposure in the neighbourhood, as schoolchildren in Italy at the time of the baseline survey were required to go to school near home. Given the stability of general traffic and of NO₂ concentrations measured at fixed sites in the city during the follow up, temporal trends in exposures are unlikely to be important. Confounding by socioeconomic status may be an issue as less advantaged families may tend to live in more polluted areas. However, we adjusted for father's level of education, as a proxy of socioeconomic status, based on a comparison between different individual and area based indicators for the same dataset.¹⁰ Finally, the size of the study was limited, and 95% CI are somewhat large because of the small number of cases detected. A longer follow up may be needed.

In conclusion, this study reveals that living close to road traffic, especially diesel truck traffic, is a risk factor for later hospitalisation for acute conditions of the upper airways. The findings were reinforced by our evaluation of NO₂, an objective measure of air pollution, and by restricting the analyses to long term residents.

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