RESEARCH PAPER

The Association Between Environmental Lead Exposure and Recurrent Respiratory Infections in Children Aged 3-7 Years in Shenyang, China

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Objectives: To investigate the lead exposure levels, and the effect of blood lead level (BLL) on recurrent respiratory infections in children aged 3-7 years in Shenyang. **Methods**: A case-control study including 78 children with recurrent respiratory infections and 141 controls was performed. Venous blood was obtained for BLL, and a questionnaire was completed. **Results**: The BLL was significantly higher in children with recurrent respiratory infections than that in the control group [Median (IQR): 2.56 (1.29-6.19) *vs* 1.99 (0.90-5.92) µg/dL, *P*=0.029]. Children with BLL ≥1.95 µg/dL were more likely to be suffering from recurrent respiratory infections (OR=2.328, 95%CI=1.228-4.413) than those with BLL <1.95 µg/dL. **Conclusions**: High lead level can increase the risk of respiratory infections in preschool children.

Keywords: *Humoral immunity, Lead toxicity, Predisposition, Risk Factors*.

Lead is harmful to children's health because of the dysfunction of various organ systems induced by lead, such as hematological, neurological, gastrointestinal, central nervous, renal and immune systems [1,2]. Studies showed that people exposed to occupational lead had impaired congenital and humoral immune responses and increased susceptibility to chronic infection [4,5]. However, there is little information about the effect of non-occupational lead exposure on humoral immunity.

At least 6% of children under 6 years old suffer from recurrent respiratory infections (RRI). We studied the blood lead and immunoglobulin levels among children aged 3 to 7 years in present study to study its relation with RRI.

METHODS

The study was done between September, 2017 and October, 2018. A case-control study was carried out in children aged 3 to 7 years. Among children diagnosed with RRI, 78 were chosen randomly from the inpatient department of our hospital, and the control group was 141 healthy children of matched age and gender who were chosen randomly from the physical examination center of the same hospital. Exclusion criteria for both case and control group were taking zinc, calcium, iron, vitamin A, vitamin D, or multivitamin supplementation in past 3 months; history of congenital malformation, such as heart disease and thoracic deformity; and history of disease associated with kidney, liver or immune system.

Ethics approval was granted by the institute ethics committee and informed written consent was obtained from the parents/caretakers of the participants. Parents/caretakers of 219 participants completed a questionnaire, including child's age, sex, BMI (kg/m^2), passive smoking and social economic status (low, middle, high income). If anyone in the family was smoking currently, it was defined as passive smoking. Children's medical histories were reviewed in particular with regard to the frequency of upper respiratory infections (cold, pharyngitis, laryngitis, tonsillitis, otitis media) and lower respiratory infections (tracheitis, bronchitis, bronchiolitis, pneumonia). RRI was defined as either upper respiratory infections at least six times within one year; or lower respiratory infections at least two times within one year [7].

The sample size was calculated according to the assumptions that alpha of 0.05, power of 0.8, odds ratio 2.5, and prevalence of exposure (lead poisoning) in the control group 20% [8]. The result was 77 children in the case group and 139 children in the control group.

Blood samples were collected in lithium heparin coated trace-metal free tubes and were transported on ice to Shenyang Harmony Health Medical Laboratory for analysis. Blood lead level (BLL) was determined by atomic absorption spectrometry through graphite furnace ionization techniques.

Since BLLs were non-normally distributed, statistical analysis was performed after logarithmic transformation. Student t-test and analysis of variance test (ANOVA) were used to evaluate the differences of indicators between different groups. Categorical variables were compared by chi-square test and Fisher's exact test. BLLs was categorized into two groups (<1.95 µg/dL and ≥1.95 µg/dL) for multiple logistic regression analysis. Data were analyzed by Statistical Package for the Social Sciences (SPSS 20.0). The results were considered statistically significant at 5%.

RESULTS

A total of 228 children were approached, of which, 5 refused to complete a questionnaire, while 4 met one of the exclusion criteria. The case-control study eventually included 78 children with RRI and 141 healthy controls (***Fig.* 1**). The percentage of passive smoking exposure was significantly lower in the control group than that of the case group (41.1% *vs* 56.4%; *P*=0.03) (***Table* I**). The median (IQR) BLL of case group was significantly higher than that of the control group [2.56 (1.29-6.19) *vs* 1.99 (0.90-5.92) µg/dL; *P*=0.029]. Children with BLL ≥1.95 µg/dL were more likely to be suffering from RRI, which was approximately 2.5 times more than those who had BLL <1.95 µg/dL.

Multivariate analysis of risk factors for recurrent respiratory infections showed that both passive smoking [OR (95% CI)=1.18 (0.98-3.20); *P*=0.057] and BLL of 1.95 µg/dL or higher [OR (95% CI) = 2.33 (1.23-4.41); *P*=0.010] had a higher risk of having recurrent respiratory infections.

DISCUSSION

Environmental lead exposure has always been one of the important public health issues in children, even at chronically low levels [5].

Table I Baseline Characteristics of Children With Recurrent Respiratory Infections and Controls

Characteristics	*Control group* (*n=141*)	*Cases* (*n=78*)
Child age		
36-47 mo	51 (36.2)	28 (35.9)
48-59 mo	31 (22.0)	26 (33.3)
60-71 mo	22 (15.6)	17 (21.8)
72-84 mo	37 (26.2)	7 (9.0)
Male gender	67 (47.5)	39 (50.0)
Passive smoking*	58 (41.1)	44 (56.4)
Socio economic status		
Low income	32 (22.7)	15 (19.2)
Middle income	103 (73.0)	57 (73.1)
High income	6 (4.3)	6 (7.7)

*All values in no. (%) except #mean (SD); All P>0.5 except *P=0.03.*

A value of 5 µg/dL US Centers for Disease Control and Prevention reference concentration) was considered as the clinical cut off for elevated BLLs [12]. This study show that the BLLs below 5 µg/dL are associated with an increased risk of RRI in preschool children. In addition, we observed that IgG levels of case group were lower than that of the control group, but the difference between these two groups was not significant (data not shown), which may be related to relatively small number of cases. The result also suggests that lead exposure may increase the risk of RRI by other means, such as by affecting cellular immunity. However, cellular immune indicators were not studied in the present study.

Previous studies [4,13,14] have shown that blood lead can affect the levels of immune cytokine, for example, reducing the production of IgG and IgM. The effects of lead on immune cytokine and other adverse

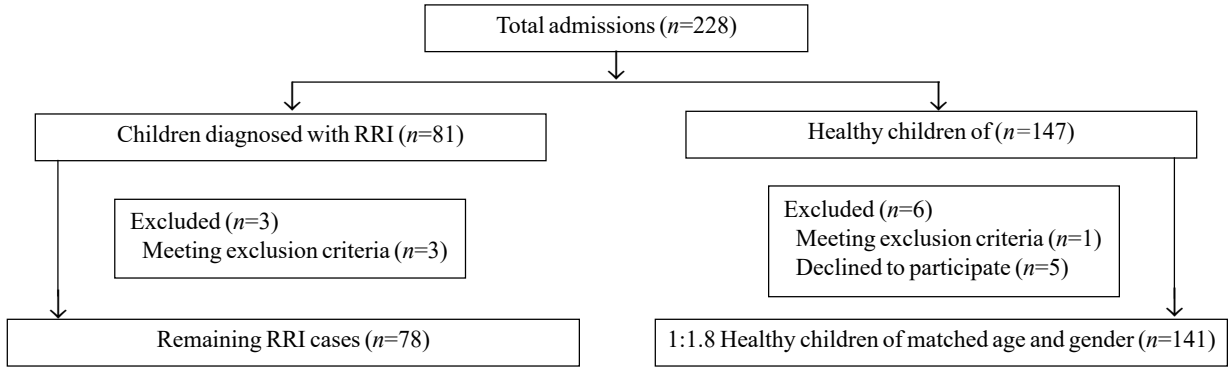

Fig.1 *Flow of participants in the study.*

WHAT THIS STUDY ADDS?

- Blood lead levels >1.95 µg/dL may increase the risk of recurrent respiratory infections in preschool children.

health are highly dose dependent. At present, the immunologic effects from low blood lead exposure (under 5 µg/dL) were poorly understood. The present study found that higher BLLs (≥1.95 µg/dL) increased the risk of RRI in preschool children, as also observed by other researchers [5]. In addition to lead exposure, some studies reported the association between other factors and RRI, such as socioeconomic status, passive smoking, air pollution, micronutrient intake of children [15,16]. Smokers often avoid children due to the increasing awareness of smoking harmfulness. So our results did not show a significant association between passive smoking and RRI.

Our findings highlight a potentially preventable cause of infectious disease in preschool-age children, findings indicate that it is necessary to control the source of lead pollution, and the harmful effects of apparently low levels of blood lead need to be further explored.

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