Allergies in the workplace

AMBIENT AIR POLLUTION AND CHILDHOOD ASTHMA: A REVIEW OF SOUTH AFRICAN EPIDEMIOLOGICAL STUDIES

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ABSTRACT

Childhood asthma is the most common chronic disease in children globally and ranks in the top 20 contributors of global disability-adjusted life years (DALY) in all children, and among the top 10 causes of DALY amongst 5-14 year olds. The growing increase in the prevalence of childhood asthma symptoms has been correlated with the increase in outdoor air pollution in developing countries. An estimated 23% of all deaths and 24% of the global burden of disease can be attributed to environmental factors, with ambient air pollution (especially particulate matter) responsible for 3.2 million deaths per year (3.1% of global total DALYs). This review focuses on epidemiological evidence from South African studies to interrogate the evidence for the link between ambient air pollution and childhood asthma. The review suggests a positive association between ambient air pollution and the risk of childhood asthma. However, the strength of this association is compromised by methodological issues related to the paucity of use of standardised instruments for assessing asthma outcomes and the lack of more detailed exposure characterisation approaches, which need to be addressed in studies contemplating further investigation into this area of research.

BACKGROUND

Childhood asthma is the most common chronic disease in children globally and ranks in the top 20 contributors of global disability-adjusted life years (DALY) in all children; and among the top 10 causes of DALY amongst 5-14 year olds. The global mortality rates of childhood asthma is approximately 0.7 per 100 000. Findings from the International Study of Asthma and Allergies in Childhood (ISAAC) showed that approximately 13% of adolescents between the ages of 13-14 years have symptoms of asthma. Previous epidemiological studies have reported five or more episodes of wheezing in one-third of asthmatic children in the first 12 months of having asthma. There is a significant global variation between countries, in the prevalence of asthma symptoms (characterised by wheezing in the past 12 months), of up to a 13-fold difference. Although symptoms of asthma are more apparent in many high-income countries (HICs), some countries in the low- and middle-income range also have a high prevalence of asthma symptoms. Africa has the highest prevalence of severe asthma symptoms among children with current wheeze. In Cape Town, asthma was prevalent in 34.4% and 17% of urban and rural children, respectively, aged 10 to 14 years. A similar distribution has been observed in children aged 8-17 years living in Kenya’s capital Nairobi, with a prevalence of 22.9% compared to 13.2% in rural Kenya.

AMBIENT AIR POLLUTION

Ambient air pollution is a major environmental health issue globally affecting the population in highly industrialised and developing countries. An estimated 23% of all deaths and 24% of the global burden of disease can be attributed to environmental factors, with ambient air pollution (especially particulate matter) responsible for 3.2 million deaths per year (3.1% of global total DALYs). The WHO reported 3.7 million premature deaths in both urban and rural areas caused by air pollution, which was mainly due to small particulate matter of 10 microns or less in diameter (PM10). It is estimated that a 15% reduction in ambient air pollution-related death can be expected from reducing ambient particulate matter from 70 to 20 µg/m3. Respiratory disease is the leading cause of deaths from ambient air pollution, responsible for over half of the deaths reported. Recent studies also show long-term exposure to nitrogen dioxide (NO2) to exacerbate bronchitis symptoms.
in asthmatic children.\textsuperscript{10-12} NO\textsubscript{2} is also linked to reduced lung function growth as reported in North America and other European cities.\textsuperscript{7,11,13} Furthermore, studies have suggested that air pollution, particularly traffic-related, contribute to the development of asthma, atopy and infant mortality (Figure 1).\textsuperscript{14} Other studies have also demonstrated that industrial air pollutants, such as emissions from refineries, are also a major source of air pollution and associated with asthma (Figure 2).\textsuperscript{15} Epidemiological studies have shown changes in respiratory symptoms and pulmonary function in individuals with asthma following exposure to sulphur dioxide (SO\textsubscript{2}) for durations as short as 10 minutes.\textsuperscript{12,15-17} High levels of ozone (O\textsubscript{3}) have also been reported to have harmful effects including breathing problems, triggering asthma and reduced lung function.\textsuperscript{18,19} Table I outlines the different ambient air quality standards for the four criteria pollutants and demonstrates that the South African standards are not as stringent as WHO standards for particulate matter, sulphur dioxide and ozone.

### METHODOLOGY

Selection criteria included peer-reviewed articles of primary research in the form of epidemiological studies, investigating the association between ambient air pollution and childhood asthma, conducted in South Africa since 2004. The rationale for inclusion of post-2004 articles was to have more recent evidence to corroborate that of a previously published review in 2004.\textsuperscript{22} Subject-specific databases (such as Medline through PubMed; CINAHL; Highwire; and the Cochrane library) were searched laterally using keywords combined by Boolean operators such as ‘AND/OR’ commands. Keywords were identified using the PICO (Population-Intervention-Comparison-Outcome) acronym and Medical Subject Headings (MeSH terms). The first stage of literature search was a sensitive (broad) search strategy with the query; ‘Children AND Air pollution AND Asthma AND South Africa’. This was followed by a more specific search including all elements of the selection criteria and different MeSH terms to narrow-down the search with the query; ‘(Child* OR Infants OR Adolescent) AND (Ambient air pollution OR Particulate Matter OR Sulphur dioxide OR Carbon monoxide OR Nitrogen dioxide) AND (Asthma OR wheezing) AND South Africa) AND “last 10 years”[PDat] AND Humans[Mesh]’. Truncations (*) were used to identify all possible endings of keyword such as ‘Child*’, whose base does not change when used differently (e.g. Child, Children, Children’s). Reference-list searching was done to identify one additional article.

### CRITICAL APPRAISAL OF RESULTS

A sum of four studies was included in this detailed review, with three of these using a cross-sectional study design and the other also including a longitudinal study component. A descriptive summary of the findings from these studies is presented in Table II.

### TABLE I: INTERNATIONAL AND NATIONAL AMBIENT AIR QUALITY GUIDELINES

<table>
<thead>
<tr>
<th>POLLUTANT</th>
<th>AVERAGING PERIOD</th>
<th>WHO AMBIENT AIR QUALITY GUIDELINES (µg/m\textsuperscript{3})\textsuperscript{20}</th>
<th>SOUTH AFRICAN NATIONAL AMBIENT AIR QUALITY STANDARDS (µg/m\textsuperscript{3})\textsuperscript{21}</th>
</tr>
</thead>
<tbody>
<tr>
<td>Particulate Matter (PM\textsubscript{10})</td>
<td>1-year 24-hour</td>
<td>20</td>
<td>40</td>
</tr>
<tr>
<td>Particulate Matter (PM\textsubscript{2.5})</td>
<td>1-year 24-hour</td>
<td>10</td>
<td>-</td>
</tr>
<tr>
<td>Sulphur dioxide (SO\textsubscript{2})</td>
<td>24-hour 10-minutes</td>
<td>20 500</td>
<td>125 500</td>
</tr>
<tr>
<td>Nitrogen dioxide (NO\textsubscript{2})</td>
<td>1-year 1-hour</td>
<td>40 200</td>
<td>40 200</td>
</tr>
<tr>
<td>Ozone (O\textsubscript{3})</td>
<td>8-hour daily maximum</td>
<td>100</td>
<td>120</td>
</tr>
</tbody>
</table>
The study by Maluleke and Worku (2009) used a cross-sectional study design to identify key predictors of asthma in children living in Polokwane province.23 The use of a cross-sectional study design limited detailed exploration of the temporal relationship between environmental pollutant exposures and childhood asthma. Furthermore, the exposure assessments used in this study were constrained by the lack of information on the proximity of the monitoring stations to the selected schools. Although the authors controlled for some covariates (socio-economic status, environmental tobacco smoke, diet and pet ownership), atopy and indoor air pollution was not controlled. Atopy and indoor air pollution may have skewed the findings positively, as it has also been shown to be independently associated with asthma.

The following table outlines the key aspects of the studies discussed:

<table>
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<tbody>
<tr>
<td>AIM OF STUDY</td>
<td>Focus on identifying key predictors of asthma in school children.</td>
<td>Assessment of asthma symptom prevalence in priority area of Cape Town (characterised by petrochemical refinery environs) compared to other places in Cape Town.</td>
<td>Association of wheeze with reported outdoor air pollution in a priority area (Ekurhuleni Metropolitan Municipality).</td>
<td>Association of respiratory outcomes in exposed children to ambient air pollution.</td>
</tr>
<tr>
<td>STUDY DESIGN</td>
<td>Cross-sectional</td>
<td>Cross-sectional</td>
<td>Cross-sectional</td>
<td>Cross-sectional and longitudinal study design (Panel Study)</td>
</tr>
<tr>
<td>STUDY POPULATION</td>
<td>Random sample of 742 school children between 13-14 years in Polokwane, Limpopo Province.</td>
<td>2361 school aged children between 11 to 14 years from 17 schools in defined areas (Cape Town).</td>
<td>3764 school aged children between 13 and 14 years from 16 selected schools in Tembisa and Kempton in Ekurhuleni Metropolitan Municipality.</td>
<td>422 school aged children in grade 3 to 6 from 4 schools in South Durban (exposed) and 3 schools in North Durban (unexposed).</td>
</tr>
<tr>
<td>EXPOSURE MEASUREMENT</td>
<td>Monthly particulate matter (PM) data from monitoring stations recorded between 2002 and 2005 to quantify pollution levels; questions on smoke in the environment was used as the exposure index in the analysis.</td>
<td>Distance from the refinery and meteorological estimates exposure index (wind speed, wind direction and proportion blown yearly) linked to each child’s residential address using the refinery as the putative point source.</td>
<td>Reported frequency of trucks passing near the home on weekdays.</td>
<td>Assessment of pollutants (SO2, PM, NOx and CO) from monitoring stations near selected schools.</td>
</tr>
<tr>
<td>POLLUTANT SOURCES</td>
<td>Silicon smelting, automobile emission, industrial activities, smoke and biomass fuels.</td>
<td>Petrochemical refinery</td>
<td>Traffic related pollutants</td>
<td>Industrial activities mainly related to petrochemical refineries and gasoline/diesel powered vehicles.</td>
</tr>
<tr>
<td>OUTCOME MEASUREMENT</td>
<td>Parental-reporting of the prevalence of cough in the child.</td>
<td>Children ISAAC written and video questionnaires to assess asthma symptoms.</td>
<td>Children ISAAC written questionnaire.</td>
<td>Standardised questionnaire, spirometry, serial peak flow and skin prick test.</td>
</tr>
<tr>
<td>RESULTS</td>
<td>Presence of smoke in the environment was strongly associated with asthma (OR; 2.39 CI: 1.34-4.98).</td>
<td>Positive associations between meteorologically estimated exposure (MEE) with having to take an inhaler to school (OR; 1.22 CI; 1.06-1.40), frequent wheezing at rest (OR; 1.27 CI; 1.05-1.54) and recent waking with wheezing (OR; 1.33 CI; 1.06-1.66). No associations were observed when simple distance from the refinery was used as a marker for exposure.</td>
<td>The frequency of trucks passing near homes during weekdays increased the likelihood of ever-wheeze (OR; 1.32 CI; 1.01-1.73), current wheeze (OR; 1.61 CI; 1.15-2.24) and current severe wheeze (OR; 2.22 CI; 1.28-3.77).</td>
<td>School children from South Durban (industrial pollutant area) were more likely to have persistent asthma (OR; 1.82 CI; 1.05-3.14) and marked airway hyper responsiveness on methacholine challenge (OR; 2.55 CI; 1.03-6.28) compared to school children in North Durban.</td>
</tr>
<tr>
<td>POTENTIAL BIAS</td>
<td>Potential bias: • Selection bias (exclusion bias); • Information bias (misclassification bias).</td>
<td>Potential bias: • Selection bias; • Information bias (recall and reporting bias).</td>
<td>Potential bias: • Selection bias; • Misclassification bias; • Information bias (recall and reporting bias).</td>
<td>Potential bias: Selection bias; Short follow-up (restricted to short term effect inference).</td>
</tr>
<tr>
<td>CONCLUSION</td>
<td>Environmental air pollution was an important risk factor for asthma in children.</td>
<td>An increased prevalence of asthma among children living around the refinery area and related to refinery emissions.</td>
<td>Children living in one of the air pollution priority areas have an increased risk of wheezing due to exposure to air pollution sources.</td>
<td>Children in South Durban, when compared to those residing in North Durban, have an increased risk of persistent asthma and airway hyper responsiveness due to ambient air pollution exposures.</td>
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</tbody>
</table>
symptoms in children.24,25 The results of the study demonstrated that children in a smoke environment were twice as likely to develop asthma, compared to unexposed children (OR; 2.39 95% CI; 1.34-4.98). The reliability of the result was constrained by the subjective assessment of asthma as reported by parental-reported cough among children, without any other objective asthma endpoints reported.

The study by White et al. (2009) also used a cross-sectional study design to determine if the prevalence of asthma in school children was higher in the Milnerton area, where a petrochemical refinery is located, compared to other areas in Cape Town.26 Furthermore, due to the lack of objective quantitative measurements of criteria air pollutants, a specific pollutant effect could not be measured. Although the authors controlled for parity, passive smoking, family history of asthma and atopic diseases, distance from major road, there was no information on smoking status and pollen data exposures in the control group. Thus, no inference about the role of both the smoking status and pollen exposures as potential confounders could be made. The overall results of the study demonstrated an eight fold increased likelihood of asthma symptoms (OR; 8.92) in the priority area compared to other areas in Cape Town. However, the wide confidence interval of 4.79 to 16.63 limited the precision of the result. Furthermore, the multivariate analysis demonstrated a positive association between meteorologically estimated exposures (MEE) but not simple distance from the refinery and the following endpoints: having to take an inhaler to school (OR; 1.22 CI; 1.06-1.40); frequent wheezing at rest (OR; 1.27 CI; 1.05-1.54); and recent waking with wheezing (OR; 1.33 CI; 1.06-1.66).

The limitation of generalisation across different socio-economic class categories was somewhat addressed in the study by Shirinde et al. (2014), which explored the association of wheeze with air pollution among children in 16 schools from two urban areas (Tembisa and Kempton Park) of different socio-economic status.27 Although the study had an appreciably large sample size of 3764, the use of cross-sectional study design limited the exploration of the temporal association between air pollution and asthma. Furthermore, a crude subjective exposure measure of exposure was used based on questions on the frequency of trucks passing by the homes of children on weekdays. This may have introduced a form of misclassification bias since children spend most of their time in school during weekdays and may, therefore, have limited insight on exposures closer to their home. There were also no questions on other sources of air pollution such as distance of industries from residential areas, nor any objective quantitative data on environmental pollution, such as data from monitoring stations to quantify specific pollutants. Although the authors took into account the presence of confounders such as residential area, sex, mother’s education level, residential history, domestic fuel exposure, diet, active and passive smoking, both in the study design and analytical approaches, there is a possibility of residual confounding due to atopic disease and unmeasured socio-economic status factors such as occupation, income levels, parity, etc. The overall findings of the study suggested that the frequency of trucks passing near homes in weekdays increased the likelihood of ever-wheeze (OR; 1.32 CI; 1.01-1.73), current wheeze (OR; 1.61 CI; 1.15-2.24) and current severe wheeze (OR; 2.22 CI; 1.28-3.77) in these children.

The only study with a longitudinal study component was reported by Naidoo et al. (2006), which investigated asthma in a representative group of school children exposed to ambient air pollution in South Durban and compared them with school children in a non-exposed area of North Durban.28 The use of a panel study design increased the power of the analysis and the ability to examine the effects of short-term fluctuations in air pollutant exposure on acute respiratory changes across the four seasons. Both selected communities had a similar socio-economic profile and the schools were randomly selected in each community area. However, recruitment of students in each area was done using a dual pronged strategy, which was characterised by inclusion of a randomly selected group of students as well as a group selected on the basis of known or probable persistent asthma. Monitoring stations located close to schools were used to assess exposure to ambient air pollution in both the exposed and non-exposed groups. Measurement bias was also reduced by random selection of schools having less than 15% of its students from surrounding communities away from the monitoring stations. Similarly, the use of an objective marker of asthma outcome (bronchial hyper responsiveness) together with a standardised validated questionnaire reduced the risk of measurement bias. The results of the study demonstrated that children from the exposed South Durban area were more likely to have persistent asthma (OR; 1.82 CI; 1.05-3.14) and marked airway hyperactivity following the methacholine challenge testing (OR; 2.55 CI; 1.03-6.28), compared to children in North Durban. Furthermore, results from the serial daily peak expiratory flow, over three consecutive weeks across the four phases (season), showed intraday variability (a marker of worsening of asthma) of mean (std. dev.) PEF [16.3 (12.4) vs 15.7 (11.9)] and mean FEV1% [18.0 (12.1) vs 17.0 (12.0)] to be marginally greater, on average, among children in South Durban, compared to those in North Durban. However, inference is limited to the short term effect of air pollution measured in the four seasons.

**DISCUSSION**

Most of the studies reviewed had methodological limitations constraining their ability of demonstrating the strength of association between ambient air pollution and childhood asthma. Three of the four studies reviewed used only a cross-sectional study design that limited the inference of a temporal relationship between air pollution on the development or presence of childhood asthma. This is important since it is possible that families, with symptomatic children at an early age, may move to homes in lower exposed areas. However, the study that used a longitudinal study compo-
nent had a short follow-up period which limited the ability to quantitatively assess the level of exposure and other covariates with the initial onset or progression of asthma. Other limitations in studies included the lack of detailed and systematic exposure assessment of criteria pollutants. This limited the ability to explore dose-response relationships and time-activity patterns in a meaningful manner. Furthermore, comparisons with other countries or regions in the world were, therefore, not possible. The use of a standardised quantitative measurement of criteria pollutants from monitoring stations located near the resident or school of the study participants could have limited exposure misclassification to the extent that it did exist.

Similarly, there were variations among studies reviewed regarding the assessment of asthma outcomes in exposed children. Asthma outcome was assessed mainly by subjective, indirect approaches using questionnaires in three of the four studies. This had the potential to introduce a form of information bias when administering questionnaires, due to possible recall and general awareness of the association between asthma with air pollution. The use of simple standardised objective measurements using peak expiratory flow measurements, spirometry and/or exhaled nitric oxide (FeNO) could have reduced such bias.

There was also evidence of selection bias operating in three of the four studies. The lack of detailed information in the inclusion and exclusion of study participants, together with a lack of randomisation of children, irrespective of known asthma-status across all socio-economic groups, limited the internal and external validity of the results. Furthermore, some studies dealt inadequately with confounding factors that were not reported on, such as socio-economic factors, smoking status, atopy and indoor air pollutants (domestic fuel combustion). These factors may have skewed the risk estimation since they are also known to be associated with childhood asthma.24,25,29 Had the data been collected for these confounders, this could have been appropriately controlled for, during statistical analysis using either stratification or multivariate analysis.

The limitations in methodology, in these studies, have also been reported by Wichmann and Voyi in their review on the effect of air pollution on ill health using evidence from South African studies.72 Their review focused on both indoor and outdoor air pollution and the health outcomes reported on all measures of ill-health, including respiratory health associated with air pollution exposure. Similar methodological issues were reported that limited the reliability and validity of the results. Future studies of the association between air pollution and childhood asthma need to address these issues to increase the strength of the evidence and render comparison with findings reported from other parts of the world, possible.

CONCLUSION

The review suggests a positive association between the risk of childhood asthma and ambient air pollution. However, the strength of this association is compromised by methodological issues that need to be addressed, in future studies, contemplating further investigations into this area of research.

It is recommended that a longitudinal study with a reasonably long follow-up period (more than 3 years) be conducted, using the following:

1. Objective standardised quantitative measurements of criteria pollutants (such as those obtained from pollutant-specific monitoring stations, supplemented by more detailed exposure characterisation studies related to both indoor and outdoor pollutant sources, using more advanced approaches in exposure modelling techniques, such as land use regression models, in addition to more traditional dispersion modelling techniques).

2. Asthma outcomes, using simple instruments according to standardised procedures (such as those obtained from serial peak expiratory flow measurements, spirometry or exhaled nitric oxide levels).

This will increase the reliability and validity of the measurements, to better quantify the risk and take into account other possible covariates that may potentially bias or confound these associations.

REFERENCES