Near Fatal and Fatal Asthma and Air Pollution – are we missing an opportunity to ask key questions?

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ABSTRACT

There is an increasing body of evidence supporting the link between asthma attacks and air pollution in children. To our knowledge, there has only been one reported case of a fatal asthma attack in a child associated with air pollution and this was in the UK. This article considers why there is a lack of evidence on fatal asthma and air pollution. We also explore three challenges. (1) Fatal and near fatal asthma events are rare and not yet well understood. (2) Measuring and interpreting personal exposure to air pollution with sufficient temporal and spatial detail is challenging to interpret in the context of individual fatal or near fatal asthma attacks. (3) Current studies are not designed to answer the question of whether or to what extent air pollution is associated with fatal/near fatal asthma attacks in children. Conclusive evidence is not yet available and systems of data collection for both air pollution and fatal and near fatal asthma attacks should be enhanced to ensure risk can be determined and impact minimised.

Introduction

Ella Kissi-Debrah was the first person in the United Kingdom (UK) whose death, at 9 years of age, was attributed to air pollution [1]. Residing in a busy, traffic dense area of London, Ella was exposed to high levels of traffic-related air pollution (TRAP). Her severe asthma symptoms and eventual death were attributed to exposure to high levels of outdoor air pollution. Asthma deaths in the UK are amongst the highest in Europe[2]. Whilst clinicians are aware of this statistic and measures have been suggested to reduce risk[3], strategies to reduce air pollution exposure are not at the forefront of our consultations and clinicians lack the tools and knowledge to limit exposure. If outdoor air pollution could be a significant

contributing factor to near fatal and fatal asthma attacks, why are we not doing more to understand and prevent further cases?

Air pollution

Hippocrates in 400BC wrote of air pollution concerns in *Air, waters and places* (400BC)[4]. A more contemporaneous, but archaic vision of air pollution is the London smog of December 1952 when a weather event combined with high levels of industrial air pollution caused a visible smoke cloud which was estimated to cause 4000 deaths[5]. Current harmful levels of air pollution are often not visible to the naked eye and yet silently contribute to an estimated 28 000 to 36 000 deaths per year in the UK[6].

Outdoor air pollution levels are a global health concern and are estimated to contribute to 4.2 million premature deaths globally[7]. Air pollution has a negative impact on health in utero, during childhood and in adulthood[8]. The World Health Organisation (WHO) identifies sulphur dioxide (SO_2), nitrogen dioxide (NO_2), Ozone (O_3) carbon monoxide (CO) and Particulate Matter (PM) as the main air pollutants negatively impacting on health outcomes. Other pollutants such as benzene have also been attributed to negative health outcomes in children with asthma[9]. The main sources of each vary (Table 1). Particulate matter (PM) is made up of solid and or liquid materials of differing size which be primary or secondary components[10] and is further quantified by size: <1 µm, ≤2.5µm and ≤10 µm. Outdoor air pollutants are typically measured from a distribution of fixed location monitoring stations. Local levels are modelled based on these measurements combined with meteorological patterns, taking into account the chemical reaction of different pollutants in the atmosphere to produce secondary pollutants[11]. In the UK, levels of air pollutants are reported in relation to the Air Quality Standards Regulations 2010 which

mandate limits for certain air pollutants. UK air pollution levels are currently higher than that recommended by the World Health Organisation (WHO) (see table 2).

Table 1 Air pollutants and sources

Pollutant	***Most common source*[10,12,13]**
Sulphur dioxide	*Combustion of sulphur containing fuels e.g. coal*
Nitrogen dioxide	*Power generation, industrial combustion and road transport*
Ozone	*Created by photochemical reactions involving nitrogen oxides and volatile organic compounds*
Carbon monoxide	*Produced from combustion of gas, oil, coal and wood*
Particulate matter	*Primary components* *Sea salt, black carbon, trace metals mineral components, road transport – fuel combustion and tyre/brake wear, road dust* *Secondary components* *Sulphate, nitrates*
Benzene	*Vehicle exhaust, evaporation of petrol*

Table 2 WHO vs UK recommended levels[7,14,15]

Air pollutant	***UK recommended level***		***European Union***		***WHO recommended level***	
Sulphur dioxide **µm/m³**	*24-hour average*	*125*	*24-hour average*	*125*	*24-hour average*	*40*
Nitrogen dioxide **µm/m³**	*Annual*	*40*	*Annual*	*40*	*Annual*	*10*
	24-hour average	*No limit set*	*24-hour average*	*No limit set*	*24-hour average*	*25*
Ozone **µm/m³**	*Annual*	*No limit set*	*Annual*	*No limit set*	*Annual*	*60*
	24-hour average	*No limit set*	*24-hour average*	*No limit set*	*24-hour average*	*100*
	8 hour mean	*100*	*8 hour mean*	*120*	*8 hour mean*	*No limit set*
Carbon monoxide **µm/m³**	*24-hour average*	*10*	*24-hour average*	*No limit set*	*24-hour average*	*4*
PM 2.5 **µm/m³**	*Annual*	*20*	*Annual*	*25*	*Annual*	*5*
	24-hour average	*No limit set*	*24-hour average*	*No limit set*	*24-hour average*	*15*
PM 10 **µm/m³**	*Annual*	*40*	*Annual*	*40*	*Annual*	*15*

	24-hour average	*50*	*24-hour average*	*50*	*24-hour average*	*45*

Asthma and air pollution

Asthma is one of the key respiratory conditions impacted by outdoor air pollutants. It is postulated that air pollutants physically obstruct and aggravate airways at bronchiole level[16]. Small particles and oxides can trigger the inflammatory cascade, resulting in acute bronchospasm in asthmatic airways[16–18]. Children are more vulnerable to the effects of air pollution compared to adults as they spend more time outdoors, have smaller airways and inhale a larger volume per kilogram per body mass compared to an adult[19]. Globally there is increasing evidence that outdoor air pollution adversely affects children with asthma. Air pollutants, such as particulate matter, have been found in placental phagocytes suggesting small particulates can enter the circulation and damage organ development[20,21]. Exposure to air pollution in pregnancy and infancy has been associated with the subsequent development of asthma, allergic sensitization and rhinitis in childhood[22–24] . Children exposed to air pollution can have lower lung function[25], increased asthma medication use[26,27], an increase in primary care, emergency care and hospital admissions[9,28–32]. The impact of viral infections in combination with air pollution has also been studied showing an increase in viral exacerbations of asthma when combined with higher air pollution exposure[33].

Challenges in interpreting air pollution data

There are several factors to be considered when applying large scale air pollution data to an individual and an asthma attack at a specific time point. Firstly, the monitoring and reporting of air pollution varies from country to country due to regional variations in the

types of air pollutants monitored and location of fixed monitoring stations. Urban areas are likely to have more stations within a smaller geographical radius compared to rural locations. Secondly, daily weather patterns are a significant contributing factor to air pollution exposure and extreme weather events such as thunderstorms, dust and sand storms will affect levels of air pollutants such as particulate matter[34]. Thirdly, air pollution is a broad term which is likely to refer to a mixture of pollutants, of which several or all may have an effect on asthmatic airways. Components such as particulate matter could refer to particles such as sea salt which is benign, or toxic industrial gaseous waste. Studies commonly address air pollutants individually and although this is useful, air pollutants are highly spatially correlated and thus the effects should be mixed together in epidemiological analyses to fully estimate the effect on a respiratory condition such as asthma. Fourthly, annual mean levels are often reported as thresholds for air pollution (see Table 2). Concentrations can vary significantly over relatively short time-scales and therefore annual means may overlook substantial peaks and troughs in a congested area. Although air pollution modelling is improving as advanced algorithms provide better spatial and temporal detail estimates (including hourly estimates at 100x100m spatial resolution), more frequently recorded, granular data would support better research though such data are less commonly available.

Personal exposure

Ideally, personal exposure to air pollutants should be considered when evaluating the impact of air pollution on health. In practice this is difficult to achieve. An individual's exposure to outdoor air pollutants will be less if they remain indoors when outdoor pollution levels are high. Children are more likely to be exposed based on activities of daily living as compared to adults, as children spend a higher proportion of their day outdoors.

Young children are closer to traffic-related air pollutants because of their small stature compared to adults which may increase exposure to air pollutants[35]. Without personal exposure measurement, the effect of air pollution globally, country wide or even regionally on an individual at the time of an attack can only be estimated based on modelled data. Exposure to indoor air pollutants have not been covered in this article but must also be taken into account when evaluating potential triggers of asthma attacks and risk factors for poor respiratory health[36].

Air pollution data related to fatal and near fatal asthma attacks is gathered retrospectively. Exposure to air pollutants around the time of an event is difficult to measure directly without personal exposure devices. Use of personal air pollution monitors has been studied in children with asthma[37,38] but it may be challenging in the context of asthma attacks which are unpredictable and may not occur when a participant is wearing a device. Measuring levels of air pollutants in a child's 'microenvironment' using personal monitoring devices may be useful when considering sources of daily exposures[38] but this has not yet been demonstrated in fatal or near fatal asthma attacks. Efforts to evaluate individual exposure (for example, from macrophages and presence of sputum carbon[39] demonstrate a possible mechanism to assess exposure, but again is of uncertain feasibility in relation to an acute severe attack. Activity diaries may be useful aids to guide personal exposure but linking personal exposure to an event will be highly individualised to each patient. The use of portable/personal devices such as spirometry may also help elucidate an association between exposure and health effects, whilst reducing exposure misclassification. Even the most robust observational study will struggle to estimate the actual exposure to air pollution around the time of an attack.

Near fatal and fatal asthma impacted by air pollution - are there more cases to come or have we missed many in the past?

Fatal and near fatal asthma attacks cause concern and anxiety for paediatric clinicians, parents, children and young people. Fatal and near fatal asthma is rare but the UK has one of the highest death rates from asthma in age 10 – 24 years[40]. Asthma attacks in children accounted for >19 000 admissions in England and Wales in 2022[41]. Despite heightened awareness of the importance of diagnosing and appropriately managing asthma, the National Review of Asthma Deaths report concluded that care was inadequate in 13 of the 28 deaths in children and young people that they investigated. People experiencing a near fatal attack are at high risk of future severe attacks and it is important for clinicians caring for children with asthma to evaluate the risk factors and features associated with near fatal and fatal attacks with an aim to reducing future risk.

Near fatal attacks are difficult to identify in the literature. The definition of near fatal asthma (and terminology used) overlaps with severe, life threatening and status asthmaticus and the use of 'diagnostic codes' to identify 'asthma' cases in routinely collected data does not further differentiate the severity of attacks within hospital. Near fatal events can be defined (see Box 1) but studies using routine data from hospital records to identify asthma attacks, typically use 'asthma' alone to find cases. Whilst this may correctly identify a case of asthma, it does not necessarily record the severity of presentation or any subsequent hospital deterioration. If a child had a sudden collapse due to asthma and required resuscitation, this would still be coded as asthma and in the same category as a child brought in to the emergency department who was discharged on the same day. This contributes to the loss of granularity of data on near fatal and fatal events,

where such attacks may exist but often poorly coded and consequently identifiable within routine data. Although large studies have demonstrated an increased frequency of acute asthma presentations associated with air pollution exposure[32], attack severity is not reported. We have only identified one study meeting the definition in Box 1 which has examined the effect of ozone and PM2.5 on near fatal asthma in children [42], which demonstrated an increase in admissions to intensive care. Two other studies included air pollution levels when assessing social deprivation and near fatal asthma, but neither focussed on this as a primary or secondary outcome[43,44]. There thus is a small body of literature examining asthma mortality and air pollution and there remains a significant and important gap in the literature regarding the impact of air pollution exposure on near fatal and fatal asthma attacks in CYP.

There are factors such as social deprivation which confound both severe asthma and air pollution. Higher concentrations of NO_2, PM10 and SO_2 are observed in areas of social deprivation in England, Scotland and Northern Ireland[45] and children from areas of higher deprivation are also more likely to be admitted to intensive care for asthma [46]. The degree of association between social deprivation, asthma and air pollution requires further observation but should be highlighted. In the UK, there is a current surveillance study examining near fatal asthma which will examine social deprivation and air pollution data around the time of event[47].

International E-Delphi defined Near Fatal Asthma Definition[48]

A near fatal asthma attack occurs in a person who is

- Exhausted, with severe dyspnoea, unable to speak with a silent chest.
- Respiratory arrest is considered imminent and invasive ventilation will likely be required.
- They will be responding poorly to emergency asthma therapies. This is associated with hypoxaemia, hypercarbia and a falling pH.

Box 1

Conclusion

We have an opportunity now to build on past work on near fatal and fatal events and air pollution. By including air pollution in the asthma risk factors assessed in a clinical history, we can start to shape the body of evidence on fatal and near fatal attacks. By increasing awareness of air pollution in conversations with our patients or their parents in the same way we would discuss smoking, atopy, pets etc. we start to highlight air pollution as a risk factor. Whilst the policy changes on air pollution exposure at local and regional levels are controlled by politicians, as clinicians we must now start to engage and consider the potential impact of air pollution for our individual patients. The question of how much exposure to air pollution is dangerous cannot yet be answered accurately, but we can start to ask the right questions (See Box 2) Some initiatives are already in place looking at 'clean air walks to school' but we need to encourage our patients that these can make a difference.

The body of evidence is growing, but better data will be required to support policy makers to deliver safer, lower exposure to air pollution levels in CYP with asthma. Reducing PM 2.5 by 1micro/hour could prevent 9300 new cases of asthma/year[49] and it is predicted if the UK becomes net zero we could reduce >20 000 cases of childhood asthma[50]. The death of Ella Kissi-Debrah has highlighted the devastating influence of outdoor air pollution and the urgent need for further research to understand the impact that air pollution may have on near fatal and fatal asthma in children. By keeping air pollution in mind in our clinical practice we can raise awareness, add to the evidence and find out more about near fatal and fatal asthma cases associated with air pollution.

Suggested questions for clinicians reviewing children experiencing asthma exacerbations
• How do you get to school? Do you walk beside a busy road? Do you travel to school by car? • Do you need your inhaler when you are walking beside a busy the road? • Do you play outside close to a busy road at break time? • Do you know about clean air walks to school? • Is your patient's home positioned beside a source of traffic related air pollution such as a busy road and if so, how do they ventilate their home i.e. windows open or closed during peak traffic times?

Box 2

Suggestions

1. Help to identify the severity of asthma attacks in routine data. We need to know more about fatal and near fatal attacks in children. Consider a coded definition for

near fatal asthma (See Box 1) to increase the granularity of future data on near fatal asthma.

2. Add air pollution questions to your asthma history (see Box 2) - think when are they exposed (day time activities, how long and how often)
3. Consider reporting any cases of e-Delphi defined near fatal asthma to the British Paediatric Surveillance Unit study (October 2022 to April 2024).

Contribution Statement

All authors contributed to the research, analysis of the results and to the writing of the manuscript. All authors reviewed and revised interim drafts of the article and approved the final version. Co Authors: Dr Tom Clemens (TC), Dr Ann McMurray (AM), Professor Hilary Pinnock (HP), Professor Jonathan Grigg (JG) and Professor Steve Cunningham (SC).

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