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A meta-analysis of blood lead levels in India and the attributable burden of disease

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ABSTRACT

Multiple studies in India have found elevated blood lead levels (BLLs) in target populations. However the data have not yet been evaluated to understand population-wide exposure levels. We used arithmetic mean blood lead data published from 2010 to 2018 on Indian populations to calculate the average BLLs for multiple subgroups. We then calculated the attributable disease burden in IQ decrement and Disability Adjusted Life Years (DALYs). Our Pubmed search yielded 1066 articles. Of these, 31 studies representing the BLLs of 5472 people in 9 states met our study criteria. Evaluating these, we found a mean BLL of 6.86 μg/dL (95% CI: 4.38–9.35) in children and 7.52 μg/dL (95% CI: 5.28–9.76) in non-occupationally exposed adults. We calculated that these exposures resulted in 4.9 million DALYs (95% CI: 3.9–5.6) in the states we evaluated. Population-wide BLLs in India remain elevated despite regulatory action to eliminate leaded petrol, the most significant historical source. The estimated attributable disease burden is larger than previously calculated, particularly with regard to associated intellectual disability outcomes in children. Larger population-wide BLL studies are required to inform future calculations. Policy responses need to be developed to mitigate the worst exposures.

1. Introduction

Lead is a naturally occurring metal with a range of industrial applications and well-documented adverse health effects when human exposure occurs (ATSDR, 2007). Its widespread use has resulted in significant contamination of natural and human environments (Needleman, 2004; Prüss-Üstün et al., 2010). Chronic lead exposure, even at very low levels, is associated with cognitive impairment, cardiovascular effects, anemia and low birth weight, among other adverse health outcomes (Budtz-Jørgensen et al., 2013; Lanphear, 2015; National Toxicology Program, 2012; United Nations Environment Programme, 2010). Lead exposure has been associated with decreased economic output, lower life expectancy and increased societal violence (Demayo et al., 1982; Landrigan and Goldman, 2011; Mielke and Zahran, 2012; Prüss-Üstün et al., 2010; Taylor et al., 2016).

The 2016 Global Burden of Disease, Injuries and Risk Factors Study by the Institute for Health Metrics and Evaluation (IHME) estimated that lead exposure resulted in 13.9 million Disability-Adjusted Life Years (DALYs) and 540,000 deaths in 2016 globally. The DALY metric is used in quantifying the burden of disease and is intended to capture morbidity and mortality attributable to a given disease or risk factor in a population (World Health Organization, 2016). In India alone, IHME found 4.6 million lead-attributable DALYs and nearly 165,000 deaths (IHME, 2017a).

The most significant historic source of global lead exposure was the use of tetraethyl lead in petrol in the 20th century (Bollhöfer and Rosman, 2001, 2000; Flegal et al., 1984; McConnell et al., 2015; Schwikowski et al., 2004; Véron et al., 1999). In cities where it was used, leaded petrol accounted for 80 to 90% of airborne lead pollution (Lovei, 1999). High-income countries began banning the use of lead in most fuels, as well as in paints, in the 1970s, resulting in significant declines in societal blood lead levels (BLLs) (Needleman, 2004). Leaded

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petrol was phased out in India from 1996 to 2000 and was similarly followed by BLL declines (Singh and Singh, 2006). Nichani et al. (2006), for instance, documented a 60% decrease in BLLs among residents of Mumbai from 1997 to 2002, following the full adoption of unleaded petrol. Similarly, Singh and Singh (2006) found a mean BLL decrease of 33% following the leaded petrol phase out in the urban centers of Mumbai, Chennai, Bangalore, Amritsar and Lucknow.

Despite these substantial improvements in exposure reduction, studies conducted more than a decade after the Indian phase out of leaded petrol continue to report elevated BLLs, often associated with proximity to lead smelting sites (Bellinger et al., 2005; Ghose et al., 2005; Sharma et al., 2005). Other sources of lead exposure to the Indian public have included ayurvedic medicine, cosmetics (kohl/surma) and contaminated foodstuffs (Goswami, 2013; Raviraja et al., 2010; Singh et al., 2010; Singhal, 2016). In some cases these exposures have found severely elevated levels in both occupational and non-occupational settings (Ghanwat et al., 2016; Goswami, 2013). Studies of environmental media have reported elevated lead concentrations in tube wells, rivers, and soil, among other media (Borah et al., 2010; Chatham-Stephens et al., 2013; Lokhande et al., 2012). With regard to lead-based paint, India currently maintains one of the stricter global limits of 90 ppm soluble lead (UNEP, 2017). However a 2015 study that assessed store-bought cans of enamel paint found that 46% of those tested contained > 10,000 ppm lead (Toxics Link, 2015). Additionally, some studies have posited lead-based paint as a possibly significant source of exposure (Ahamed et al., 2009; Khan et al., 2010).

Few studies have attempted to calculate population-wide mean BLLs in low- and middle-income countries (LMICs), with most focusing on discrete cohorts of exposed individuals (Olympio et al., 2017). Caravanos et al. (2014) conducted a meta-analysis of BLLs in Mexico, finding a mean concentration of 5.36 μg/dL in urban areas after the phase out of leaded petrol. A 2009 study of Chinese BLLs reviewed published papers and found a mean BLL of 7.93 μg/dL for male children and 7.69 μg/dL for female children living in urban areas (He et al., 2009).

In this assessment we reviewed existing studies on BLLs to infer broader conclusions about the population of a subset of India. We first conducted a literature review and meta-analysis of Indian BLLs published between 2010 and 2018. We then used the results to quantify the disease burden in terms of IQ decrement and attributable DALYs. The objective of this study was to quantify the potential public health impacts of lead exposure in India and to stimulate policies, education, and, where appropriate, remediation of contaminated sites.

2. Methods and approach

2.1. Literature review and data selection

We conducted a PubMed search in April 2018 using the terms blood (subheading, all fields, MeSH terms) lead (all fields, MeSH terms), and India (all fields, MeSH terms, abstract text) between 1 January 2010 and 1 January 2018 (National Library of Medicine (US), 1946). We then assessed each article by a the following 6 criteria: 1) the study published BLL data from human populations residing in India; 2) the study included at least 30 participants; 3) BLL data were derived from venous, capillary, or umbilical cord samples (bone, organ or tissue samples were excluded); 4) the utilized data were collected after 2005; 5) the study was published in English; 6) the study contained a statistical mean and standard deviation (SD) or standard error (SE) for the original data set. Articles that did not meet one or more of the above criteria were excluded from the meta-analysis.

2.2. Subgroup rational

The BLL data for each study were analyzed by certain demographic categories following the literature review. Where possible samples were disaggregated by the following four subgroups: gender, age, urbanicity, and occupation.

Age categories were defined using United Nations Children's Fund's parameters outlined in the Convention on the Rights of the Child. An individual was considered a “child” if he or she was at or below the age of 17 at the time of the original study, and an “adult” if he or she was identified as at or above 18 (United Nations General Assembly, 1989). Gender was stratified into four different categories: female, male, both and unspecified. Urbanicity was determined by a review of studies for ‘urban’ or ‘rural’ keywords. If this was not indicated in the article, the study location was used to make this determination. The Census of India classification of 400 people per square kilometer was used as the threshold for an urban area (India, 2011). Finally samples were coded as occupational if the relevant occupation substantively involved lead and therefore a higher risk of elevated BLLs. Samples comprised of battery recyclers for instance were coded as occupational, while studies of teachers were coded as non-occupational.

2.3. Identification and use of sample means

Where possible, the mean and SD/SE were derived for our specific subgroups. In cases where the subgroups used by study were incongruous with our own, the mean and SD/SE were taken for a larger subset, such as the study population.

If the same population was assessed multiple times, and treatment was not provided in between assessments, the mean for all analyses was used. In cases where the mean for all analyses could not be taken, the most conservative value (i.e. lowest) value was used. If treatment was provided to the patients with the intent of lowering BLLs, pre-treatment values were used.

Three studies assessed the BLLs of the same large cohort of untreated children at different points (Palaniappan et al., 2011; Roy et al., 2013, 2009). In this case, one study had a slightly larger sample size than the other two and all presented similar overall results with regard to BLLs. The study with the largest population was thus included and the other two were excluded.

In one case, BLLs were assessed at the same point using multiple methods having different results (Reddy et al., 2014). In this case we selected the most conservative (i.e. lowest) value.

Some studies segregated the sample exclusively based on the results of the BLL test (e.g. high and low subgroups). In these cases we took the pooled BLL for the study. In one study (Ravibabu et al., 2015), the pooled mean was not available. We therefore used both subgroups as discrete samples. Other studies disaggregated the sample by health outcome. Tiwari et al. (2012), for instance analyzed BLLs for three groups of anemic women (mild, moderate, severe) and one control group. A pooled mean was not available for the study as a whole, so we used the means for each subgroup and presented them as discrete samples.

Two studies, Goswami et al. (2013) and Chaudhary et al. (2017), found exceptionally high BLLs in children. While the exposures that result in these BLLs were not occupational they do represent an acute scenario that is not representative of the general population, thus justifying their exclusion. Goswami et al. (2013) looked at children that apply surma (kohl) as a cosmetic, which has long been identified as an acute source of lead exposure, and a control group of children that do not apply surma (Ali et al., 1978; Gogte et al., 1991). In this case a study mean was not available, so we utilized the control group and excluded the exposed group. Chaudhary et al. (2017) assessed the BLLs of 260 children (age 6 months to 12 years) attending the pediatrics outpatient department at a hospital in Lucknow, Uttar Pradesh. The study reported a mean BLL of 55.7 μg/dL (SD: 227.38). We were unable to identify a comparably high value of a general population in the literature. Other studies in Lucknow have found much lower levels. Ahamed et al. (2011) assessed the BLLs of 68 children (age 3–12 years) in Lucknow, finding BLLs of 4.23–9.86 μg/dL. An earlier study by the same authors