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Risk-Factor Based Lead Screening and Correlation with Blood Lead Levels in Pregnancy

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Abstract

Objectives Lead exposure has devastating neurologic consequences for children and may begin in utero. The American College of Obstetricians and Gynecologists recommends prenatal lead screening using a risk factor-based approach rather than universal blood testing. The clinical utility of this approach has not been studied. We evaluated a risk-factor based questionnaire to detect elevated blood lead levels in pregnancy.

Methods We performed a secondary analysis of a cohort of parturients enrolled to evaluate the association of lead with hypertensive disorders of pregnancy. We included participants in this analysis if they had a singleton pregnancy ≥ 34 weeks' gestation with blood lead levels recorded. Participants completed a lead risk factor survey modified for pregnancy. We defined elevated blood lead as ≥ 2 µg/dL, as this was the clinically reportable level.

Results Of 102 participants enrolled in the cohort, 92 had blood lead measured as part of the study. The vast majority (78%) had 1 or more risk factor for elevated lead using the questionnaire yet none had clinical blood lead testing during routine visits. Only two participants (2.2%) had elevated blood lead levels. The questionnaire had high sensitivity but poor specificity for predicting detectable lead levels (sensitivity 100%, specificity 22%).

Conclusions for Practice Prenatal risk-factor based lead screening appears underutilized in practice and does not adequately discriminate between those with and without elevated blood levels. Given the complexity of the risk factor-based approach and underutilization, the benefit and cost-effectiveness of universal lead testing should be further explored.

Keywords Lead exposure · Prenatal screening · Pregnancy · Risk factors

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Significance

Lead exposure has devastating neurologic consequences for children and may begin in utero. Risk factor-based screening is recommended in the prenatal population, rather than universal testing. This study assessed test characteristics of a risk-factor based questionnaire, using blood lead levels as the gold standard for exposure. The authors demonstrated underutilization of the risk factor-based approach in their clinical setting and poor performance of the tool to discriminate elevated from undetectable lead levels. Alternative strategies to identify and ameliorate prenatal lead exposure are needed, particularly when prevalence of elevated lead is low.

Introduction

Public health efforts have dramatically decreased lead levels in the U.S. population over the past three decades (*Fourth National Report on Human Exposure to Environmental Chemicals Update*, 2019), primarily through removal of lead from gasoline and phasing out lead-based paint for commercial and residential purposes (Egan et al., 2021). Nevertheless, due to the neurotoxic effects of lead on the developing brain, even at very low levels, exposure during early life is particularly devastating (Dórea, 2019). These effects can lead to learning and behavior differences, as well as impaired growth and hearing (Ettinger & Wengrovitz, 2010). While most pediatric exposure occurs from ingestion of contaminated dust or soil in older homes through hand-mouth behaviors in early childhood (Hauptman et al., 2017), prenatal exposure may be independently neurotoxic (Bellinger et al., 1987) and can contribute to the overall body burden. Elevated lead levels during pregnancy also appears to be associated with a range of adverse pregnancy outcomes including preterm birth, impaired fetal growth and possibly hypertensive complications of pregnancy and have been observed across a range of exposures, including as low as 2.3 µg/dL (Ettinger & Wengrovitz, 2010; Jusko et al., 2008; Liu et al., 2013).

The American College of Obstetricians and Gynecologists (ACOG) recommends prenatal lead screening using a risk factor-based approach rather than universal blood lead testing (Fig. 1) (Committee on Obstetric Practice, 2012). Risk factors include prior residence in countries with high lead contamination, pica behavior, renovation of older housing stock, use of some imported cosmetics or herbal remedies, engaging in high risk hobbies like pottery making with leaded glazes, and high risk occupations (battery manufacturing, ship building, ammunition production) (Ettinger & Wengrovitz, 2010). As is evident from Fig. 1, translating these risk factors into simple screening questions is not straightforward (Ettinger & Wengrovitz, 2010). Furthermore, no questionnaires have been validated in pregnancy (US Preventive Services Task Force et al., 2019).

We undertook this study to (1) ascertain whether risk factor-based lead screening was routinely performed in pregnancy at an urban tertiary medical institution and (2) evaluate the ability of a risk assessment questionnaire to identify clinically reportable prenatal lead levels.

Methods

Enrollment

We performed a secondary analysis of a cohort of patients originally enrolled in the primary study to evaluate the association of lead levels with hypertensive disorders of pregnancy (Johnson et al., 2020). Detailed methods for recruitment of parturients have been published, but in brief, individuals were approached for inclusion in the primary study over a six-month period from 2018 to 2019 at a single institution (Boston) if they presented for obstetric admission or triage of an acute issue, were at least 34 weeks' gestation, had a singleton pregnancy, and planned delivery at the study site. For this secondary analysis, we included all participants who had blood lead levels measured in the original study. At the time of recruitment, all eligible participants were offered written material about the risks of lead exposure in pregnancy, as well as the risks of lead to their families. Participants provided written informed consent. We utilized trained medical interpreters to approach and consent participants whose preferred language was not English. The institutional review board at the primary study site approved this study. The institutional review board at the affiliated school of public health ceded review.

Questionnaire

The participant was asked to fill out a brief questionnaire postpartum. The questionnaire included a screening for lead, modified from the New York City Department of Health Lead Risk Assessment Questions for Pregnant Women (Ettinger & Wengrovitz, 2010). This questionnaire was chosen because it was specifically designed for pregnant women and also because it was one of two questionnaires highlighted in the landmark Centers for Disease Control and Prevention (CDC) document on lead screening in pregnancy (Ettinger & Wengrovitz, 2010). We modified the questionnaire slightly, in that we separated the question regarding time spent abroad and birth abroad into separate questions.

Box 1: Risk Factors for Lead Exposure in Pregnant and Lactating Women

- Recent emigration from or residency in areas where ambient lead contamination is high—women from countries where leaded gasoline is still being used (or was recently phased out) or where industrial emissions are not well controlled.
- Living near a point source of lead—examples include lead mines, smelters, or battery recycling plants (even in the establishment is closed).
- Working with lead or living with someone who does—women who work in or who have family members who work in an industry that uses lead (e.g., lead production, battery manufacturing, paint manufacturing, ship building, ammunition production, or plastic manufacturing) and do not practice OSHA-recommended guidance in industrial hygiene.
- Women who work in security or as police officers or in the military and engage in target practice using firearms in improperly cleaned or ventilated indoor ranges without appropriate gloves and other personal protective clothing.
- Using lead-glazed ceramic pottery—women who cook, store, or serve food in lead-glazed ceramic pottery made in a traditional process and usually imported by individuals outside the normal commercial channels.
- Eating nonfood substances (pica)—women who eat or mouth nonfood items that may be contaminated with lead, such as soil or lead-glazed ceramic pottery.
- Using alternative or complementary substances, herbs or therapies—women who use imported home remedies or certain therapeutic herbs traditionally used by East Indian, Indian, Middle Eastern, West Asian, and Hispanic cultures that may be contaminated with lead.
- Using imported cosmetics or certain food products—women who use imported cosmetics, such as tiro or kohl or surma or certain imported foods or spices that may be contaminated with lead. Lead-acetate containing hair dyes can also be sources of contamination.
- Engaging in certain high-risk hobbies or recreational activities—women who engage in high-risk activities (e.g. stained glass production or pottery making with certain leaded glazes and paints or amateur firearms marksmanship activities using indoor gun ranges) or have family members who do
- Renovating or remodeling older homes without lead hazard controls in place—women who have been disturbing lead paint or plaster and/or creating lead dust by sanding or scraping painted, varnished, or plastered surfaces or participating in demolition work.
- Consumption of lead-contaminated drinking water—women whose homes have leaded pipes or sources lines with lead.
- Having a history of previous lead exposure or evidence of elevated body burden of lead—women who have high body burdens of lead from past exposure, particularly those who have deficiencies in certain key nutrients (calcium or iron).
- Living with someone identified with an elevated lead level—women who may have exposure in common with a child, close fried, or other relative living in the same environment.

Fig. 1 Risk factors for lead exposure in pregnant and lactating women. Adapted from The American College of Obstetricians and Gynecologists Committee Opinion Number 533, August 2012, reaffirmed 2016. This box was modified by ACOG from the Centers for Disease Control and Prevention, Guidelines for the identification and management of lead exposure in pregnant and lactating women. (Committee on Obstetric Practice, 2012)

Table 1 Questionnaire questions and how population responded

Question	Blood lead available, n = 92
Any question answered "yes"	
Yes	72 (78)
No	20 (22)
More than 2 "yes" responses	
Yes	48 (52)
No	44 (48)
In the last 12 months, has there been any renovation or repair work in your home or apartment building?	
Yes	40 (43)
No	50 (54)
Unsure	2 (2)
Have you ever had a job or hobby that involved possible lead exposure, such as home renovation or working with glass, ceramics, or jewellery?	
Yes	7 (8)
No	84 (91)
Unsure	1 (1)
At any time during your pregnancy did you eat, chew on, or mouth non-food items such as clay, crushed pottery, soil, or paint chips?	
Yes	0 (0)
No	92 (100)
Unsure	0 (0)
During the past 12 months, did you use any imported health remedies, spices, foods, ceramics, or cosmetics?	
Yes	9 (10)
No	78 (85)
Unsure	5 (5)
Were you born outside of the United States?	
Yes	28 (30)
No	64 (70)
Unsure	0 (0)
Have you spent time living for an extended period of time (more than 1 month) outside of the United States?	
Yes	47 (51)
No	45 (49)
Unsure	0 (0)

Data presented are n (%)

The questions are listed in Table 1. Participants were also asked to identify their race, ethnicity, place of birth, and occupation. A medical record review was performed to ascertain medical history, obstetrical history, medication use, delivery outcomes, and neonatal outcomes. All data were stored in REDCap (Harris et al., 2009).

Blood Lead Measurement

Venous blood was collected prior to delivery in the third trimester as part of the original study, with methods detailed elsewhere (Johnson et al., 2020). In brief, an aliquot of 100 µl of whole blood was stored at -80 ˚C for later blood lead testing, performed at a CLIA-certified clinical laboratory.

Statistical Analysis

Blood lead ≥ 2 µg/dL was clinically reportable by the local Clinical Laboratory Improvement Amendments of 1988 (CLIA) certified laboratory, although the limit of detection was as low as 0.1 µg/dL. Because there is no safe level of lead (Prevention of Childhood Lead Toxicity, 2016) and ever increasing improvement in methods to detect lead (Caldwell et al., 2017), we used the clinically reportable level to define elevated blood lead for our analysis. Data are reported as proportion or median (interquartile range, IQR). We calculated sensitivity, specificity, positive predictive value and negative predictive value (with 95% confidence intervals) for any positive response on the questionnaire.

Results

Out of an annual delivery volume of approximately 5000 patients, 150 were approached and 102 enrolled and constituted a convenience sample over a 6-month time period. One participant withdrew consent prior to participation. Of the 101 remaining participants, 9 did not have a blood measurement performed due to inability to obtain blood sample prior to delivery, leaving 92 participants for assessment of blood lead concentrations prior to delivery and inclusion in this analysis.

Participant characteristics are shown in Table 2. Most participants were Caucasian. A majority of participants were employed in the healthcare or educational setting. None of the participants had blood lead testing done during pregnancy as part of routine clinical care. Seventy eight percent of participants reported at least one risk factor for lead, with 46% reporting 2 or more risk factors. The most common reported risk factors were renovation or repair work in the home (43%) or time spent outside of the United States (51%) (Table 1). The question regarding use of imported health remedies, spices, or cosmetics generated the most "Unsure" responses (n = 5).

Median blood lead was 0.2 µg/dL (IQR 0.2–0.4), with a range of 0 to 6.4 µg/dL. Two participants (2.2%) had clinically reportable (≥ 2 µg/dL) blood lead, with only one of these participants with a blood lead level above 5 µg/dL, which is the CDC actionable blood lead level in pregnancy (Ettinger & Wengrovitz, 2010). The two participants with elevated blood lead both spent extended time abroad (one through travel and one through birth abroad), but did not answer yes to any other questions on the risk factor questionnaire (Table 3). Sensitivity for identifying detectable maternal lead levels was high with any positive response on the questionnaire; however, the corresponding specificity was low (Table 3). None of the individual components of the questionnaire had more than 50% sensitivity to detect elevated blood lead, although the negative predictive value in this population was overall good, likely due to low prevalence of lead exposure.

Table 2 Participant characteristics

Characteristics	Overalln = 92	Positive screen[a] n = 72	Negative screen n = 20
Demographics			
Maternal age	34 (31–36)	34 (31–36)	33 (30–35.5)
Race			
Caucasian	62 (67)	50 (69)	12 (60)
African American	7 (8)	4 (6)	3 (15)
Asian	11 (12)	9 (12)	2 (10)
Other	12 (13)	9 (12)	3 (15)
Hispanic	8 (9)	7 10)	1 (5)
Nulliparous	56 (61)	47 (65)	9 (45)
Occupation			
Healthcare	19 (21)	12 (17)	7 (35)
Education, arts, media, legal	30 (33)	27 (37)	3 (15)
Service	7 (8)	4 (6)	3 (15)
Management, business, financial	10 (11)	8 (11)	2 (10)
Sales and office	7 (8)	6 (8)	1 (5)
Computer, engineering, science	5 (5)	4 (6)	1 (5)
Not employed[b]	14 (15)	11 (15)	3 (15)
Medical factors			
BMI > 30 at delivery	56 (61)	42 (58)	14 (70)
Anemia (Hematocrit < 33)	19 (21)	12 (17)	7 (35)
Smoking status			
Never smoker	83 (90)	65 (90)	18 (90)
Ever smoker	9 (10)	7 (10)	2 (10)
Gestational age at blood draw	38.6 (36.9–40.1)	38.9 (35.9–40.4)	37.0 (36.1–39.6)

Data presented as median (interquartile range) or n (%)

[a]Positive screen if any answers were yes to risk assessment questionnaire

[b]Not employed = student, homemaker, and no occupation listed

Table 3 Proportion with detectable blood lead and testing characteristics among those who answered positively to questionnaire, stratified by individual questions

Question	Blood lead ≥ 2 µg/dL, n = 2	Blood lead < 2 µg/dL, n = 90	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
Any positive response	2	70	100 (16–100)	22 (14–32)	3 (0–10)	100 (83–100)
Two positive responses	0	40	0 (0–84)	47 (36–58)	0 (0–7.4)	96 (85–99)
Individual components of the questionnaire						
In the last 12 months, has there been any renovation or repair work in your home or apartment building?	0	40	0 (0–84)	56 (45–66)	0 (0–9)	96 (87–100)
Have you ever had a job or hobby that involved possible lead exposure, such as home renovation or working with glass, ceramics, or jewelry?	0	7	0 (0–84)	92 (85–97)	0 (0–41)	98 (92–100)
At any time during your pregnancy did you eat, chew on, or mouth non-food items such as clay, crushed pottery, soil, or paint chips?	0	0	n/a	n/a	n/a	n/a
During the past 12 months, did you use any imported health remedies, spices, foods, ceramics, or cosmetics?	0	9	0 (0–84)	90 (82–95)	0 (0–34)	98 (92–100)
Were you born outside of the United States?	1	27	50 (1–99)	70 (59–79)	4 (0–18)	98 (92–100)
Have you spent time living for an extended period of time (more than 1 month) outside of the United States?	1	46	50 (1–99)	49 (38–60)	2 (0–11)	98 (88–100)

Discussion

Among a population of parturients presenting to a single Boston-based hospital for admission in the third trimester, we found that a risk-factor based approach for detecting lead exposure identified all parturients with elevated lead levels. Nevertheless, only a small number had detectable lead (2.2%) and thus the specificity and positive predictive value of the screening test was poor. Moreover, the recommended prenatal risk factor-based lead screening appears underutilized in practice. Among parturients presenting for admission in the third trimester, none of the 72 with identifiable risk factors had lead measured during routine prenatal care; though only 2 of those 72 had reportable lead levels.

Though the questionnaire identified all parturients with elevated blood lead, the questionnaire was not specific, and nearly 4 of 5 individuals screened positive and would require blood lead testing with this approach. No single question alone had high enough sensitivity to justify eliminating the others. Validated questionnaires do not exist in pregnancy, limiting comparison of our results with those of others. A recent systematic review by the United States Preventive Services Task Force (Cantor et al., 2019) included only one observational study, which assessed the utility of a questionnaire in screening for lead exposure in pregnancy (Stefanak et al., 1996). In a population with a 13% prevalence of elevated lead, which is much higher than in our study, the questionnaire performed poorly, with a sensitivity of about 76% and specificity of 46% (Stefanak et al., 1996). The questionnaire evaluated by these authors was modified from the CDC questionnaire used for children, and interestingly identified many families with elevated lead in both children and pregnant women. The questionnaire in our study, however, took into account more pregnancy-specific behaviors and notably included the risk factor of birth abroad, which has been associated with elevated blood lead levels in U.S. populations (Klitzman et al., 2002).

Risk factors for lead exposure are better studied among children, and most screening questionnaires focus on identifying sources of lead exposure in the pediatric population (Cantor et al., 2019). Limited information about risk factors in pregnancy exist, but the existing information suggests that behaviors such as pica and occupational exposures likely contribute (Bakhireva et al., 2013; Fletcher et al., 1999). In another study, there was not an identifiable current source of lead exposure among a third of women who screened positive (Fletcher et al., 1999). Interestingly, none of the parturients in our study reported pica. Our finding may be because women are unlikely to report pica if asked about it directly (Simpson et al., 2000) or it may be that the population studied is not one in which pica is common. There also did not appear to be a high proportion of participants with occupational or hobby exposures to lead, limiting the generalizability of this study to populations with more exposure to occupational or hobby risk factors. Of all the risk factors evaluated in our study, the most commonly identified ones were home renovation and travel abroad, factors that turn out to be nonspecific and suggest that over three-quarters of

the prenatal population is at risk for elevated lead. Refinement of these questions to include just repair work on homes built prior to elimination of lead paint or residence abroad in places with high lead levels may improve specificity and deserves further study.

Risk-factor based screening identifies cases of elevated blood lead, but is not specific. Given the complexity of the risk factor-based approach, it is understandable that obstetric providers have not operationalized it. Limited utility of questionnaires for children (Kazal, 1997; Ossiander, 2013) has led to universal screening in many states. Blood lead screening in pregnancy, however, is not recommended (Cantor et al., 2019; Committee on Obstetric Practice, 2012; Ettinger & Wengrovitz, 2010). Universal lead testing would be easier to operationalize, as adding one more test to the prenatal panel would be straightforward. However, the benefit and cost-effectiveness of such an approach in improving outcomes and preventing childhood lead neurotoxicity remains unclear (Cantor et al., 2019) and warrants future research.

Strengths

Strengths of our study include utilization of a pregnancy-specific questionnaire to assess utility of a risk-factor based approach to screening for lead, an understudied question. Our study adds to the body of knowledge about this approach. Moreover, compared to the CDC questionnaire on childhood lead exposure evaluated in other studies in pregnancy, (Stefanak et al., 1996) the questionnaire utilized in our study was more specific to pregnancy. In addition, while our sample was overall small, it was similar to the institution's obstetric population in general with respect to maternal age, race, ethnicity, and body mass index (BMI) (Modest et al., 2019).

Limitations

Our population overall had a low level of lead exposure, and thus our findings regarding the testing characteristics of the questionnaire, cannot be generalized to a population with different characteristics or where pica or occupational exposures may be more prevalent. Moreover, our study was limited to a single center, which overall limits generalizability. Nevertheless, the blood lead levels we observed were comparable to the U.S. population overall. The mean U.S. blood lead in a 2015–2016 cohort of adults was 0.82 µg/dL (95% CI 0.77–0.87) (*Fourth National Report on Human Exposure to Environmental Chemicals Update*, 2019). In addition, we utilized just one questionnaire and thus can only apply our findings to the performance of a single questionnaire adopted from New York State's prenatal screening efforts.

In summary, we found that risk-factor based screening is underutilized in practice at our tertiary institution. Use of a pregnancy-specific questionnaire to perform risk-factor based screening for elevated lead identifies parturients with elevated blood lead levels with good sensitivity but poor specificity. Future studies should correlate prenatal screening with lead detection among children, given the potential benefit for earlier identification of at-risk infants and also to determine the true costs associated with different screening strategies.

Author Contributions KMJ, AJS, MRH, SAK, KO and BJW contributed to all aspects of the manuscript, from design, planning, conduct, data analysis and manuscript writing. JMH and SS contributed to the conduct and manuscript writing. ALE contributed to the design, data analysis, and manuscript writing. ADW and MH contributed to design, conduct and manuscript writing.

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Declarations

Conflict of interests The authors declare that they have no conflict of interest.

Ethical Approval The institutional review board at the Beth Israel Deaconess Medical Center approved this study. The institutional review board at the Harvard T. H. Chan School of Public Health ceded review.

Consent to Participate All enrolled participants provided written informed consent.

Data Availability Data is not available for sharing.

Code Availability Code is not available for sharing.

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