Heliyon 8 (2023) e12582

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Research article

The construction and validation of a lead exposure screening tool for pregnant women in Thailand (ThaiL8Is)

Donrawee Waeyeng [a], Tanaporn Khamphaya [a], Phisit Pouyfung [b], Udomratana Vattanasit [c], Walaiporn Pramchoo [d], Supabhorn Yimthiang [a,*]

[a] Environmental, Safety Technology and Health Program, School of Public Health, Walailak University, Thaiburi, Thasala, Nakhon Si Thammarat 80160, Thailand
[b] Occupational Health and Safety Department, School of Public Health, Walailak University, Thaiburi, Thasala, Nakhon Si Thammarat 80160, Thailand
[c] Environmental Health and Technology Department, School of Public Health, Walailak University, Thaiburi, Thasala, Nakhon Si Thammarat 80160, Thailand
[d] Community Public Health, Faculty of Science and Technology, Hat Yai University, Kho Hong, Hatyai, Songkhla, 90110, Thailand

ARTICLE INFO

Keywords:
Blood lead levels
Lead exposure
Screening tool
Pregnant women

ABSTRACT

Objectives: To construct, validate, and implement a new screening tool for lead exposure in Thai pregnant women.
Methods: A cross-sectional study that included three processes: screening tool development, validation, and implementation. The participants were pregnant women who had received antenatal care at district health promotion hospitals. There were 100 pregnant women in Nakhon Si Thammarat province during the validation process, and 30 pregnant women in Phang Nga province during the implementation process. Blood lead levels (BLLs) were analysed by atomic absorption spectrophotometry. The sensitivity and specificity of the screening instrument, as well as the Area Under the Curve (AUC), demonstrate its validity.
Results: There were 80 BLL-related items found through the collection of primary and secondary data and examined for validity and inter-rater reliability by five experts. Six items were excluded because the values were less than the criteria set. Seventy-four items remained with the Item Content Validity Index (I-CVI) = 0.80–1.00, the Content Validity Index Average (S-CVI/Ave) = 0.91, and Kappa scores = 0.76–1.00. After using 74 items collected on pregnant women, only 31 items were included in the validation process. Following that, the pooled eight items with cut-off point scores of 1 had the highest validity, which included systolic blood pressure, diastolic blood pressure, urine sugar, haemoglobin level, occupation, drinking coffee, using chemical products, and education level (ThaiL8Is). The ThaiL8Is in the validation process yielded sensitivity = 80.9%, specificity = 69.8%, and an AUC (95%CI) = 0.78 (0.69–0.87). The implementation process has confirmed the validity of the screening tool; sensitivity = 78.9%, specificity = 81.8%, and the AUC (95%CI) = 0.80 (0.63–0.97).
Conclusions: The ThaiL8Is a valid screening tool for Thai pregnant women. ThaiL8Is' sensitivity in detecting the risk groups for lead exposure can be enhanced by a combination of biochemical markers used in routine prenatal screening. It can be used to screen pregnant women for early indicators of lead exposure prior to a blood lead test.

1. Introduction

Lead (Pb) is a toxin that can be transferred from a pregnant woman's placenta to a foetus or from the mother's breast milk to a baby [1] Its teratogenic effects have also been demonstrated in several rodent and human studies [2, 3]. Pregnant women who are exposed to lead, even at low levels, are at risk of developing gestational hypertension, anaemia, and spontaneous abortion [4, 5]. Infants with lead exposure from mothers during the first trimester had significantly more pronounced adverse neurological development effects than those in other trimesters [6]. Historically, the main source of lead was known to be from gasoline, but more recent studies have pointed to a considerably broader range of sources, including contaminated food and beverages, fishery occupations, and cosmetics products such as lipstick, mascara, and hair dye [7, 8, 9, 10]. As it currently stands, no safe threshold for blood lead levels (BLLs) has been identified [11].

High BLLs in pregnant women are a concern in many countries. Pregnant women in Asia, such as in China and India, have average BLLs of 2.40–9.20 μg/dL [12, 13]. In Thailand, there is currently limited data available on BLLs in pregnant women. However, one study in 1993

* Corresponding author.
E-mail address: ksupapor@mail.wu.ac.th (S. Yimthiang).

https://doi.org/10.1016/j.heliyon.2022.e12582
Received 24 July 2022; Received in revised form 11 October 2022; Accepted 15 December 2022

Table 1. The definition and formula of I-CVI, S-CVI/Ave and K.

Index	Definition	Formula
I-CVI	The proportion of content experts giving item a relevance rating of 4.	I-CVI = (agreed item)/(number of expert)
S-CVI/Ave	The average of the I-CVI scores for all items on the scale or the average of proportion relevance judged by all experts. The proportion relevant is the average of relevance rating by individual expert.	S-CVI/Ave = (sum of I-CVI scores)/(number of item)
K	The Kappa statistic, a consensus index of interrater agreement that adjusts for chance agreement.	$(\text{I-CVI-}p_c)/(1\text{-}p_c)$; $p_c = [N!/A!(NA)!]*.5^N$ where N = number of experts and A = Number agreeing

reported that the average BLL in pregnant women in Bangkok was 6.20 ± 2.00 μg/dL and there was a direct relationship between maternal BLLs and umbilical cord BLLs [14]. Furthermore, recent studies in 2019 in Nakhon Si Thammarat province and in 2020 in Phuket and Phang Nga revealed that children are exposed to lead, with BLLs ranging between 0.03 and 26.40 μg/dL [15, 16]. This is especially significant because lead in the mother's blood can enter the foetus through the placenta. Therefore, screening pregnant women for lead exposure will help identify those at risk and encourage protective behaviors to lessen the risk of the mother and foetus being exposed to lead. In addition, those that are identified as being at risk of having high BLLs can undergo a blood test and, if applicable, be referred for treatment.

Screening is an approach to monitor and prevent risk from lead exposure [17]. Blood lead screening is considered the gold standard method for detecting lead in the body. However, due to the high cost and limited availability of equipment, it is not possible to screen all pregnant women and have their blood tested for lead. Another method is questionnaire-based screening, a tool which is recommended for the first stage of screening for lead exposure [18]. It is a fast, simple, non-invasive and inexpensive method. Although screening tools for lead exposure in pregnant women have been developed in several countries, including the United States of America (USA) and France [18, 19], distinct lead risk factors must be evaluated for each group as the screening tools will produce different results in various populations [20]. Moreover, the technique of selecting the items affects the performance of the test. Therefore, we aimed to construct, validate, and implement a new lead exposure screening method for Thai pregnant women in order to enable early detection of lead exposure in pregnant women and children.

2. Materials and methods

This study aimed at the construction (1), validation (2) and implementation (3) of a lead exposure screening tool. This study was approved by the Human Research Ethics Committee (approval ID 20-275-02, approval date 8 September 2021).

2.1. Construction of the lead exposure screening tool

By gathering both primary and secondary data, we were able to determine the variables that were related to BLLs during pregnancy. For primary data, we conducted a review of the literature using national and international electronic databases including ThaiJo (Thai Journal online), PubMed, and ScienceDirect by using the keywords “pregnancy blood lead levels”, “maternal blood lead levels", and “prenatal lead exposure” during the years 1990–2020, as well as the Thai government reports on lead exposure [21]. For secondary data, we interviewed five experts in Thailand with expertise in lead research. The experts were asked open-ended questions about the BLL factors and sources of lead that contributed to their experience. Then, we compiled a list of the factors. The factors identified were examined for validity and interrater reliability with the Item Content Validity Index (I-CVI), the Scale Content Validity Index Average (S– CVI/Ave), and the Kappa statistic (K) by five more experts in Thailand with expertise in lead research. Items with an I-CVI of less than 0.78 and a K of less than 0.6 were excluded [22]. The definition and formula of I-CVI, S-CVI/Ave and K are explained in Table 1 [22,23].

2.2. Validation of the lead exposure screening tool

This process was conducted among 100 pregnant women who received antenatal care at district health promotion hospitals in Mueang

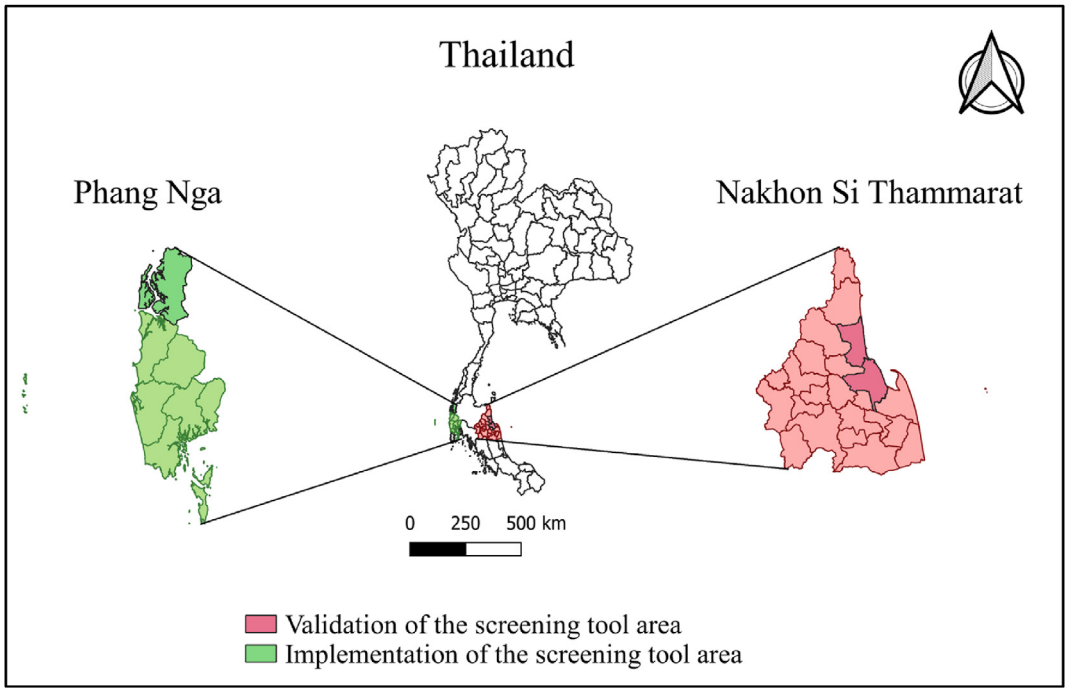

Figure 1. The study areas of validation and implementation of the screening tool.

Table 2. Characteristics and BLLs of pregnant women enrolled for the validation and implementation of the lead exposure screening tool, Thailand, 2022.

Characteristics	%	Validation area (n = 100)		%	Implementation area (n = 30)		p
		BLLs (μg/dL)			BLLs (μg/dL)		
		Mean ± SD	95%CI		Mean ± SD	95%CI	
Age (yr)							
≤19	11	5.64 ± 2.01	4.28–6.99	7	4.50 ± 2.12	-	0.474
20-30	60	4.68 ± 1.51	4.29–5.07	53	6.12 ± 2.33	4.88–7.37	
≥31	29	4.86 ± 1.62	4.25–5.48	40	5.75 ± 1.91	4.53–6.96	
Education[a]							
Primary	18	5.00 ± 1.45	4.28–5.72	10	5.67 ± 2.89	-1.50–12.83	0.487
Lower-secondary	43	5.05 ± 1.73	4.51–5.58	47	6.50 ± 1.99	5.35–7.64	
Upper-secondary	20	5.00 ± 1.30	4.39–5.61	30	6.00 ± 2.06	4.41–7.58	
Higher education	19	4.05 ± 1.65	3.26–4.85	13	3.50 ± 0.58	2.58–4.41	
Occupation							
Unemployed	59	4.85 ± 1.67	4.41–5.28	57	5.53 ± 2.37	4.31–7.75	0.820
Employed	41	4.83 ± 1.54	4.34–5.32	43	6.31 ± 1.75	5.25–7.36	
Household income per month							
<396.15 USD	62	4.84 ± 1.49	4.46–5.22	73	5.59 ± 2.26	4.59–6.59	0.255
≥396.15 USD	38	4.84 ± 1.81	4.25–5.44	27	6.62 ± 1.60	5.29–7.96	
Trimester							
First trimester	33	4.82 ± 1.49	4.29–5.35	17	7.00 ± 1.87	4.68–9.32	0.206
Second trimester	38	5.21 ± 1.90	4.58–5.84	43	6.61 ± 1.94	5.44–7.79	
Third trimester	29	4.29 ± 1.12	3.85–4.72	40	4.58 ± 1.88	3.39–5.78	
Underlying disease							
No	90	4.86 ± 1.58	4.52–5.19	90	5.74 ± 2.16	4.89–6.59	1.000[b]
Yes	10	4.70 ± 1.94	3.31–6.09	10	7.00 ± 1.73	2.70–11.30	
Parity							
Primiparous	44	4.93 ± 1.48	4.48–5.38	30	5.22 ± 1.72	3.90–6.54	0.171
Multiparous	56	4.77 ± 1.72	4.31–5.23	70	6.14 ± 2.26	5.11–7.17	
Pre-pregnancy BMI (kgm^{-2})							
<18.5	9	3.67 ± 1.00	2.90–4.44	17	6.00 ± 2.55	2.83–9.16	0.808
18.5–22.9	33	5.15 ± 1.60	4.58–5.72	27	5.62 ± 2.13	3.84–7.40	
23.0–29.9	46	4.74 ± 1.66	4.24–5.23	40	5.58 ± 2.02	4.30–6.87	
≥30.0	12	5.25 ± 1.48	4.31–6.19	17	3.80 ± 2.39	3.83–9.76	
Systolic blood pressure							
<120 mmHg	69	4.45 ± 1.38	4.12–4.78	73	5.54 ± 2.18	4.58–6.51	0.695
120–129 mmHg	20	5.55 ± 1.93	4.65–6.45	13	5.50 ± 1.73	2.74–8.26	
≥130 mmHg	11	6.00 ± 1.48	5.00–7.00	13	8.00 ± 0.82	6.70–9.30	
Diastolic blood pressure							
<80 mmHg	85	4.71 ± 1.61	4.36–5.05	93	5.68 ± 2.07	4.87–6.48	0.382
80–89 mmHg	12	5.33 ± 1.37	4.46–6.20	3	-	-	
≥90 mmHg	3	6.67 ± 1.53	2.87–10.46	3	-	-	
Haemoglobin level							
<11 g/dL	13	5.54 ± 1.94	4.37–6.71	7	5.50 ± 0.71	-	0.518[b]
≥11 g/dL	87	4.74 ± 1.54	4.41–5.06	93	5.89 ± 2.20	5.04–6.75	
Urine sugar level							
Normal	93	4.78 ± 1.52	4.47–5.10	97	5.86 ± 2.16	5.04–5.59	0.681[b]
Abnormal	7	5.57 ± 2.57	3.19–7.95	3	-	-	
BLLs							
<5 μg/dL	53	3.58 ± 0.57	3.43–3.74	37	3.54 ± 0.52	3.19–3.90	0.146
≥5 μg/dL	47	6.26 ± 1.17	5.91–6.60	63	7.21 ± 1.40	6.54–7.88	
Mean BLLs (μg/dL)	100	4.84 ± 1.61	4.52–5.16	100	5.87 ± 2.13	5.07–6.66	0.019[c]*

[a] Education: primary = ages 7–12, lower-secondary = ages 13–15, upper-secondary = ages 16–18, higher education > age 18.
[b] Fisher's exact test.
[c] Independent t-test, *p < 0.05.

district, Nakhon Si Thammarat province (Figure 1). Participants had to have lived in those areas for at least one year and be aged 18 or over. The sample size in this process was calculated for estimating sensitivity (Se) and specificity (Sp) [24]. There are no criteria for the optimum Se and Sp. However, if the sum of Se and Sp is equal to or more than 1.5, the test is regarded appropriate [25]. In a previous meta-analysis study screening lead exposure, the pooled results of Se and Sp were 48.0% (95%CI 31.40–65.60) and 58.0% (95%CI 39.90–74.00) respectively [11]. Therefore, we set the Se and Sp higher than these results, at 90%, to improve the performance of the screening tool. Pregnant women were

Table 3. Acceptable I-CVI, S-CVI/Ave and K indexes by five experts for a blood lead level screening test.

Item	Factor	∑ Agree	I-CVI	K
1. Personal factors				
I1-1	Age	5	1.00	1.00
I1-2	Education	5	1.00	1.00
I1-3	Household income	5	1.00	1.00
2. Health factors				
I2-1	Gestational age	5	1.00	1.00
I2-2	Pre-pregnancy BMI	5	1.00	1.00
I2-3	Parity	5	1.00	1.00
I2-4	Underlying disease	5	1.00	1.00
I2-5	Systolic blood pressure	4	0.80	0.76
I2-6	Diastolic blood pressure	4	0.80	0.76
I2-7	Urine protein	4	0.80	0.76
I2-8	Urine sugar	4	0.80	0.76
I2-9	Haemoglobin level	4	0.80	0.76
3. Occupational factors Have you or any family members worked in these occupations?				
I3-1	Fishing net sinker worker	4	0.80	0.76
I3-2	Boat repair worker	4	0.80	0.76
I3-3	Any industry related to lead	4	0.80	0.76
I3-4	Mining worker	4	0.80	0.76
I3-5	Farmer (chemical use)	4	0.80	0.76
I3-6	Automotive worker	4	0.80	0.76
I3-7	Antique dealer	4	0.80	0.76
I3-8	Vinyl shop owner	4	0.80	0.76
I3-9	Street sweeper	4	0.80	0.76
I3-10	Jewellery maker	4	0.80	0.76
I3-11	Fishing rod maker	4	0.80	0.76
I3-12	Salon worker	4	0.80	0.76
4. Living area factors Are you living close to or within these places?				
I4-1	Fishing net sinker workplace	5	1.00	1.00
I4-2	Boat repair site	5	1.00	1.00
I4-3	Workplaces related to lead or mining such as the battery industry	5	1.00	1.00
I4-4	Farm (using chemicals)	5	1.00	1.00
I4-5	Car or motorcycle shop	5	1.00	1.00
I4-6	Antiques shop	5	1.00	1.00
I4-7	Vinyl shop	5	1.00	1.00
I4-8	Landfill	5	1.00	1.00
I4-9	Garbage burning site	5	1.00	1.00
I4-10	Sorting shop	5	1.00	1.00
I4-11	Main road	5	1.00	1.00
I4-12	Living in a house painted within 1 year	5	1.00	1.00
I4-13	Living in a painted house	5	1.00	1.00
I4-14	Living in a house with oil paint	5	1.00	1.00
I4-15	Living in a house with peeling paint	5	1.00	1.00
I4-16	Living with a pet	4	0.80	0.76
I4-17	Living with a smoker	5	1.00	1.00
5. Consumption factors In the past month have you consumed or used the following?				
I5-1	Rain water	4	0.80	0.76
I5-2	Well water	4	0.80	0.76
I5-3	Tap water	4	0.80	0.76
I5-4	Seafood	4	0.80	0.76
I5-5	Canned food	4	0.80	0.76
I5-6	Smoking	5	1.00	1.00
I5-7	Drinking liquor	4	0.80	0.76
I5-8	Drinking wine	4	0.80	0.76
I5-9	Drinking beer	4	0.80	0.76
I5-10	Drinking coffee	4	0.80	0.76

(*continued on next page*)

Table 3 (*continued*)

Item	Factor	∑ Agree	I-CVI	K
I5-11	Drinking milk	4	0.80	0.76
I5-12	Iron supplements	5	1.00	1.00
I5-13	Calcium supplements	5	1.00	1.00
I5-14	Zinc supplements	4	0.80	0.76
I5-15	Vitamin C supplements	5	1.00	1.00
I5-16	Vitamin D supplements	5	1.00	1.00
I5-17	Herbs (not approved by the FDA Thailand)	5	1.00	1.00
I5-18	Fungicide	5	1.00	1.00
I5-19	Pesticide	5	1.00	1.00
I5-20	Insecticide	5	1.00	1.00
I5-21	Eyeliner	5	1.00	1.00
I5-22	Brush-on	5	1.00	1.00
I5-23	Nail polish	5	1.00	1.00
I5-24	Lipstick	5	1.00	1.00
I5-25	Concealer	5	1.00	1.00
I5-26	Hair dye	5	1.00	1.00
6. Other factors				
I6-1	Do you know what lead is?	5	1.00	1.00
I6-2	Have you ever had knowledge of lead hazards?	4	0.80	0.76
I6-3	Do you know how to protect yourself from lead?	4	0.80	0.76
I6-4	Do you wash hands before eating or drinking?	5	1.00	1.00
I6-5	Have you ever lived in a lead contaminated area?	4	0.80	0.76
I6-6	Have you ever been diagnosed as having a high blood lead level?	4	0.80	0.76
I6-7	Do you live with someone who has BLL >10 μg/dL?	4	0.80	0.76
S– CVI/Ave		**0.91**		

interviewed using the screening tool constructed in the previous process (2.1) and had biological samples collected, including urine and blood. In terms of biological indicators, blood pressure, urine protein, urine sugar, and haemoglobin levels were evaluated by health professionals as routine lab check-ups for pregnancy. Next, we selected items for the screening tool that have a Diagnostic Odds Ratio (DOR) of ≥2 to distinguish between pregnant women with and without high BLLs (≥5 μg/dL) [26]. Receiver Operating Characteristic (ROC) curves were used to evaluate the performance of the items and AUC was used to summarize overall screening tool accuracy [27, 28].

Sample size calculation formulae.

• Specifications.

n_{se} = the sample size required for sensitivity
n_{sp} = the sample size required for specificity
Se = Expected sensitivity
Sp = Expected specificity
$Z^2_{1-\frac{\alpha}{2}}$ = Z-score for type I error
w = the maximum clinically acceptable width of the 95% CI
P = an estimate for the prevalence of BLLs in Thai's pregnant women

$$n_{se} = \frac{Z^2_{1-\frac{\alpha}{2}} \times Se \times (1 - Se)}{w^2 \times P} \quad (1)$$

$$n_{sp} = \frac{Z^2_{1-\frac{\alpha}{2}} \times Sp \times (1 - Sp)}{w^2 \times (1 - P)} \quad (2)$$

$$n_{se} = \frac{1.96^2 \times 0.90 \times (1 - 0.90)}{0.10^2 \times 0.40}$$

$$n_{se} = 87$$

$$n_{sp} = \frac{1.96^2 \times 0.90 \times (1 - 0.90)}{0.10^2 \times (1 - 0.40)}$$

$$n_{sp} = 58$$

Since $n_{se} > n_{sp}$, the sample size in this study was 87 subjects. The sample size was increased by 20%, in case some subjects had incomplete data, to 105 subjects. Five subjects had incomplete data, which gave a final number of 100 subjects.

2.3. Implementation of the lead exposure screening tool

The screening tool was implemented on a population of 30 pregnant women who received antenatal care at district health promotion hospitals in Kuraburi district, Phang Nga province. This area shares similar characteristics and sources of lead exposure [15, 16] with the validation area (Figure 1). We interviewed pregnant women using the validated screening tool from the previous process (2.2) and also collected biological indicators and blood samples for blood lead analysis (as in process 2.2) to analyse the performance of the screening tool.

2.4. Measurement of blood lead

The pregnant women's blood samples were collected by nurses at each district health promotion hospital. An anticoagulant, ethylene diamine tetra-acetic acid, was used to collect approximately 3 ml of venous blood from each pregnant woman. Blood samples were stored at -20 °C in a sealed tube to avoid contamination during storage and transport. Blood samples were sent to the Bangkok RIA Laboratory in Thailand for a graphite furnace atomic absorption spectrophotometry assay for BLLs. The detection limit was 1.0 μg/dL.

2.5. Assessment of pregnant women's biological indicators

Pregnant women's biological indicators, including blood pressure, urine protein and sugar levels, and haemoglobin levels, were assessed as part of a routine lab check-up for pregnant women by a health professional at district health promotion hospitals. Blood pressure was measured by a sphygmomanometer. In this study, abnormal systolic blood pressure was defined as ≥ 130 mmHg and abnormal diastolic

Table 4. Validity of the items for screening lead exposure in pregnant women, Thailand, 2022.

Item	Positive screen	Se (%)	Sp (%)	LR+	LR-	DOR
I1-1	1 = ≥ 30 year	36.20	71.70	1.28	0.89	1.44
I1-2	1 = Primary to upper-secondary level	89.40	26.40	1.21	0.40	**3.03**
I1-3	1 = < 396.15 USD	36.20	58.50	0.87	1.09	0.80
I2-1	1 = 1&3 trimester	57.40	34.00	0.87	1.25	0.69
I2-2	1 = ≥30	14.90	90.60	1.59	0.94	1.69
I2-3	1 = Primiparous	44.70	56.60	1.03	0.98	1.05
I2-4	1 = No	91.50	11.30	1.03	0.75	1.37
I2-5	1 = ≥ 130 mmHg	19.10	96.20	5.03	0.84	**5.98**
I2-6	1 = ≥ 80 mmHg	31.90	84.90	2.11	0.80	**2.63**
I2-7	1 = Abnormal	14.90	86.80	1.13	0.98	1.15
I2-8	1 = Abnormal	10.60	96.20	2.79	0.93	**3.00**
I2-9	1 = Abnormal	19.10	92.50	2.55	0.87	**2.91**
I3-1-12[a]	1 = Yes	17.00	92.50	2.27	0.90	**2.53**
I4-1-11[b]	1 = Yes	53.20	37.70	0.85	1.24	0.69
I4-12-15[c]	1 = Yes	12.80	84.90	0.85	1.03	0.83
I4-16	1 = Yes	48.90	58.50	1.18	0.87	1.35
I4-17	1 = Yes	68.10	20.80	0.86	1.53	0.56
I5-1	1 = Yes	6.40	96.20	1.68	0.97	1.73
I5-2	1 = Yes	8.50	92.50	1.13	0.99	1.15
I5-3	1 = Yes	6.40	84.90	0.42	1.10	0.38
I5-4	1 = Yes	83.00	20.80	1.05	0.82	1.28
I5-5	1 = Yes	19.10	69.80	0.63	1.16	0.55
I5-10	1 = Yes	8.50	98.10	4.47	0.93	**4.80**
I5-13	1 = Yes	21.30	84.90	1.41	0.93	1.52
I5-14	1 = Yes	80.90	17.00	0.97	1.12	0.87
I5-15	1 = Yes	85.10	9.40	0.94	1.59	0.59
I5-16	1 = Yes	89.40	5.70	0.95	1.86	0.51
I5-18-20[d]	1 = Yes	17.00	92.50	2.27	0.90	**2.53**
I5-21-26[e]	1 = Yes	46.80	43.40	0.83	1.23	0.67
I6-1-3[f]	1 = No	80.90	15.10	0.95	1.26	0.75
I6-4	1 = No	19.10	73.60	0.72	1.10	0.66

Bold font in the DOR column indicates items included in the screening tool.
[a] Pooled occupation item (I3-1 to I3-12).
[b] Pooled living near lead source item (I4-1 to I4-11).
[c] Pooled living in a house lead contamination item (I4-12 to I4-15).
[d] Pooled using chemical product item (I5-18 to I5-20).
[e] Pooled using cosmetic product item (I5-21 to I5-26).
[f] Pooled knowledge of lead item (I6-1 to I6-3).

blood pressure was defined as ≥ 80 mmHg. Urine protein and sugar levels were measured using the urine dipstick and the results were read by the reflectance photometer technique [29], with abnormal urine protein levels defined as ≥ 15 mg/dL and abnormal urine sugar levels defined as ≥ 50 mg/dL. Haemoglobin was measured using the sodium lauryl sulphate (SLS) method [30], with abnormal levels defined as < 11 g/dL.

2.6. Data analysis method

Data were analysed with SPSS software version 28 (SPSS Inc., Chicago, IL, USA). Percentage, mean, and standard deviation were used to describe the variables. Chi-squared test and Fisher's exact test were used to compare the characteristic differences. An independent t-test was used to compare the mean difference in BLLs in pregnant women between the validation and implementation screening tool areas. We used BLLs as a categorial variable (<5 and ≥5 μg/dL) to classify lead exposure in pregnant women. Logistic regression analysis was used to predict the association between BLLs and screening items. The Se and Sp, positive likelihood ratio (LR+), negative likelihood ratio (LR-), DOR, ROC, and AUC indicate the validity of the screening tool.

3. Results

3.1. Characteristics and BLLs of pregnant women compared between the validation and implementation of the screening tool areas

Pregnant women in both the validation and implementation areas of the screening tool have similar characteristics; most of them fall in the age range of 20–30 years, have a lower secondary education level, are unemployed, and have a household income of less than 396.15 USD (minimum wage) per month. In terms of health status, most of them were in their second trimester, don't have underlying disease, are multiparous, and have normal levels of pre-pregnancy BMI [31], systolic blood pressure, diastolic blood pressure, hemoglobin levels and urine sugar. However, despite having similar characteristics, the BLLs of pregnant women in the implementation area (5.87 ± 2.13 μg/dL) were significantly higher than those in the validation area (4.84 ± 1.61 μg/dL) (p = 0.019) (Table 2).

3.2. Construction of the lead exposure screening tool

In these processes, we identified 80 items consisting of six categories related to BLLs; (1) personal factors (three items); (2) health factors (nine

Table 5. Crude Odds Ratio (cOR) and Adjusted Odds Ratio (aOR) for association between eight items and high BLLs ≥5 μg/dL (n = 100), Thailand, 2022.

Screening items	cOR	95%CI	p	aOR[a]	95%CI	p
Systolic blood pressure						
<130 mmHg	Ref			Ref		
≥130 mmHg	6.04	1.23–29.58	0.027**	8.60	1.13–65.35	0.038**
Diastolic blood pressure						
<80 mmHg	Ref			Ref		
≥80 mmHg	2.64	1.00–6.96	0.050*	5.72	1.49–21.87	0.011**
Urine sugar						
Normal	Ref			Ref		
Abnormal	3.04	0.56–16.45	0.198	10.37	0.83–129.03	0.069*
Haemoglobin level						
≥11 g/dL	Ref			Ref		
<11 g/dL	2.90	0.83–10.14	0.095*	5.47	1.09–27.30	0.038**
Occupations related to lead exposure						
No	Ref			Ref		
Yes	2.51	0.70–8.96	0.156	3.10	0.57–16.87	0.190
Occupations related to lead exposure >5 years (n = 30)						
No	Ref			-	-	-
Yes	4.00	0.85–18.84	0.080*	-	-	-
Drinking coffee (in the past month)						
No	Ref			Ref		
Yes	4.84	0.52–44.91	0.166	8.01	0.66–97.70	0.103
Using chemical products (in the past month)						
No	Ref			Ref		
Yes	2.51	0.70–8.96	0.156	8.09	1.59–41.15	0.012**
Education						
Primary to upper-secondary level	Ref			Ref		
Higher education level	0.33	0.11–1.00	0.051*	0.11	0.02–0.61	0.012**

*p < 0.1, **p < 0.05.
[a] In addition to the variables shown, the model contained age, trimester, parity, and underlying disease.

items); (3) occupational factors (12 items); (4) living area factors (18 items); (5) consumption factors (31 items); and (6) other factors (seven items). After experts validated the items, six were excluded because the I-CVI conformance criteria was less than 0.78, namely; living in a renovated house with lacquer, soil consumption, stone consumption, mud consumption, ceramic consumption, and drinking milk during adolescence. Thus, there were still 74 items. Forty items had a I-CVI index equal to 1, 34 items had an index equal to 0.80, the S-CVI/Ave was equal to 0.91 and the K more than 0.6 in every item (Table 3).

3.3. Validation and implementation of the lead exposure screening tool

In the validation process, eight items were excluded because no pregnant women answered "yes", or only one person answered "yes", including; I5-6 smoking, I5-7 drinking liquor, I5-8 drinking wine, I5-9 drinking beer, I5-17 herbs (not approved by the FDA Thailand), I6-5 have you ever lived in a lead contamination area? I6-6 have you ever been diagnosed as having a high blood lead level? And I6-7 do you live with someone who has BLL >10 μg/dL? There were two items excluded because everyone answered "yes" in these items, including; I5-12 consuming iron and I5-11 drinking milk. In addition, we pooled items that are the same type together (described below in Table 4). Finally, we reached a total of 31 items. From 31 items, we included eight items in the screening tool, selected by estimate values of DOR ≥2, which were; I1-2 education, I2-5 systolic blood pressure, I2-6 diastolic blood pressure, I2-8 urine sugar, I2-9 haemoglobin level, I3-1-12 occupation, I5-10 drinking coffee and I5-18-20 using chemical products (Table 4). We also calculated the crude odds ratio (cOR) and adjusted odds ratio (aOR) of those eight items. After adjustments, six items were associated with high BLLs including; systolic blood pressure, diastolic blood pressure, urine sugar, haemoglobin level, using chemical products and education level (Table 5). According to the included eight items we set the cut-off point score as 1, as this yielded the best Se (80.9%) and Sp (69.8%) (Table 6). For the ROC and AUC analysis, we found using eight items gave us the highest performance AUC (95%CI) = 0.78 (0.69–0.87) (Figure 2). Therefore, we used these eight items in the screening tool (ThaiL8Is) implemented in Kuraburi district, Phang Nga province. The performance of the ThaiL8Is gave Se = 78.9% and Sp = 81.8%, and the AUC (95%CI) = 0.80 (0.63–0.97) (Tables 7 and 8 and Figure 3).

Table 6. The cut-off point score of sums eight items.

Cut-off point score	Se (%)	Sp (%)	LR+	LR-	DOR
≥1	80.90	69.80	2.68	0.27	9.93
≥2	23.40	96.20	6.20	0.80	7.75
≥3	8.50	100.00	Infinity	0.91	Infinity

4. Discussion

Pb exposure among pregnant women is still a public health problem, leading to complications including preeclampsia and abnormal neurodevelopment of their children [32, 33]. The policies on the prevention of lead poisoning in Thailand focus on the population who work or live in lead-contaminated areas, and there are no guidelines for lead exposure for pregnant women [21]. In this cross-sectional study, we validated the ThaiL8Is screening tool in the province of Nakhon Si Thammarat and then used it in the province of Phang Nga. Both provinces are in southern Thailand, and subjects have similar education, occupation, income, and health status. We included all pregnant women, regardless of whether their occupation is associated with a high risk of lead exposure. Thus, we

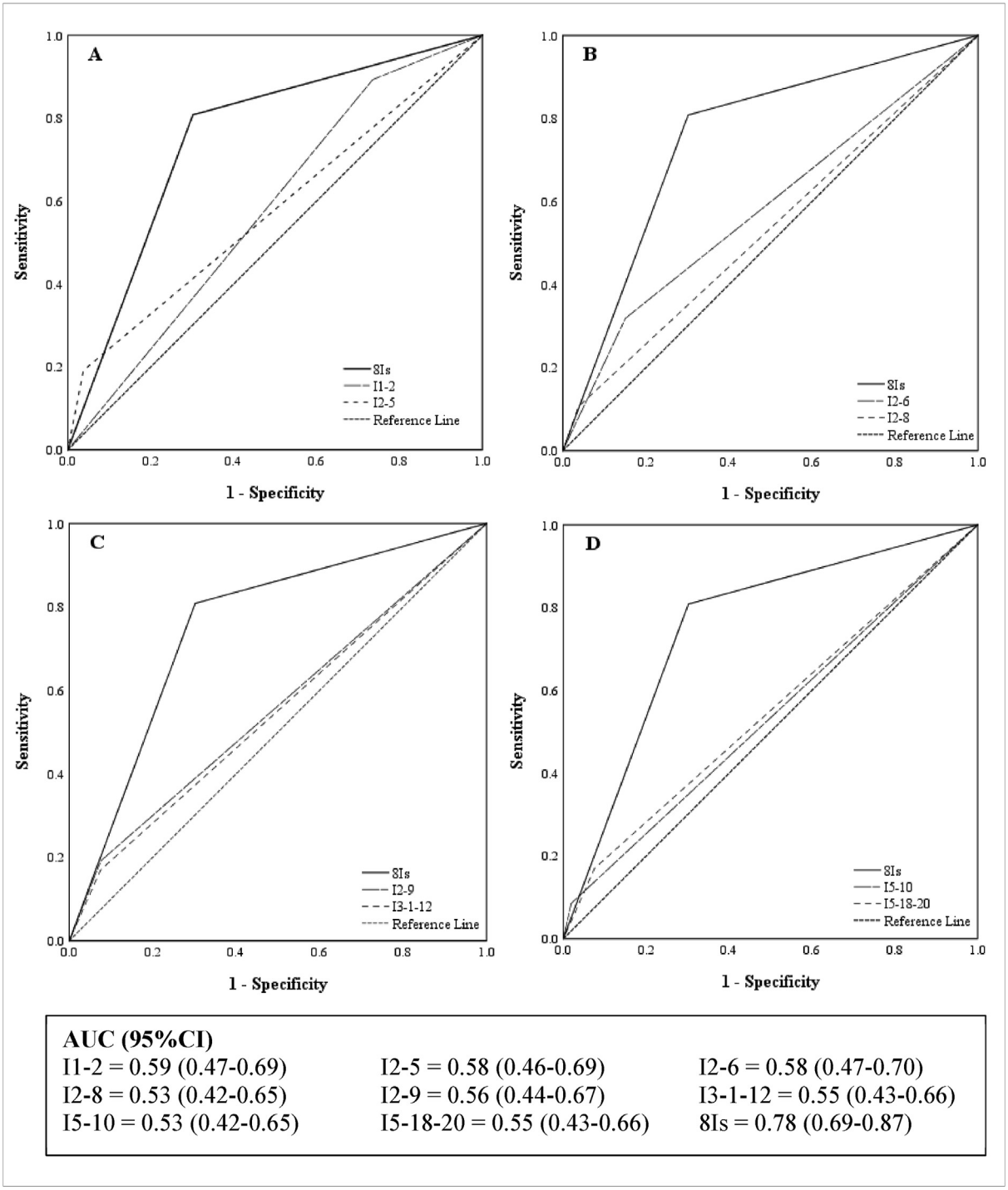

Figure 2. Comparison of ROC curve and AUC between single item and 8 items (8Is), Thailand, 2022 (A) comparison between 8Is, I1-2 and I2-5 (B) comparison between 8Is, I2-6 and I2-8 (C) comparison between 8Is, I2-9 and I3-1-12 (D) comparison between 8Is, I5-10 and I5-18-20.

obtained a sample of pregnant women with high and low BLLs, which is suitable for the construction of a screening tool [34]. The mean BLLs in pregnant women in the validation area was 4.84 ± 1.61 μg/dL and in the implementation area, 5.87 ± 2.13 μg/dL. Both areas have BLLs higher than pregnant women in Japan (the median was 0.63 μg/dL, with a range of 0.16–7.50 μg/dL) [35] and the United States (the median was 0.20 μg/dL, with a range of 0.00–6.40 μg/dL) [19]. This demonstrates the need for urgent action to protect pregnant women from lead exposure. The ThaiL8Is showed strong results in both the validation area (Se = 80.9%, Sp = 69.8%, AUC (95%CI) = 0.78 (0.69–0.87)) and implementation area (Se = 78.9%, Sp = 81.8%, AUC (95%CI) = 0.80 (0.63–0.97)). The result was comparable with previous studies [11, 18], or at least for the characteristics of Thai women in the locations studied. This is potentially due to the screening items being appropriate for the characteristics of pregnant women living in Thailand. Furthermore, ThaiL8Is include biological indicators, which are routine lab tests for pregnant women, whereas previous studies considered only risk factors [18, 19], such as one study in France, which recommended three items: the use of traditional cosmetics, degraded old housing, and eating bread more than twice a day [18]. In addition, the technique of selecting the items affects the performance of the test [36]. Our study used the DOR as a criterion to select items because the DOR is a global measure of diagnostic accuracy that indicates better

Table 7. Eight items for lead exposure screening in pregnant women (ThaiL8Is).

Items	Answer	
	Yes	No
1. Do you have a systolic blood pressure of ≥130 mmHg?	1 ☐	0 ☐
2. Do you have a diastolic blood pressure of ≥80 mmHg?	1 ☐	0 ☐
3. Do you have abnormal urine sugar results?	1 ☐	0 ☐
4. Do you have a haemoglobin level <of 11 g/dL?	1 ☐	0 ☐
5. Have you or family members worked in these occupations for *more than five years?* Fishing net sinker worker, boat repair worker, any industry related to lead, mining worker, farmer (chemical use), automotive worker, antique dealer, vinyl shop staff, street sweeper, jewellery maker, fishing rod maker, and salon worker	1 ☐	0 ☐
6. In the past one month have you consumed coffee regularly?	1 ☐	0 ☐
7. In the past one month have you been exposed to chemical products such as fungicide, pesticide or insecticide?	1 ☐	0 ☐
8. Did you graduate in higher education?	-1 ☐	0 ☐
Total scores		
Interpretation: If the total score ≥1, pregnancy women may have a blood lead levels ≥5 μg/dL.		

Table 8. Cross-classification of pregnant women in implementation area by using ThaiL8Is and blood lead test.

	Blood lead test		
	≥5 μg/dL	<5 μg/dL	total
ThaiL8Is			
Score ≥1	15	2	17
Score <1	4	9	13
Total	19	11	30
	Se = 78.9%	Sp = 81.8%	

discriminatory test performance and combines the strengths of Se and Sp as prevalence independent indicators [26]. ThaiL8Is consist of eight items: (1) systolic blood pressure (SBP), (2) diastolic blood pressure (DBP), (3) urine sugar, and (4) haemoglobin level, which are biological indicators related to lead exposure. These biological indicators were recorded in maternal and children's health notebooks by a nurse, which is standard procedure, simplifying the process of screening. Numerous studies have shown that lead causes abnormalities in these biological indicators. A study by Vaziri (2008) described the multiple mechanisms of lead promoting hypertension through oxidative stress, impaired nitric oxide (NO) system, inflammation, dysregulation of vasoactive hormones, and alteration of cellular Ca^{2+} transport and intracellular Ca^{2+} distribution [37]. This was consistent with our findings: pregnant women with systolic blood pressure ≥130 mmHg and diastolic blood pressure ≥80 mmHg had high BLLs (≥5 μg/dL) 8.6 times and 5.7 times more than those with lower systolic and diastolic blood pressure, respectively. Urine sugar is also a biological indicator which can be used for screening for gestational diabetes mellitus, as lead inhibits insulin signaling by reactive oxygen species

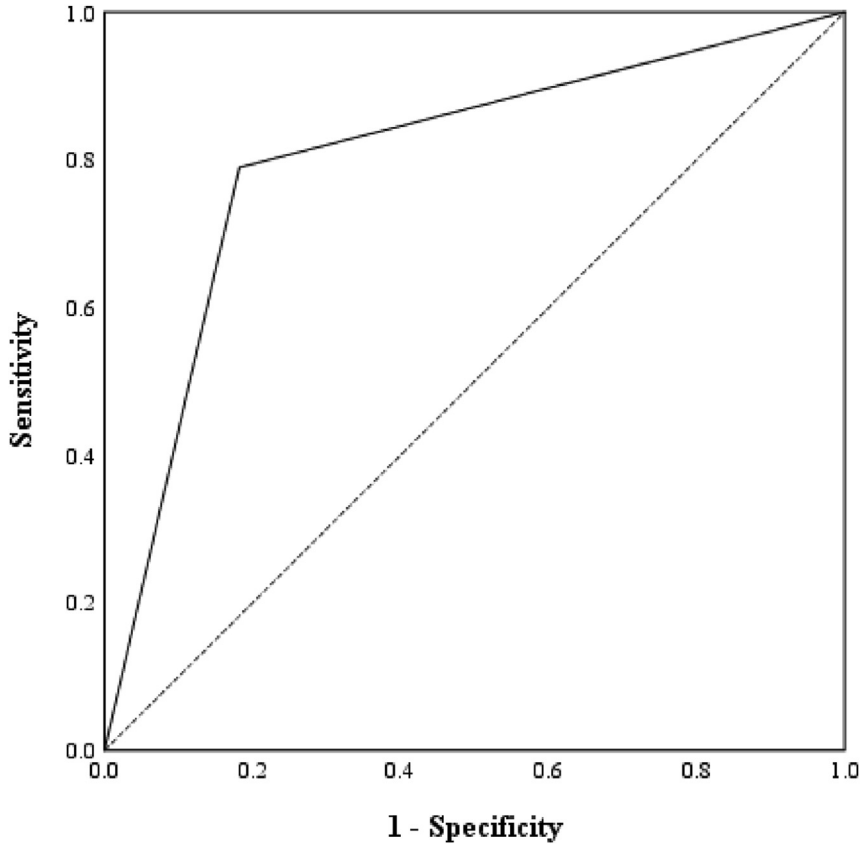

Figure 3. The results of the implementation of the screening tool (ThaiL8Is), the AUC (95%CI) = 0.80 (0.63–0.97).

(ROS), promoting the development of insulin resistance and diabetes [38]. This result is consistent with a study by Soomro et al. (2019) who found that lead exposure may cause gestational diabetes mellitus, which disrupts glucose absorption and alters glucose regulation [39]. Furthermore, haemoglobin levels in pregnancy under 11 g/dL are considered anaemia, caused by lead being taken up by the iron absorption machinery (DTM1), which blocks iron through competitive inhibition and interferes with heme biosynthesis, therefore decreasing red blood cell survival [5, 40, 41]. The next items, (5) to (7), are considered to be risk factors, namely: occupation, drinking coffee, and using chemical products. The occupations (5) related to lead exposure in this study area includes fishing net sinkers, boat repair workers, farmers (chemical use), automotive workers, and salon workers. These occupations have been reported to have potential lead exposure [15, 42, 43]. In addition, we are not only concerned about pregnant women's occupations but also concerned about cohabiting family members. Since lead dust from the workplace can become attached to clothes or personal items, this can result in other family members becoming at risk of lead exposure [44]. Moreover, our study found that pregnant women who have lived with those who work in lead-related occupations or have themselves worked in lead-related occupations for five years or more had four times higher levels of lead in their blood (Table 5). Coffee (6) is a popular beverage in Thailand, especially among the working-age population [45]. It is well known that coffee contains caffeine and might be contaminated with lead in some areas. However, the risk of lead exposure is low unless consumed in excess [46, 47]. It has been reported that caffeine may interfere with calcium absorption, leading to an increase in bone resorption and lead, resulting in increased BLLs [48, 49]. Chemical products (7) such as fungicides, pesticides, and insecticides contain lead [50] which, if used unprotected, can cause lead to enter the body. This correlates with a study of pregnant women in Indonesia which found high BLLs (46.24 ± 22.33 μg/dL) that may be caused by pesticides [42]. The last items, (8), is education, which is considered to be a protective factor. Our study found that higher education was associated with an 89.0% reduction in the risk of having high BLLs (Table 5). As education is one of the most important factors in health and wellness behaviour, generally, people with higher education tend to be healthier and more likely to engage in healthy behaviours [51]. The level of education is also used as an indirect measure of social and economic class; that is, the majority of people with a good education also have a higher socio-economic class [52]. Moreover, people with higher education have greater access to health information. Likewise, pregnant women with a higher level of education may be able to get information about lead hazards and avoid the risk of lead exposure [53].

To the best of our knowledge, this is the first report that shows a valid lead exposure screening tool for pregnant Thai women. The ThaiL8Is can be used in routine pregnancy surveillance systems by health officials in both primary healthcare centres and hospitals. The pregnant women who are identified as being in a high-risk group need to be confirmed by a blood lead test. By using the ThaiL8Is, every pregnant woman has the opportunity to get tested for lead exposure. This could lower the cost of blood lead and prevent negative effects for pregnant mothers and their children. Nevertheless, the present study has the following limitations: the sample size in this study was the minimum sample size required for calculating the sensitivity and specificity of screening parameters, the small number of subjects used in this study may have implications for its sensitivity and specificity if it ever gets adopted. In addition, the coastal nature of both the development area and the validation area may limit its generalizability.

5. Conclusions

The ThaiL8Is a lead exposure screening tool for pregnant Thai women which includes eight items; (1) systolic blood pressure (2) diastolic blood pressure (3) urine sugar (4) haemoglobin level (5) occupation (6) drinking coffee (7) using chemical products and (8) education level, with an acceptable effective test [28]. The ThaiL8Is can classify pregnant women who need a blood lead test. Local health centres should employ ThaiL8Is in surveillance processes to lessen the negative effects of lead exposure on health.

Declarations

Author contribution statement

Donrawee Waeyeng: Conceived and designed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Supabhorn Yimthiang: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Tanaporn Khamphaya: Analyzed and interpreted the data.

Phisit Pouyfung: Analyzed and interpreted the data; Wrote the paper.

Udomratana Vattanasit: Performed the experiments; Analyzed and interpreted the data; Wrote the paper.

Walaiporn Pramchoo: Contributed reagents, materials, analysis tools or data.

Funding statement

This work was supported by Walailak University Graduate Research Fund [CGS-RF-2020/12].

Data availability statement

Data included in article/supp. material/referenced in article.

Declaration of interest's statement

The authors declare no competing interests.

Additional information

No additional information is available for this paper.

References

[1] V. Rísová, The pathway of lead through the mother's body to the child, Interdiscip. Toxicol. 12 (2019) 1–6.
[2] D.C. Bellinger, Teratogen update: lead and pregnancy, Birth Defects Res A Clin Mol Teratol 73 (2005) 409–420.
[3] A.M. Taiwo, E.A. Aluko, O.O. Babalola, Investigations into the teratogenic potentials of lead in pregnant rabbit, Int J Biol Chem Sci 4 (2010).
[4] D.A. Kennedy, C. Woodland, G. Koren, Lead exposure, gestational hypertension and pre-eclampsia: a systematic review of cause and effect, J. Obstet. Gynaecol. 32 (2012) 512–517.
[5] N.H. Hsieh, S.H. Chung, S.C. Chen, W.Y. Chen, Y.H. Cheng, Y.J. Lin, S.H. You, C.M. Liao, Anemia risk in relation to lead exposure in lead-related manufacturing, BMC Publ. Health 17 (2017).
[6] H. Hu, M.M. Tellez-Rojo, D. Bellinger, D. Smith, A.S. Ettinger, H. Lamadrid-Figueroa, J. Schwartz, L. Schnaas, A. Mercado-Garcia, M. Hernandez-Avila, Fetal lead exposure at each stage of pregnancy as a predictor of infant mental development, Environ. Health Perspect. 114 (2006) 1730–1735.
[7] E. Obeng-Gyasi, Sources of lead exposure in various countries, Rev. Environ. Health 34 (2019) 25–34.
[8] M.G. Parizi, Z. Sedaghat, M. Mazloomi, M. Fararouei, Serum level of lead and cadmium is linked to facial cosmetics use among Iranian young women, Environ. Sci. Pollut. Control Ser. 28 (2021) 13913–13918.
[9] C. Thanapop, A.F. Geater, M.G. Robson, P. Phakthongsuk, D. Viroonudomphol, Exposure to lead of boatyard workers in southern Thailand, J. Occup. Health 49 (5) (2007 Sep) 345–352.
[10] D.M. Chirinos-Peinado, J.I. Castro-Bedrinana, Lead and cadmium blood levels and transfer to milk in cattle reared in a mining area, Heliyon 6 (2020).
[11] S.J. Curry, A.H. Krist, D.K. Owens, M.J. Barry, M. Cabana, A.B. Caughey, C.A. Doubeni, J.W. Epling, A.R. Kemper, M. Kubik, C.S. Landefeld, C.M. Mangione, L. Pbert, M. Silverstein, M.A. Simon, C.W. Tseng, J.B. Wong, Screening for elevated blood lead levels in children and pregnant women: US preventive services task force recommendation statement, JAMA, J. Am. Med. Assoc. 321 (2019) 1502–1509.
[12] M.K. Silver, X. Li, Y. Liu, M. Li, X. Mai, N. Kaciroti, P. Kileny, T. Tardif, J.D. Meeker, B. Lozoff, Low-level prenatal lead exposure and infant sensory function, Environ. Health 15 (2016).

[13] K.N. Sindhu, J.D. Bondu, S.K. Ganesan, C. Syed, G. Kang, V.R. Mohan, Blood lead levels in mother-infant pairs, Indian J. Pediatr. 85 (2018) 1143–1144.

[14] W. Phuapradit, T. Jetsawangsri, K. Chaturachinda, N. Noinongyao, Maternal and umbilical cord blood lead levels in Ramathibodi Hospital, 1993, J. Med. Assoc. Thai. 77 (7) (1994 Jul) 368–372.

[15] S. Yimthiang, D. Waeyang, S. Kuraeiad, Screening for elevated blood lead levels and related risk factors among Thai children residing in a fishing community, Toxics 7 (2019).

[16] T. Chantian, W. Saetia, J. Srisaeng, P. Siripongpokin, P. Thammawijaya, S. Siriratanapruk, Predicting Blood Lead Levels Among Children Living in Households Making Fishing Nets with Lead Weights in Phuket and Phang Nga Provinces, 2020.

[17] G. Wang, J. Dibari, E. Bind, A.M. Steffens, J. Mukherjee, R.E. Azuine, G.K. Singh, X. Hong, Y. Ji, H. Ji, C. Pearson, B.S. Zuckerman, T.L. Cheng, X. Wang, Association between maternal exposure to lead, maternal folate status, and intergenerational risk of childhood overweight and obesity, JAMA Netw. Open 2 (2019).

[18] E. Coiplet, M. Freuchet, C. Sunyach, J. Mancini, J. Perrin, B. Courbiere, H. Heckenroth, C. Pissier, N. Hamdaoui, F. Bretelle, Assessment of a screening questionnaire to identify exposure to lead in pregnant women, Int. J. Environ. Res. Publ. Health 17 (2020) 1–12.

[19] K.M. Johnson, A.J. Specht, J.M. Hart, S. Salahuddin, A.L. Erlinger, M.R. Hacker, A.D. Woolf, M. Hauptman, S.A. Karumanchi, K. O'Brien, B.J. Wylie, Risk-factor based lead screening and correlation with blood lead levels in pregnancy, Matern. Child Health J. 26 (2022) 185–192.

[20] WHO, Screening programme, Increase Effectiveness, Maximize Benefits and Minimize Harm Screening Programmes: a Short Guide, 2020 (accessed June 12, 2022), https://apps.who.int/iris/handle/10665/330829.

[21] Department of Disease Control of Thailand, Guidelines for Surveillance, Prevention and Control of lead Poisoning in the Working Age Group, 2021 (accessed June 7, 2022), http://envocc.ddc.moph.go.th/contents/view/1118.

[22] D.F. Polit, C.T. Beck, S.v. Owen, Focus on research methods: is the CVI an acceptable indicator of content validity? Appraisal and recommendations, Res. Nurs. Health 30 (2007) 459–467.

[23] M.S.B. Yusoff, ABC of content validation and content validity index calculation, Education in Medicine Journal 11 (2019) 49–54.

[24] N.M. Fenn Buderer, Statistical Methodology: I. Incorporating the Prevalence of Disease into the Sample Size Calculation for Sensitivity and Specificity, 1996.

[25] M. Power, G. Fell, M. Wright, Principles for high-quality, high-value testing, Evid. Base Med. 18 (2013) 5–10.

[26] A.S. Glas, J.G. Lijmer, M.H. Prins, G.J. Bonsel, P.M.M. Bossuyt, The diagnostic odds ratio: a single indicator of test performance, J. Clin. Epidemiol. 56 (2003) 1129–1135.

[27] K.H. Zou, A.J. O'Malley, L. Mauri, Receiver-operating characteristic analysis for evaluating diagnostic tests and predictive models, Circulation 115 (2007) 654–657.

[28] J.N. Mandrekar, Receiver Operating Characteristic Curve in Diagnostic Test Assessment, 2010.

[29] M. Oyaert, J.R. Delanghe, Semiquantitative, fully automated urine test strip analysis, J. Clin. Lab. Anal. 33 (2019).

[30] A. Karsan, I. Maclaren, D. Conn, L. Wadsworth, An evaluation of hemoglobin determination using sodium lauryl sulfate, Am. J. Clin. Pathol. 100 (1993) 123–126.

[31] WHO, The Asia-Pacific Perspective: Redefining Obeseity and its Treatment, 2000. https://apps.who.int/iris/bitstream/handle/10665/206936/0957708211_eng.pdf?sequence1 (accessed June 7, 2022).

[32] S. Shah-Kulkarni, M. Ha, B.M. Kim, E. Kim, Y.C. Hong, H. Park, Y. Kim, B.N. Kim, N. Chang, S.Y. Oh, Y.J. Kim's, B. Lee, E.H. Ha, Neurodevelopment in Early Childhood Affected by Prenatal lead Exposure and Iron Intake, Medicine 95 (2016).

[33] A.E. Poropat, M.A.S. Laidlaw, B. Lanphear, A. Ball, H.W. Mielke, Blood lead and preeclampsia: a meta-analysis and review of implications, Environ. Res. 160 (2018) 12–19.

[34] P. Eusebi, Diagnostic accuracy measures, Cerebrovasc. Dis. 36 (2013) 267–272.

[35] Y. Goto, M. Mandai, T. Nakayama, S. Yamazaki, S.F. Nakayama, T. Isobe, T. Sato, H. Nitta, Association of prenatal maternal blood lead levels with birth outcomes in the Japan Environment and Children's Study (JECS): a nationwide birth cohort study, Int. J. Epidemiol. 50 (2021) 156–164.

[36] M.S. Pepe, H. Janes, G. Longton, W. Leisenring, P. Newcomb, Limitations of the odds ratio in gauging the performance of a diagnostic, prognostic, or screening marker, Am. J. Epidemiol. 159 (2004) 882–890.

[37] N.D. Vaziri, Mechanisms of lead-induced hypertension and cardiovascular disease, Am. J. Physiol. Heart Circ. Physiol. 295 (2008) 454–465.

[38] T. Leff, P. Stemmer, J. Tyrrell, R. Jog, Diabetes and exposure to environmental lead (Pb), Toxics 6 (2018).

[39] M.H. Soomro, N. Baiz, G. Huel, C. Yazbeck, J. Botton, B. Heude, C.G. Bornehag, I. Annesi-Maesano, Exposure to heavy metals during pregnancy related to gestational diabetes mellitus in diabetes-free mothers, Sci. Total Environ. 656 (2019) 870–876.

[40] G. Yadav, S. Chambial, N. Agrawal, M. Gothwal, P. Kathuria, P. Singh, P. Sharma, P. Sharma, Blood lead levels in antenatal women and its association with iron deficiency anemia and adverse pregnancy outcomes, J. Fam. Med. Prim. Care 9 (2020) 3106.

[41] N. Abbaspour, R. Hurrell, R. Kelishadi, Review on iron and its importance for human health, J. Res. Med. Sci. 19 (2) (2014) 164–174.

[42] N.A. Sakina, Blood lead levels of pregnant women in agricultural and coastal area: a SDG's indicator for health and pollution in brebes district, in: IOP Conf Ser Earth Environ Sci, IOP Publishing Ltd, 2021.

[43] S. Nakhaee, A. Amirabadizadeh, S. Nakhaee, M. Zardast, J. Schimmel, J. Ahmadian-Moghadam, A. Akbari, H. Mohammadian Darmian, M. Mohammadi, O. Mehrpour, Blood lead level risk factors and reference value derivation in a cross-sectional study of potentially lead-exposed workers in Iran, BMJ Open 9 (2019).

[44] J.L. Rinsky, S. Higgins, K. Angelon-Gaetz, D. Hogan, P. Lauffer, M. Davies, A. Fleischauer, K. Musolin, J. Gibbins, J. MacFarquhar, Z. Moore, Occupational and take-home lead exposure among lead oxide manufacturing employees, North Carolina, 2016, Publ. Health Rep. 133 (2018) 700–706.

[45] P. Polsripradist, K. Tantayaporn, P. Homchampa, Caffeine consumption behaviors of the working-age population in rural communities in northeastern Thailand, J. Med. Assoc. Thai. 99 (7) (2016 Jul) 839–851.

[46] A. Winiarska-Mieczan, K. Kwiatkowska, M. Kwiecień, E. Zaricka, Assessment of the Risk of Exposure to Cadmium and lead as a Result of the Consumption of Coffee Infusions, 2011.

[47] A. Winiarska-Mieczan, K. Jachimowicz, S. Kislova, M. Kwiecień, Z. Zasadna, D. Yanovych, Cadmium and lead concentration in drinking instant coffee, instant coffee drinks and coffee substitutes: safety and health risk assessment, Biol. Trace Elem. Res. (2022) 1–10.

[48] C.M. Taylor, J. Golding, J. Hibbeln, A.M. Emond, Environmental factors predicting blood lead levels in pregnant women in the UK: the ALSPAC study, PLoS One 8 (2013).

[49] C.S. Riedt, B.T. Buckley, R.E. Brolin, H. Ambia-Sobhan, G.G. Rhoads, S.A. Shapses, Blood lead levels and bone turnover with weight reduction in women, J. Expo. Sci. Environ. Epidemiol. 19 (2009) 90–96.

[50] J. Guo, C. Wu, J. Zhang, X. Qi, S. Lv, S. Jiang, T. Zhou, D. Lu, C. Feng, X. Chang, Y. Zhang, Y. Cao, G. Wang, Z. Zhou, Prenatal exposure to mixture of heavy metals, pesticides and phenols and IQ in children at 7 years of age: the SMBCS study, Environ. Int. 139 (2020).

[51] A.J. Cowell, The relationship between education and health behavior: some empirical evidence, Health Econ. 15 (2006) 125–146.

[52] J.I. Ladele, I.B. Fajolu, V.C. Ezeaka, Determination of lead levels in maternal and umbilical cord blood at birth at the Lagos University Teaching Hospital, Lagos, PLoS One 14 (2019).

[53] K. Polanska, W. Hanke, W. Sobala, M. Trzcinka-Ochocka, D. Ligocka, H. Strugala-Stawik, P. Magnus, Predictors of environmental lead exposure among pregnant women - a prospective cohort study in Poland, Ann. Agric. Environ. Med. 21 (1) (2014) 49–54.