

Screening the risk factors for methamphetamine use in pregnant women not receiving prenatal care

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Abstract

Objective: To develop a screening tool for the risk factors potentially indicating methamphetamine use in pregnant women who are not receiving prenatal care.

Method: This prospective cohort, Institutional Review Board-approved study was performed at a university hospital in Thailand between January 2017 and January 2019. A screening tool was developed using data from 125 pregnant women not receiving prenatal care upon their first admission for childbearing at the hospital delivery room. Potential factors obtained from the patient's history, physical examination, and methamphetamine use in pregnancy or had a urine amphetamine test positive were entered into a logistic regression analysis. The discriminative ability of the screening tool was expressed by the area under the receiver operating characteristic curve (AUROC) sensitivity and specificity, while bootstrapping was used for internal validation.

Results: The screening covered four factors: smoking (odds ratio 7.73, score = 2), drinking (3.81, score = 1), living with a spouse or friend who uses methamphetamine (17.28, score = 3), BP \geq 130/90 mmHg (2.47, score = 1). The AUROC for the model was 0.87, 95% CI, 0.81–0.93 (SE: 0.03). A total points score \geq 3 represented the best cut-off value, with a sensitivity of 81% and specificity of 82%. Across the bootstrapping, the C-statistic for the full screening was 0.86, 95% CI, 0.81–0.93 (SE: 0.03).

Conclusion: A screening tool was developed with an excellent ability to discriminate the risk factors potentially indicating methamphetamine use in pregnant women not receiving prenatal care. Validation in pregnant women receiving prenatal care still needs to be performed.

Key words: pregnant women not receiving prenatal care, risk of methamphetamine use, screening risk factors.

Introduction

Methamphetamine is the most widely abused illicit drug in Thailand and indeed in the world. The clinical symptoms of methamphetamine use at low doses generally involve some seemingly positive effects, such as increased alertness, energy, euphoria, elevated self-confidence, persistent activity, increased talkativeness, increased

sexual pleasure and hypersexuality, a sense of well-being, increased strength, and a loss of appetite. The egosyntonic, pleasurable nature of methamphetamine intoxication explains its persistence as a drug of choice for many as well as the addictive cycle that usually emerges among users.¹ Perinatal methamphetamine exposure introduces neurostimulants and neurotoxins to the fetus that carry a high risk of causing psychiatric co-morbidities, and

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evidence suggests that it is associated with poor pregnancy outcomes,² including the following effects: reduced blood flow caused by a narrowing of the blood vessels, limited oxygen and nutrient supply, resulting in reduced growth and a smaller head circumference of the baby, antepartum bleeding conditions, and behavioral and learning difficulties in children who are exposed in utero. Pregnancy complications include miscarriage and preterm labor, an increased risk of fetal abnormalities (i.e., heart abnormalities), an altered fetal nervous system as the drug acts as a stressor to the baby, and alteration of the baby's brain structure and development.³⁻⁸

An increasing number of babies are exposed to these risks from maternal methamphetamine use during pregnancy. Some exposed babies may have sleep disturbances and feeding problems. Babies may be born drug-affected, such as overactive and agitated.⁹ A study of the outcomes in pregnancies complicated by methamphetamine use found that methamphetamine use among pregnant women led to greater odds of gestational hypertension (odds ratio [OR], 1.8; 95% confidence interval [CI], 1.6–2.0), preeclampsia (OR, 2.7; 95% CI, 2.4–3.0), intrauterine fetal death (OR, 5.1; 95% CI, 3.7–7.2), and abruption (OR, 5.5; 95% CI, 4.9–6.3). In addition, these patients had higher odds of preterm birth (OR, 2.9; 95% CI, 2.7–3.1), neonatal death (OR, 3.1; 95% CI, 2.3–4.2), and infant death (OR, 2.5; 95% CI, 1.7–3.7).¹⁰ Babies with perinatal methamphetamine exposure may escape detection because their signs of withdrawal are usually less pronounced than those of opiate-exposed babies. Also, there is little evidence of amphetamine-induced neurotoxicity or of a long-term neurodevelopmental impact, but this may be because data are scarce and difficult to extricate from the influence of other factors associated with children living in households where one or more parents uses drugs, such as the effects of poverty and neglect.

Improving the early detection of perinatal exposure could increase the provision of early-intervention services for the affected children and their families. Siriraj Hospital has a guideline for maternal and newborn care for drug-use mothers. As part of this, pregnant women who use recreational drugs are sent for a urine test to check for drug use, such as methamphetamine use. In addition, parents and families need to take part in a consultation with an adult psychiatric doctor and child psychiatric doctor, as well as a social worker, to allow an assessment of their ability to care for a newborn and to ensure the baby will not be subject to poverty and neglect abuse issues after

discharge from the hospital. Screening pregnant women during the prenatal period for substance use could help to prevent the newborn from receiving drugs through the mother's milk, as well as help to ensure that mothers and newborn babies can receive continuous care after the birth. Data from Siriraj Hospital from 2010 to 2014 showed that among 1057 pregnant women attending the institute who were not receiving prenatal care, 35.1% [371/1057] had a previous history of using recreational drugs, almost all of whom had used methamphetamine during pregnancy [359/1057], and 20.8% [220/1057] had a positive urine amphetamine test; whereas only 1.3% [599/46 486] of the pregnant women attending the institute who were receiving prenatal care had used recreational drugs.¹¹ The incidence of recreational drugs use in pregnant women receiving prenatal care was perhaps much higher because it is difficult to detect the signs and symptoms in pregnant women, while self-reports of substance use may be misleading or infrequently elicited, physicians may fail to routinely screen for use, and as substance-abusing pregnant women may seek little or no prenatal care. However, most pregnant women who use methamphetamines during pregnancy will eventually have to be screened when they come to the hospital for their delivery.

At present, screening on the labor ward for drug use is performed through a patient interview and history-taking related to substance abuse, through physical examination, and by laboratory investigation. A key problem though is that pregnant women with a history of substance abuse are usually unlikely to give true information. Health professionals must therefore try to observe the patients for signs of drug abuse, which can depend on their experience. Pregnant women who do not have abnormal symptoms, such as restlessness, and who do not reveal a drug-use history will often not have screening performed or screening after the birth will be promoted before breastfeeding. Therefore, this study aimed to develop a screening tool for the risk factors potentially indicating methamphetamine use in pregnant women not receiving prenatal care. Here, it is considered that an assessment of methamphetamine use should be the first step toward ensuring all pregnant women and newborns to receive quality care.

Materials and Methods

A screening tool for the risk factors potentially indicating methamphetamine use was developed with a

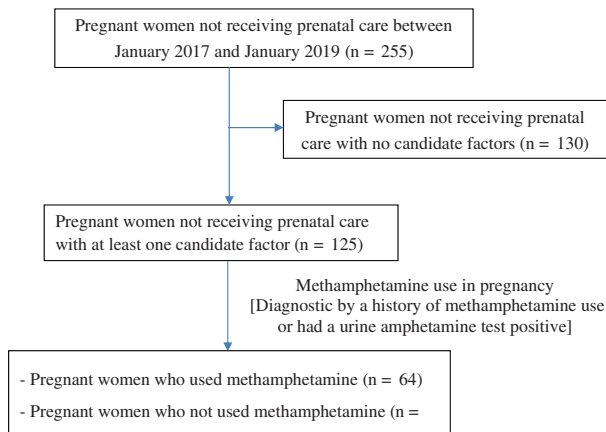


Figure 1 Flow diagram of patient selection for inclusion in the study

prospective cohort of 125 pregnant women attending the labor ward in Siriraj Hospital, Thailand, between January 2017 and January 2019, who were not receiving prenatal care. The sample size estimation was based on the incidence of pregnant women not receiving prenatal care who were determined to carry a risk of having used recreational drugs as assessed by the labor nurses at Siriraj Hospital in 2016 (30% of all the pregnant women according to the annual statistics at Siriraj Hospital 2016).¹² We enrolled 125 pregnant women, who were asked about their current and previous history of drug use in an initial assessment. The eligibility criteria from the Human Research Protection Unit were vulnerable subjects aged over 18 years old with at least one candidate factor. The exclusion criteria were a history of hypertension and the use of

certain drugs that may impact them having a false-positive urine amphetamine test, such as ephedrine or phenylpropanolamine. The principle that there are seven key risk factors that may indicate potential drug use in a patient was noted in this study in line with a previous pilot study and the reviewed literature about screening for substance abuse during pregnancy.¹³ Consequently, the following seven risk factors were considered in the present study: have a tattoo; smoking; drinking; have abnormal symptoms and signs of methamphetamine use, such as displaying inappropriate behaviors (restlessness, disorientation, dilated pupils); living with a spouse or friend who uses recreational drugs; BP \geq 130/90 mmHg; and pulse \geq 100/min. Methamphetamine use in pregnancy was diagnosed by a history of methamphetamine use or had a urine amphetamine test positive. After all, the potential subjects had given their informed consent, but with a waiver for documentation to conceal the secret of their drug use, they were enrolled on the study and followed up with a urine amphetamine test, analyzed by GC/MS (gas chromatography/mass spectrometry). Data were obtained from the pregnant women's medical records as completed by the midwives, who had been given training in data collection during labor. Ethical approval for this study was granted by the ethical review committee of the Human Research Protection Unit, Faculty of Medicine Siriraj Hospital, Mahidol University (Certificate of Approval number: Si 697/2016).

A screening tool for assessing the risk of methamphetamine use was developed using the results from a multiple logistic regression analysis of the data of all the participating pregnant women. Selection of the

Table 1 Characteristics of the pregnant women by methamphetamine use

Characteristics	% Not used (n = 61)	% Used (n = 64)	p-value
Age, mean \pm SD	26.9 \pm 6.9	27.9 \pm 5.8	0.38
Gravida, mean \pm SD	2.5 \pm 1.3	3.3 \pm 1.4	0.00
GA, mean \pm SD	36.4 \pm 3.0	36.3 \pm 3.0	0.83
Family income (100 Bath), mean \pm SD	16.4 \pm 16.2	13.4 \pm 10.5	0.22
Marital status: married	88.5	84.4	0.34
Education: secondary school	67.2	60.9	0.09
Occupation: Unemployment	47.5	59.4	0.03
Have a tattoo: Yes	39.3	60.9	0.02
Smoking: Yes	18.0	60.9	0.00
Drinking: Yes	4.9	31.3	0.00
Abnormal symptoms: Yes	13.1	25.0	0.09
Living with a spouse/friend who uses drugs: Yes	11.5	59.4	0.00
BP \geq 130/90 mmHg: Yes	45.9	45.3	0.95
Pulse \geq 100/min: Yes	47.5	29.7	0.04
Total	48.8	51.2	0.86

Table 2 Logistic regression analysis of the risk factors related to methamphetamine use in pregnant women

Predictor	Odds ratio	SE	<i>p</i> -value	95% CI	
				Lower	Upper
Smoking: Yes	7.73	4.45	0.00	2.50	23.91
Drinking: Yes	3.81	2.88	0.08	0.87	16.78
Living with a spouse/friend who uses drugs: Yes	17.28	10.08	0.00	5.51	54.20
BP \geq 130/90 mmHg: Yes	2.47	1.31	0.09	0.87	6.99

final risk factors potentially indicating methamphetamine use took place through a backward selection of the candidate factors, using a *p*-value of ≥ 0.10 for exclusion. The results of the multivariable regression model were then used to develop a scoring system for the factors using a regression coefficient-based scoring method. Integer scores were assigned by dividing the risk-factor coefficients by the smallest coefficient and then rounding up the result to the nearest integer. The screening tool was internally validated. The discriminative power was assessed using the area under the receiver operating characteristic curve (AUROC) sensitivity and specificity. Calibration was assessed graphically by plotting the observed outcome frequencies against the mean predicted outcome probabilities or risks within subgroups of patients, ranked by increasing estimated probability. To evaluate the predictive value of the screening for the risk of methamphetamine use, the discriminatory power of the resulting score was assessed with both derivation and internal validation sets by calculating the cross-validated C-statistic, which could indicate the ability to differentiate the risks potentially indicating methamphetamine use. Data were analyzed using IBM SPSS Statistics v.23 and Stata for Windows special edition. In this study, we used the transparent reporting offered by a multivariable prediction model for an individual prognosis or diagnosis (TRIPOD), representing a strict methodology for data reporting, to check our adherence to the suggested optimal

levels of transparency and completeness of reporting of the screening of the risk factors.^{14–17}

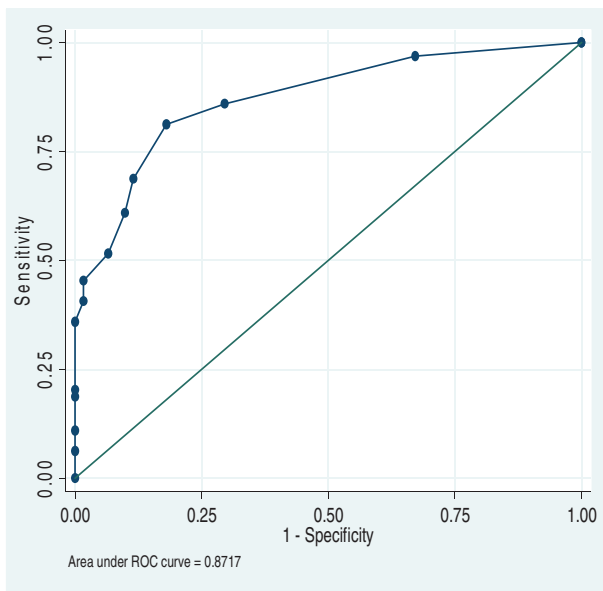
Results

In total, 255 pregnant women who attended Siriraj Hospital between January 2017 and January 2019 and who were not receiving prenatal care were considered for inclusion in the study. The prevalence of methamphetamine use in pregnancy was diagnosed by a history of methamphetamine use or had a urine amphetamine test positive was 25.1% [64/255], compared with 20.8% [220/1057] in our previous report.¹¹ A total of 125 pregnant women who had at least one candidate predictor included in the study had a urine amphetamine test positive 36.0% [45/125]. See Figure 1 for a schematic of the cohort selection.

Table 1 presents the characteristics of the pregnant women who had not used methamphetamine and those who had used methamphetamine. There were no differences based on age, family income, marital status, education, gestational age, abnormal symptoms, and BP \geq 130/90 mmHg among the two groups of pregnant women not receiving prenatal care with at least one candidate factor, while gravida, occupation, have a tattoo, smoking, drinking, living with a spouse or friend who uses recreational drugs, and pulse \geq 100/min were significantly associated with methamphetamine use by the pregnant women.

Table 3 Regression coefficients of the risk factors for the methamphetamine use screening

Predictor	Beta coef.	SE	Coef. adjusted	Score	<i>p</i> -value	95% CI	
						Lower	Upper
Smoking	2.05	0.58	1.92	2	0.00	0.92	3.17
Drinking	1.34	0.76	1.25	1	0.08	-0.15	2.82
Living with a spouse/friend who uses drugs	2.85	0.58	2.67	3	0.00	1.71	3.99
BP \geq 130/90 mmHg	0.90	0.53	0.85	1	0.09	-0.14	1.94
Constant	-2.28	0.52			0.00	-3.31	-1.25



BP \geq 130/90 mmHg ($R^2 = 0.37$, $\chi^2 = 63.78$, p -value = 0.00, AUROC curve = 0.87).

The formula used to screen the risk factors for methamphetamine use in pregnant women from the data development set in Table 3 was:

$$\text{Risk of methamphetamine use} = 1/[1 + e^{-(2.28 + 2.05 \times \text{Smoking} + 1.34 \times \text{Drinking} + 2.85 \times \text{Living with spouse/friend who uses drugs} + 0.90 \times \text{BP} \geq 130/90)}]$$

The discriminatory power of the final model was refitted using 200 repeat internal validation samples. The model performed well in all forms with the C-statistic. The AUROC for the model was 0.87, 95% CI 0.81–0.93 (SE: 0.03) and across the bootstrapping, the C-statistic for the full model was 0.86, 95% CI 0.81–0.93 (SE: 0.03) (Figure 2).

An internal validation cohort calibration plot was performed to fit the model. As shown in Figure 2, the slope of the model was 1.00 with an intercept of 0.00.

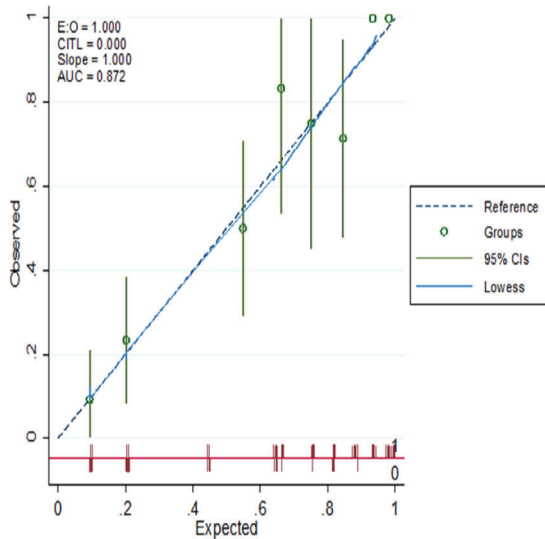


Figure 2 Area under the receiver operating characteristic curve (AUROC) for the development dataset (AUROC = 0.87), and calibration plot and the best fit line for the final model

Application of the screening tool

We developed a bedside screening tool that can be applied using either a pocket card or a handheld device. The factors were given weighted scores based on each factor’s coefficient. The screening tool considers the factors taken from the final model by assigning a point total to each factor, which allowed a total point score for each pregnant woman to be calculated. The results from the screening card show up as a nomogram of the estimated probability of methamphetamine use that the medical professionals can use in their decision-making about the need for further investigation, see Figure 3. Alternatively, the risk of methamphetamine use could be calculated using a handheld device.

The total points of the four factors were given weighted scores from the adjusted coefficient and cut-off points at ≥ 2 , ≥ 3 , and ≥ 4 points. We found that a total point score ≥ 3 points seemed to be the best cut-off, with a sensitivity of 81%, specificity of 82%, and AUROC of 0.82. To compare the performance of our screening tool with the traditional screening approach involving labor nurses, we asked the attending labor room nurses to screen the risk of methamphetamine use by using the same data of the 125 pregnant women within 1 h of the patient admission and before getting back the results of the urine amphetamine test. The sensitivity of prediction by the labor nurses was 0.95, the specificity was = 0.23, and the AUROC was = 0.59, which were significantly inferior to the results from the developed screening tool.

Table 2 presents the results of the logistic regression analysis. Here, the risk factors for potentially indicating methamphetamine use were selected in the final model, which took place through a manual backward selection of the candidate factors using a p -value of ≥ 0.10 for exclusion. The four factors that were found to be significant for screening the risk of methamphetamine use were smoking, drinking, living with a spouse or friend who uses recreational drugs, and

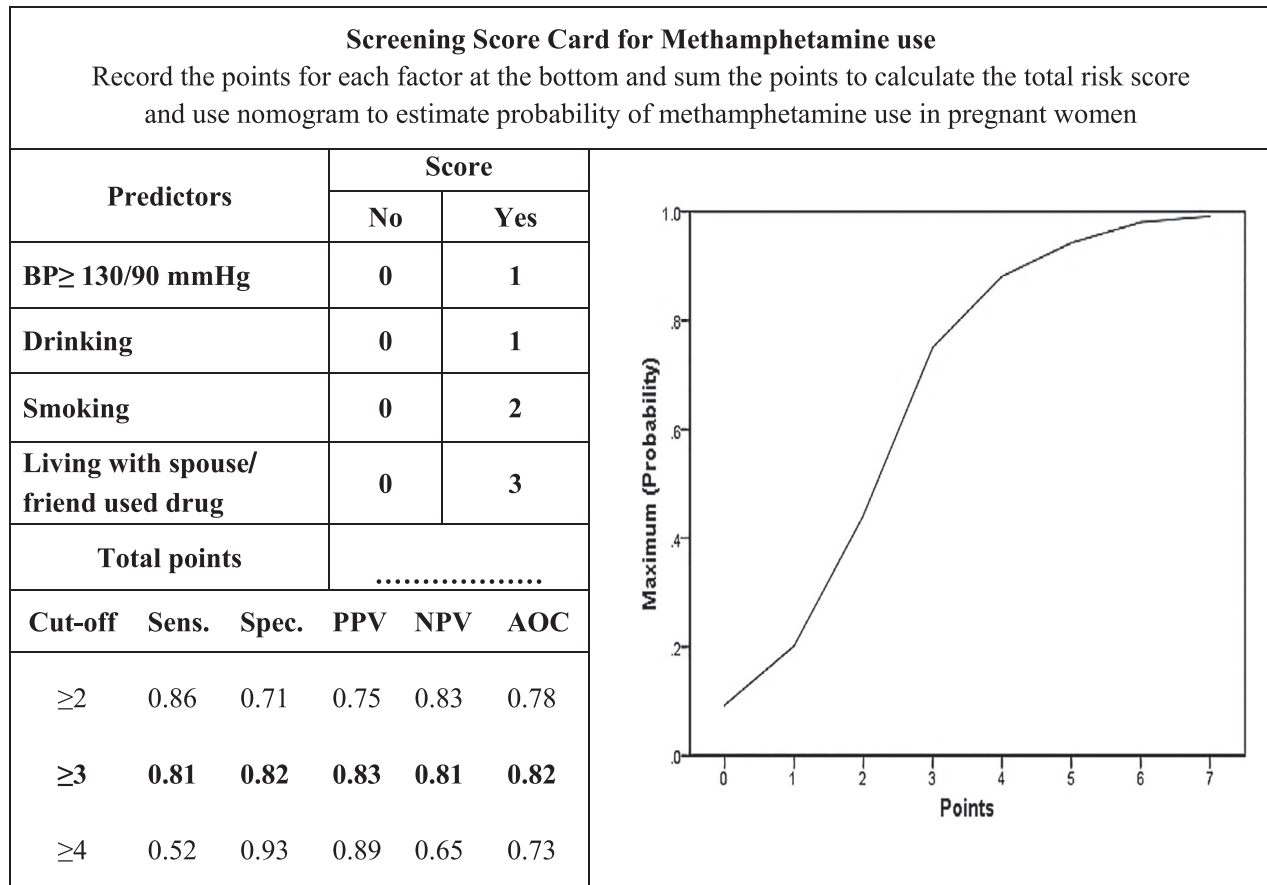


Figure 3 Methamphetamine use screening score card

Discussion

The main outcomes in the present study are the risk factors that could be used to screen the risk of methamphetamine use in pregnant women who are not receiving prenatal care. Early detection of perinatal exposure could increase the quality of care for affected mothers and newborns through following the guidelines for drug-use mothers at the labor ward. To the best of our knowledge, this is the first study for screening the risk factors potentially indicating methamphetamine use in pregnant women. Although the number of pregnant women considered in this study was less than in our previous study, mostly because Siriraj Hospital had raised the price for delivery, resulting in a decrease in the number of pregnant women attending Siriraj Hospital, and despite Thailand having active campaigns against drugs, our study still supports that there is an increased number of drug-exposed babies from maternal methamphetamine

use in pregnancy.¹⁰ This is consistent with a study in the United States, which reported that the percentage of pregnant women admitted to hospital for the treatment of methamphetamine abuse in the USA increased from 8% in 1994 to 24% by 2006.¹⁸

From the result of the present logistic regression analysis, four predictors were selected for inclusion in the final model. These confirmed the suggestion from a previous study that medical professionals should ask all pregnant women about past and recent smoking, alcohol use, and other drug use as part of the prenatal history-taking and should also ask about partner substance use as this may aid patient disclosure of personal drug use.^{19,20}

Although a cut-off at ≥4 points was a higher specificity of 0.93, the sensitivity was only 0.52. That means it has a high false-negative rate which many pregnant women would be lost to screening. On the other hand, the sensitivity of the current prediction approach by the labor nurses suggests a high false-positive rate, which

would incur a higher operation cost from performing unnecessary screening urine amphetamine tests. Therefore, it is good that medical professionals should use the total risk score and the estimated probability of methamphetamine use in pregnant women in their decision-making to consider the pros and cons of further investigation and management. Even though pregnant women who had negative urine amphetamine tests would not be diagnostic as methamphetamine users, no prenatal care is the biggest risk factor for methamphetamine use. So it would be great to give care and counsel about drug abuse even to those pregnant women with negative urine amphetamine tests.

Conclusion

A screening tool for the risk factors potentially indicating methamphetamine use was developed in this study and was shown to be able to perform significantly better than the previous screening approach used by the medical professionals. The new screening tool has the potential to be used daily in prenatal care and in the labor room. This would facilitate the targeted initiation of preventive measures. Our study showed that this screening tool had limitations to use with all pregnant women, and validation in pregnant women receiving prenatal care still needs to be performed. However, its use would be important in clinical implementation because it could increase the quality of care for affected mothers and newborns through supporting the guidelines for drug-use mothers.

Limitations of the Study

This study had a few limitations to note. First, although the screening tool for the risk factors of methamphetamine use demonstrated a high sensitivity and specificity, it had a high cost of screening related to the need for a urine amphetamine test. Therefore, we need to choose only potential participants with at least one candidate predictor. That means pregnant women not receiving prenatal care without candidate predictors were not selected for inclusion in this study. Hence, we do not know the true incidence of methamphetamine use in pregnant women not receiving prenatal care.

Second, adding covariates to the screening tool would decrease its sensitivity to the other covariates. For these reasons, we did not include demographic

data in the screening tool for assessing the risk factors potentially indicating methamphetamine use.

Finally, because of the limitation of the participant cohort, we used data collected in this study for the developed and internal validations of the model.

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Conflict of Interest

None to declare.

Author Contributions

The new screening tool has the potential to be used daily in prenatal care and in the labor room. Early detection of perinatal exposure could increase the quality of care for affected mothers and newborns through following the guidelines for drug used mothers.

Data availability statement

The data that support the findings of this study are openly available in figshare at <https://doi.org/10.6084/m9.figshare.14531895.v3>.

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