นิพนธ์ต้นฉบับ

การศึกษาย้อนหลังเรื่องผลกระทบของการใช้แอมเฟตามีนในหญิงตั้งครรภ์ต่อพัฒนาการเด็กอายุน้อยกว่า 5 ปี

ธิดารัตน์ พันธุ์แก้ว[1], จิตราภรณ์ ปัทมานุกูล[2]

[1] นายแพทย์ชำนาญการพิเศษ กลุ่มงานกุมารเวชกรรม โรงพยาบาลอุตรดิตถ์

[2] พยาบาลวิชาชีพชำนาญการ กลุ่มงานกุมารเวชกรรม โรงพยาบาลอุตรดิตถ์

Received November 16, 2024 Revised March 18, 2025 Accepted March 26, 2025

บทคัดย่อ

ความเป็นมา: แอมเฟตามีนในครอบครัวส่งผลกระทบต่อเด็กหลายด้าน โดยเฉพาะอย่างยิ่งเมื่อได้รับตั้งแต่อยู่ในครรภ์ อย่างไรก็ตาม ข้อมูลเกี่ยวกับผลระยะยาวยังมีข้อจำกัดและจำเป็นต้องศึกษาเพิ่มเติม

วัตถุประสงค์: ศึกษาพัฒนาการของเด็กที่เกิดจากมารดาที่มีและไม่มีประวัติใช้แอมเฟตามีน เพื่อให้เข้าใจผลกระทบและแนวทางดูแลที่เหมาะสม

วิธีการ: เป็นการศึกษาย้อนหลังที่ใช้ข้อมูลจากเวชระเบียนของโรงพยาบาลอุตรดิตถ์ โดยวิเคราะห์ข้อมูลเด็กที่มีทะเบียนบ้านในจังหวัดอุตรดิตถ์ระหว่างวันที่ 1 ตุลาคม 2560 ถึง 30 กันยายน 2565 การรวบรวมข้อมูลใช้ผลจากคู่มือการเฝ้าระวังและส่งเสริมพัฒนาการ (the Developmental Surveillance and Promotion Manual, DSPM) ของศูนย์ข้อมูลสุขภาพอุตรดิตถ์ (Health Data Center, HDC) และเปรียบเทียบทางสถิติโดยใช้ risk regression ภายใต้ Poisson distribution เพื่อนำเสนอ effect size ด้วย risk ratio ในพัฒนาการ 5 ด้าน

ผลลัพธ์: กลุ่มตัวอย่างประกอบด้วยเด็ก 8,453 คนที่ได้รับการดูแลแรกเกิดที่โรงพยาบาลอุตรดิตถ์ และ 6,860 คนมีบันทึก DSPM ใน HDC อุตรดิตถ์ โดยแบ่งเป็นสองกลุ่มตามประวัติการเสพแอมเฟตามีนของมารดา ได้แก่ 6,798 คนที่มารดาไม่มีประวัติเสพ และ 62 คนที่มารดามีประวัติเสพแอมเฟตามีน (48 คนมีตรวจพบแอมเฟตามีนในปัสสาวะ และ 14 คนตรวจไม่พบ) เด็กที่มารดามีประวัติการเสพมีน้ำหนักแรกเกิดต่ำกว่าและแสดงพัฒนาการล่าช้าอย่างมีนัยสำคัญเมื่ออายุ 9 เดือน รวมถึงเด็กที่ไม่พบแอมเฟตามีนในปัสสาวะเมื่อแรกเกิดก็ยังแสดงพัฒนาการล่าช้าอย่างมีนัยสำคัญในทุกด้าน (3.31-7.33 เท่า) เทียบกับกลุ่มที่มารดาไม่มีประวัติการเสพ ในขณะที่เด็กที่มีผลตรวจแอมเฟตามีนเป็นบวกแสดงความล่าช้าอย่างมีนัยสำคัญในด้านกล้ามเนื้อมัดเล็ก การสื่อภาษา และสังคม-การช่วยเหลือตนเอง

สรุป: จากการศึกษาแสดงให้เห็นว่าเด็กที่เกิดจากมารดาที่มีประวัติการใช้แอมเฟตามีนมีพัฒนาการล่าช้าอย่างมีนัยสำคัญที่อายุ 9 เดือน แม้ว่าผลการตรวจปัสสาวะแอมเฟตามีนแรกเกิดจะเป็นลบ

คำสำคัญ: แอมเฟตามีน, DSPM พัฒนาการ, การตั้งครรภ์, เสพแอมเฟตามีนก่อนคลอด

A retrospective study on the impact of prenatal amphetamine exposure on child development under five years of age

Thidarat Pankaew[1], Jitraporn Pattamanukul[2]

[1] Developmental and Behavioral Pediatrician, Department of Pediatrics, Uttaradit Hospital, Uttaradit, Thailand

[2] Registered nurse (RN), Department of Pediatrics, Uttaradit Hospital, Uttaradit, Thailand

Abstracts

Background: Amphetamine use within families can impact various aspects of child development, especially when exposure occurs in utero. However, data on its long-term effects remain limited, necessitating further research.

Objectives: To examine the impact of maternal amphetamine use during pregnancy on early childhood development, focusing on its association with developmental delays in gross motor, fine motor, receptive language, expressive language, and personal-social skills.

Method: This retrospective study utilized medical records from Uttaradit Hospital, focusing on children registered in Uttaradit Province between October 1, 2017, and September 30, 2022. Data were collected using the Developmental Surveillance and Promotion Manual (DSPM) from the Uttaradit Health Data Center (HDC). Statistical comparisons were made using risk regression under Poisson distribution, presenting effect sizes with risk ratios across five developmental domains.

Results: A total of 8,453 infants received care at Uttaradit Hospital, with 6,860 having DSPM records in the HDC. The children were divided into two groups based on their mothers' amphetamine use history: 6,798 children whose mothers had no history of use, and 62 children whose mothers had a history of use (48 tested positive for amphetamines in urine, and 14 tested negative). Infants born to mothers with a history of amphetamine use exhibited significantly lower birth weights and developmental delays in the DSPM at 9 months. Additionally, children whose urine did not test positive for amphetamines at birth demonstrated significant developmental delays (3.31-7.33 times) across all domains compared to the group with mothers without a history of use. On the other hand, infants with positive urine tests at birth showed significant delays in fine motor skills, expressive language, and personal-social skills.

Conclusion: The study highlights that children born to mothers with a history of amphetamine use demonstrate significant developmental delays at 9 months of age, even when initial urine tests for amphetamines are negative.

Keywords: Amphetamine, DSPM, Development, Pregnancy, Prenatal Amphetamine

Introduction

Amphetamine, a synthetic non-catecholamine sympathomimetic amine, was first discovered in the United States about a century ago. It exerts psychostimulant effects on the sympathetic nervous system, enhancing alertness and concentration. Initially, amphetamine was widely used, but it later became a controlled substance due to its potential for both therapeutic benefits and harm. Lisdexamfetamine, a prodrug of d-amphetamine, is the first of its kind approved for the treatment of attention deficit hyperactivity disorder (ADHD) and narcolepsy in children, adolescents, and adults in the United States.

In Thailand, amphetamine is classified strictly as an illegal substance. Historically, laborers commonly consumed it in tablet form. Over time, modifications to its chemical structure enhanced its psychotropic effects while reducing cardiovascular side effects, resulting in methamphetamine, which remains a significant public health issue today.

An alarming trend is the increasing use of amphetamines by pregnant women.[1,2] Infants born to mothers who used amphetamines during pregnancy frequently exhibit a range of neonatal complications,[3-8] including low birth weight, intrauterine growth restriction, preterm birth, respiratory distress, microcephaly, and Neonatal Abstinence Syndrome (NAS), depending on the half-life of the drug (48-60 hours for methamphetamine).[9,10] Systematic effects on newborns include impacts on the nervous, gastrointestinal, and respiratory systems. Furthermore, mothers who use amphetamines during pregnancy often exhibit delayed or inadequate prenatal care, are more likely to have multiple pregnancies, and are at greater risk for severe maternal morbidity and mortality, including gestational hypertension and preeclampsia with severe features.[2,11]

Long-term studies have followed children exposed to amphetamines in utero through ages 8 and 14.[12,13] These studies have found significant associations between maternal amphetamine use (both in quantity and duration) and adverse psychological outcomes, including aggressive behavior, adjustment difficulties, and impaired growth in various domains. While maternal amphetamine misuse is likely linked to neurodevelopmental deficits, it remains unclear whether these outcomes are due to amphetamine exposure itself or related familial factors,[14,15] such as the increased risk of child abuse (physical, emotional, neglect, and sexual) in mothers who use methamphetamines during pregnancy.

Children born to mothers who use amphetamines are at higher risk for congenital abnormalities and suboptimal care, which may hinder their development. Given that child development is a critical predictor of the quality of the future population, developmental disorders increase the likelihood of

academic difficulties, substance abuse, and risky adolescent behaviors, such as unprotected sex, teenage pregnancy, accidents, and violence. These risks further predispose individuals to mental health problems, psychiatric disorders, and chronic physical illnesses in adulthood. Once these issues arise, they are often difficult and costly to address, making early intervention crucial, particularly during brain development in the first 5-6 years of life.

Further research is needed to fully assess the long-term developmental consequences in children prenatally exposed to amphetamines. This study aimed to examine the impact of maternal amphetamine use during pregnancy on early childhood development, focusing on its association with developmental delays in gross motor, fine motor, receptive language, expressive language, and personal-social skills.

Methods

Design

This study employed a retrospective design to investigate prognostic factors associated with developmental outcomes in children. Data were systematically collected from the Child Development Promotion Project in honor of Her Royal Highness Princess Maha Chakri Sirindhorn, commemorating Her Majesty's five-cycle celebration on April 2, 2015.

Setting

Data were obtained from the medical records of pediatric patients born or receiving neonatal care at Uttaradit Hospital, Thailand, between October 1, 2017, and September 30, 2022. Eligible participants were those with a registered address in Uttaradit Province and at least one documented developmental assessment using the Developmental Surveillance and Promotion Manual (DSPM) conducted by medical personnel aged 9, 18, 30, 42, or 60 months. Patients were excluded if no DSPM data were available in the Health Data Center (HDC) of Uttaradit Hospital.

Definition

Amphetamine-related history referred to children whose mothers had a positive urine test for amphetamine during pregnancy or who self-reported amphetamine use during pregnancy despite negative urine results. It also included mothers diagnosed with amphetamine dependence or abuse (ICD-10 code: F15) based on medical records. At birth, the presence of amphetamine in the child's urine might or might not have been detected.

Positive urine amphetamine referred to children who had detectable levels of amphetamine in their urine at birth.

Negative urine amphetamine referred to children who had no detectable levels of amphetamine in their urine at birth.

No amphetamine-related history referred to children whose urine was not tested for amphetamine at birth and whose mothers had no reported history of amphetamine use or a diagnosis of amphetamine abuse.

Data collection

Clinical information collected for each patient included gender, age, date of birth, birth weight, and maternal age. Developmental data were assessed using the Developmental Surveillance and Promotion Manual (DSPM) across five domains: gross motor development, fine motor development, receptive language development, expressive language development, and personal-social development. The overall developmental outcomes were also recorded.

This study was approved by the Human Research Ethics Committee of Uttaradit Hospital (Project No. 15/2023) and the Uttaradit Provincial Public Health Office (UPHO REC No. 060/2566).

Sample size and statistical analysis

Based on the assumption that developmental delays would be observed in 60% of children born to mothers with a history of amphetamine use and in 20% of children born to mothers without such a history, a two-sided test with a significance level of 0.05 and a power of 0.80 was used. The ratio of children with and without a maternal amphetamine history was set at 1:136. Using these parameters, the required sample size was calculated to be 45 in the exposed group (amphetamine-related history) and 6,120 in the unexposed group (no amphetamine-related history). To account for a 10% rate of incomplete data, the final sample size was adjusted to 50 cases in the exposed group and 6,800 cases in the unexposed group. Sample size calculation was performed using Stata version 16.1.

Continuous variables were reported as means with standard deviations (SD), and categorical variables were presented as percentages. Statistical comparisons were made using risk regression based on the Poisson distribution, with effect sizes reported as risk ratios (RR).

Results

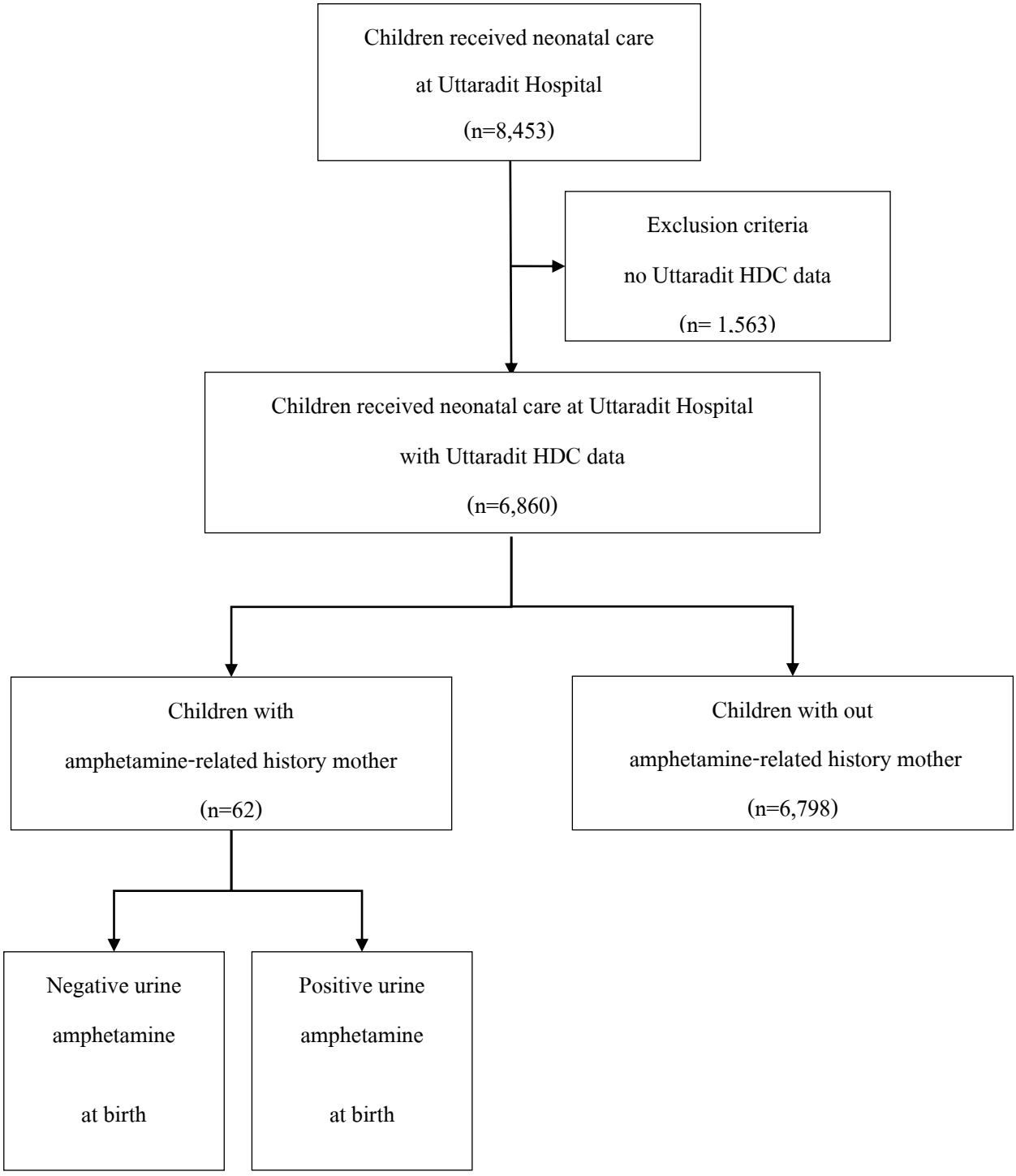

Figure 1 Study flow diagram

Total of 8 ,4 5 3 children were born or received neonatal care at Uttaradit Hospital, residing in Uttaradit Province, between October 1, 2017, and September 30, 2022 (over the past five fiscal years). Of

these, 6,860 children (81.12%) had recorded developmental surveillance data in the Health Data Center (HDC) in Uttaradit Province (Figure 1).

Table 1 Demographic data

Characters	Amphetamine-related history		p value
	Related history n=62	No history n=6,798	
	n (%)	n (%)	
Male	32 (51.6)	3,561 (52.4)	0.766
Birthweight (g, mean±SD)	2,594.4±576.3	3,044.4±470.4	<0.001**
Maternal age (yr, mean±SD)	29.7±7.8	28.1±6.4	0.258

*p value < 0.05, **p value <0.001

There were no significant differences in maternal age and gender between groups. However, children born to mothers with a history of amphetamine use had significantly lower birth weights compared to those born to mothers without such a history (Table 1).

Table 2 Interpretation of development by DSPM

Interpretation		Amphetamine-related history		
		Related history n (%)	No history n (%)	p value
Age	9 months	n=24	n=1,891	
	Normal surveillance	13 (54.2)	1,382 (73.1)	reference
	Abnormal surveillance	11 (45.8)	509 (26.9)	0.036
	Gross motor delay	2 (8.3)	62 (3.3)	0.026
	Fine motor delay	7 (29.2)	111 (5.9)	<0.001
	Receptive language delay	3 (12.5)	43 (2.3)	0.005
	Expressive language delay	3 (12.5)	35 (1.9)	<0.001
	Personal-social delay	3 (12.5)	28 (1.5)	0.002
	Unspecified	11 (45.8)	469 (24.8)	0.044

Interpretation		Amphetamine-related history		
		Related history	No history	p value
		n (%)	n (%)	
Age	18 months	n=34	n=2,208	
	Normal surveillance	17 (50.0)	1,533 (69.4)	reference
	Abnormal surveillance	17 (50.0)	675 (30.6)	0.008
	Gross motor delay	0 (0)	22 (1.0)	1.000
	Fine motor delay	4 (11.7)	67 (3.0)	0.023
	Receptive language delay	3 (8.8)	119 (5.4)	0.355
	Expressive language delay	1 (2.9)	72 (3.3)	1.000
	Personal-social delay	1 (2.9)	55 (2.5)	0.580
	Unspecified	17 (50.0)	641 (29.1)	0.005
Age	30 months	n=18	n=2,353	
	Normal surveillance	10 (55.5)	1,728 (73.4)	reference
	Abnormal surveillance	8 (44.4)	625 (26.6)	0.192
	Gross motor delay	0 (0)	24 (1.0)	1.000
	Fine motor delay	1 (5.5)	38 (1.6)	0.259
	Receptive language delay	1 (5.5)	69 (2.9)	0.418
	Expressive language delay	0 (0)	62 (2.6)	1.000
	Personal-social delay	0 (0)	67 (2.8)	1.000
	Unspecified	8(44.4)	613(26.0)	0.121
Age	42 months	n=15	n=2,130	
	Normal surveillance	12 (80.0)	1,556 (73.1)	reference
	Abnormal surveillance	3 (20.0)	574 (26.9)	0.708
	Gross motor delay	0 (0)	10 (0.5)	1.000
	Fine motor delay	1 (6.7)	67 (3.2)	0.384
	Receptive language delay	0 (0)	89 (4.2)	1.000
	Expressive language delay	0 (0)	52 (2.4)	1.000
	Personal-social delay	0 (0)	62 (2.9)	1.000
	Unspecified	2 (13.3)	555 (26.1)	0.629

Interpretation		Amphetamine-related history		
		Related history	No history	p value
		n (%)	n (%)	
Age	60 months	n=4	n=1,083	
	Normal surveillance	3 (75.0)	897 (82.9)	reference
	Abnormal surveillance	1 (25.0)	186 (17.1)	0.237
	Gross motor delay	0 (0)	3 (0.3)	1.000
	Fine motor delay	0 (0)	9 (0.8)	1.000
	Receptive language delay	0 (0)	24 (2.2)	1.000
	Expressive language delay	0 (0)	31 (2.8)	1.000
	Personal-social delay	0 (0)	31 (2.8)	1.000
	Unspecified	1 (25.0)	180 (16.6)	0.228

Fisher's Exact Test

At 9 months, children born to mothers with a history of amphetamine use exhibited significantly more frequent abnormal surveillance compared to those without such a history (45.8% vs. 26.9%, p value 0.036) (Table 2) . Specific developmental delays were observed, with gross motor delay being more common in the amphetamine-related history group (8.3% vs. 3.3%, p value 0.026) and expressive language delay (12.5% vs. 1.9%, p <0.001) (Table 2).

At 18 months, the trend of developmental delays persisted. Abnormal surveillance remained significantly higher in children with a maternal history of amphetamine use (50.0% vs. 30.6%, p value 0.008). Fine motor delays were more frequent in the amphetamine-related group (11.7% vs. 3.0%, p value 0.023) (Table 2).

At 30, 42, and 60 months, no significant differences in abnormal surveillance or developmental delays were observed between the two groups across the various developmental domains.

Table 3 Effect of maternal amphetamine use on children under 5 years old in 5 domains of development, and mothers without a history of amphetamine use.

Domain	Negative urine amphetamine N= 14			Positive urine amphetamine N=48		
	OR	95% CI	p value	OR	95% CI	p value
Gross motor	6.14	1.51, 25.00	0.011	NA	NA	0.984
Fine motor	4.40	1.41, 13.75	0.011	4.10	2.11, 7.98	<0.001
Receptive language	3.31	0.82,13.30	0.092	1.56	0.58, 4.18	0.380
Expressive language	7.33	2.34, 22.93	0.001	0.60	0.08, 4.27	0.608
Personal Social	4.83	1.20, 19.45	0.027	1.28	0.32, 5.17	0.726

†mOR: multivariable Odds ratio

The five developmental domains in children of mothers with a history of amphetamine use, and children whose mothers had no amphetamine-related history was analyzed in Table 3.

A significant association was found between negative urine amphetamine and gross motor skills delays (mOR 6.14, 95% CI 1.51–25.00, p value 0.011), while no significant association was observed with positive urine amphetamine results (mOR NA, p value 0.984).

Both negative (mOR 4.40, 95% CI 1.41–13.75, p value 0.011) and positive urine amphetamine results (mOR 4.10, 95% CI 2.11–7.98, p <0.001) were significantly associated with fine motor skills delays.

There was no significant association for either negative (mOR 3.31, 95% CI 0.82–13.30, p value 0.092) or positive urine amphetamine (mOR 1.56, 95% CI 0.58–4.18, p value 0.380) with the receptive language delay.

A significant association was found in negative urine amphetamine with expressive language delay (mOR 7.33, 95% CI 2.34–22.93, p value 0.001), but not in positive results (mOR 0.60, 95% CI 0.08–4.27, p value 0.608).

Significant personal social skills delays were observed in children of mothers with negative urine amphetamine (mOR 4.83, 95% CI 1.20–19.45, p value 0.027), while no association was observed with positive results (mOR 1.28, 95% CI 0.32–5.17, p value 0.726).

Discussion

This study found that children born to mothers with a history of amphetamine use were more frequently delayed than children born to mothers without such a history. These results are consistent with previous research[16] that suggests that prenatal amphetamine exposure may have transient effects on gross motor development but have little effect on early life behavior and executive function. Our results indicate that infants are delayed in gross motor development at 9 months of age, but not significantly delayed after 18 months of age. However, further studies are needed.

Studies have reported structural brain abnormalities in children exposed to amphetamines in utero, including reductions in cortical gray matter volume, which may indicate characteristics associated with substance dependence.[17] There have also been reports of congenital malformations, such as gastroschisis,[3] as well as behavioral and cognitive impairments in animal models, potentially linked to dysfunction in hippocampal synaptic function.[18]

One notable case in this study involved a preterm infant, born at 24 weeks of gestation (Ballard score) with a birth weight of 730 grams, who was diagnosed with schizencephaly. However, since structural brain anomalies were not systematically examined across all cases, the significance of this finding remains uncertain.

Animal studies have provided additional insights into the impact of amphetamine exposure on offspring. Research suggests that both maternal and paternal amphetamine use can negatively affect neurological and reproductive functions. Paternal amphetamine use[19-20] before conception has been linked to impaired intelligence in offspring, while maternal amphetamine use[21] is associated with disrupted ovarian function, oocyte maturation, and fetal development. Furthermore, studies in pregnant sheep[22] have demonstrated significant cardiovascular effects in both mothers and fetuses, highlighting the rapid placental transfer of amphetamines and their prolonged clearance from the amniotic fluid.

In this study, many mothers also reported a history of drug use by the fathers, which may have affected sperm quality and contributed to developmental abnormalities in their children. Additionally, case reports[23] suggest that children prenatally exposed to amphetamines require significantly higher public healthcare expenditures. However, due to ethical constraints, direct research on the effects of amphetamines during pregnancy remains limited. Moreover, self-reported data from substance users are often unreliable due to legal and social stigmatization.

The existing literature indicates that women who use amphetamines frequently experience multiple unplanned pregnancies with different partners and often lack adequate prenatal care.[6] Notably,

these characteristics overlap with those of women with undiagnosed ADHD, a population at increased risk for early sexual activity, teenage pregnancies, and sexually transmitted diseases. Early diagnosis and appropriate treatment of ADHD could potentially reduce amphetamine misuse and improve both maternal and fetal health outcomes.

Importantly, therapeutic doses of ADHD medications, including amphetamines,[24-25] have not been associated with adverse fetal effects. Some evidence[26] also suggests that medications such as methylphenidate may help reduce amphetamine use disorder. Further research is necessary to explore the potential benefits of ADHD treatment in this population as a strategy to mitigate amphetamine abuse and improve child developmental outcomes.

One notable finding was that children whose mothers had a history of amphetamine use but whose newborns tested negative for amphetamines in their urine exhibited the most developmental delays. This might be due to less rigorous follow-up in the negative urine group compared to the positive urine group. Additionally, there was qualitative evidence suggesting that some caregivers might have concealed information by not submitting urine samples during the newborn period, which could have affected follow-up data. If such information was concealed early on, other developmental concerns might also be underreported.

In terms of child development, children whose mothers had a clear history of amphetamine use showed delays at 9 months, but some showed improvements with age. However, the cause remained unknown. These children allowed ongoing follow-up to fully understand long-term outcomes.

This study had some limitations. Being a retrospective study, some information was incomplete or missing. Data was collected by various personnel, including doctors, nurses, psychologists, and public health officers, using the same manual. However, there were variations in evaluations. In the earlier years, such as 2017, some personnel misunderstood or incompletely recorded information, resulting in inaccuracies, such as misclassification of developmental delays or missing details. Children of mothers who used amphetamines are often difficult to track due to neglect, family resistance, or safety concerns for medical personnel, making comprehensive follow-up challenging. The developmental surveillance over the 5 fiscal years included children of different ages, leading to inconsistencies in the number of DSPM (Developmental Surveillance and Promotion Manual) assessments. Very few children of maternal amphetamine use had assessments at 60 months of age. The exact dosage, duration, and timing of amphetamine use were difficult to determine due to reliance on potentially inaccurate self-reported data, complicating clear correlations with developmental outcomes.

The strength of this research lied in its large dataset of child development surveillance across Uttaradit Province, facilitated by medical personnel. This allowed for fast and broad data processing, saving time compared to individual case tracking from birth to five years. Nevertheless, a prospective cohort study is recommended to obtain more comprehensive data.

Implications for Practice

The findings should inform the development of guidelines in Thailand aimed at preventing maternal amphetamine use during pregnancy. These guidelines should emphasize the potential harm to child development, even if amphetamines were not detected in the newborn's urine. Both groups,positive and negative urine amphetamines,required close and long-term developmental monitoring.

Conclusion

Children born to mothers with a history of amphetamine use were at an elevated risk of developmental delays, particularly in gross motor, fine motor, and expressive language skills during the early years of life (9 and 18 months). These differences were no longer significant by 30 months.

The findings emphasize that maternal amphetamine use, regardless of whether the child tests positive at birth, could have detrimental effects on early development. Raising awareness and providing education on the harmful impact of amphetamines could reduce long-term societal and healthcare costs while protecting future outcomes for children and society. Further research was needed to explore the specific effects of varying levels of amphetamine exposure on different developmental domains.

Acknowledgments

We thank Dr. Thanin Loketkrawee, Prof. Dr. Chayanthorn Pathummanon, and the Research Unit of the Center for Clinical Medicine, Buddhachinnarat Hospital, Phitsanulok, for supervising data analysis and interpretation.

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

1. Jarlenski MP, Paul NC, Krans EE. Polysubstance use among pregnant women with opioid use disorder in the United States, 2007–2016. Obstet Gynecol. 2020;136:556–64.
2. Admon LK, Bart G, Kozhimannil KB, Richardson CR, Dalton VK, Winkelman TNA. Amphetamine- and opioid-affected births: Incidence, outcomes, and costs, United States, 2004–2015. Am J Public Health. 2019;109:148–54.
3. Garey JD, Lusskin SI, Scialli AR. Teratogen update: Amphetamines. Birth Defects Res. 2020;112:1171–82.
4. Maranella E, Mareri A, Nardi V, Di Natale C, Di Luca L, Conte E, et al. Severe neurologic and hepatic toxicity in a newborn prenatally exposed to methamphetamine: A case report. Brain Dev. 2019;41:191–4.
5. Perez FA, Blythe S, Wouldes T, McNamara K, Black KI, Oei JL. Prenatal methamphetamine impact on the mother and child: A review. Addiction. 2022;117:250–60.
6. Notethasoung C. Neonatal outcomes and factors affecting the severity of amphetamine withdrawal symptoms in antenatal maternal amphetamine use. Chiangrai Med J. 2022;14:118–30.
7. Maranella E, Basti C, Di Fabio S. Methamphetamine abuse during pregnancy and its effect on fetal and neonatal outcome: A review. J Case Rep Clin Images. 2022;5:1104–9.
8. Sankaran D, Lakshminrusimha S, Manja V. Methamphetamine: Burden, mechanism, and impact on pregnancy, the fetus, and newborn. J Perinatol. 2022;42:293–9.
9. Chaiverapundech J, Kanchanabat S. Prenatal methamphetamine exposure and neonatal outcomes. Vajira Med J. 2017;60:53–64.
10. Schep LJ, Slaughter RJ, Beasley MG. The clinical toxicology of methamphetamine. Clin Toxicol (Phila). 2010;48:675–94.
11. Speranza RJ, Greiner KS, Rincon M, Beeraka SS, Burwick RM. Association between amphetamine use and pregnancy outcomes in women with a hypertensive disorder of pregnancy [24A]. Obstet Gynecol. 2019;133(Suppl 1):16.
12. Billing L, Eriksson M, Jonsson B, Steneroth G, Zetterström R. The influence of environmental factors on behavioral problems in 8-year-old children exposed to amphetamine during fetal life. Child Abuse Negl. 1994;18:3–9.

13. Cernerud L, Eriksson M, Jonsson B, Steneroth G, Zetterström R. Amphetamine addiction during pregnancy: 14-year follow-up of growth and school performance. Acta Paediatr. 1996;85:204–8.
14. Oei JL, Kingsbury A, Dhawan A, Burns L, Feller JM, Clews S, et al. Amphetamines, the pregnant woman, and her children: A review. J Perinatol. 2012;32:737–47.
15. Patcharoros N, Chulakadabba S, Manorom NN, Boon-Yasidhi V. Assessing child maltreatment in children born to mothers who used methamphetamine during pregnancy at Siriraj Hospital, Bangkok, Thailand: A pilot study. Int Sch Res Notices. 2014:406208.
16. Smith LM, LaGasse LL, Derauf C, Newman E, Shah R, et al. Motor and cognitive outcomes through three years of age in children exposed to prenatal methamphetamine. Neurotoxicol teratol. 2011;33:176-184.
17. Berman S, O'Neill J, Fears S, Bartzokis G, London ED. Abuse of amphetamines and structural abnormalities in the brain. Ann N Y Acad Sci. 2008;1141:195–220.
18. Aghazadeh R, Roshan-Milani S, Derafshpour L, Saboory E. Effects of prenatal methamphetamine exposure on spatial cognition and hippocampal synaptic plasticity in adolescent rats. Int J Dev Neurosci. 2022;82:471–85.
19. Verstegen RHJ, Wang G, Langenberg-Ververgaert KPS, Ren LY, Nulman I. Paternal exposure to recreational drugs before conception and its effect on live-born offspring: A scoping review. Birth Defects Res. 2020;112:970–88.
20. Khoshgoftar Some Saraii Z, Dianaty S, Rouhollah F, Zare N, Ghorbani Yekta B. Reproductive status of male rat offspring following exposure to methamphetamine during intrauterine life: An experimental study. Int J Reprod Biomed. 2023;21:175–84.
21. Rezazadeh M, Hajikhani R, Vaezi G, Bananej M. Evaluation of the effects of methamphetamine on amniotic sac composition in pregnant mice and their offspring. J Anim Biol. 2022;14:195–206.
22. Stek AM, Fisher BK, Baker RS, Lang U, Tseng CY, Clark KE. Maternal and fetal cardiovascular responses to methamphetamine in the pregnant sheep. Am J Obstet Gynecol. 1993;169:888–97.
23. Pankaew T, Jongatchariyakul P, Funoi M, Jiamsajjamongkol C, Budcha N. Bio-psycho-social health problems related to maternal amphetamine use in pediatric patients: A case report. J Phayao Hosp. 2023;2:29–36.

24. Rose SJ, Hathcock MA, White WM, Borowski K, Rivera-Chiauzzi EY. Amphetamine-dextroamphetamine and pregnancy: Neonatal outcomes after prenatal prescription mixed amphetamine exposure. J Atten Disord. 2021;25:1295–301.
25. Bang Madsen K, Robakis TK, Liu X, Momen N, Larsson H, Dreier JW, et al. In utero exposure to ADHD medication and long-term offspring outcomes. Mol Psychiatry. 2023;28:1739–46.
26. Chan B, Freeman M, Kondo K, Ayers C, Montgomery J, Paynter R, et al. Pharmacotherapy for methamphetamine/amphetamine use disorder: A systematic review and meta-analysis. Addiction. 2019;114:2122–36.