Perinatal Effects of Amphetamine and Heroin Use during Pregnancy on the Mother and Infant

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Objectives: *To determine the perinatal impacts of heroin and amphetamine on both mothers and infants.*
Material and Method: *This is a retrospective study on the influence of amphetamine and heroin on pregnant women and their newborn infants at King Chulalongkorn Memorial Hospital in Bangkok, Thailand, between January 1997 and December 2002. The medical and demographic data of both mothers and infants were evaluated. Comparison of the consistent drug effects of these 2 drugs on the mothers and infants were also performed.*
Results: *Two hundred and eleven women were identified. There were 178 (84.4%) and 33 (15.6%) women addicted to amphetamine and heroin respectively. Sixty one (28.9%) of them were polydrug users. There were more polydrug users among heroin addicts than amphetamine addicts, (43.7% vs 27.2%, $p < 0.05$). Poor obstetric history were noted in both groups of women including lack of prenatal care (74.9%), a high incidence of previous abortion (22.3%), positive HIV serology test (11.1%), pre-eclampsia (5.2%), infection (3.3%) and antepartum hemorrhage (1.9%). Drug intoxication was found in 11 amphetamine addicted mothers, whereas 2 heroin addicts developed withdrawal symptoms during intrapartum and postpartum periods. All infants were singleton. There was one stillbirth and 2 neonatal deaths. There was no statistical difference in terms of sex ratio, mean birth weight, gestational age, length, head circumference and Apgar score between the groups of amphetamine and heroin exposed infants.*

The incidence of prematurity, low birth weight, IUGR and microcephaly were not statistically different between both groups of infants. The overall incidence was 31.7%, 31.7%, 9.5% and 8.6% respectively.

Congenital anomalies were found in 5 (2.8%) amphetamine exposed infants. Thirty one out of 33 heroin exposed infants (93.9%)and 4 out of 178 amphetamine exposed infants (2.2%) developed drug withdrawal symptoms with the mean onset of 21.5 ± 16.5 hours and 10.3 ± 7.5 hours respectively, $p > 0.05$. All heroin withdrawal infants were successfully treated with Phenobarbital with the mean duration of treatment of 23.7 ± 11.5 days. None of the amphetamine withdrawal infants needed specific treatment. They recovered spontaneously within 6.0 ± 5.3 days. Eighteen infants were left in an orphanage or under the custody of their relatives.
Conclusion: *Amphetamine or heroin use during pregnancy can cause many serious adverse effects on both mothers and infants. The findings in the present study are consistent with previous reports, although they seemed to be more common and severe. Increasing awareness and improving understanding of drug abuse in the medical, legal and social aspects are needed in order to reduce these impacts.*

Keywords: *Perinatal effect, Amphetamine, Heroin, Pregnancy*

J Med Assoc Thai 2005; 88 (11): 1506-13
Full text. e-Journal: *http://www.medassocthai.org/journal*

Amphetamine and heroin are the 2 major illicit drugs use that can cause many serious health problems and enormous financial and social burdens. Perinatal exposure to amphetamine or heroin may lead to maternal and neonatal intoxication or withdrawal. Consistent health problems include risk of contracting human immunodeficiency virus (HIV), hepatitis B and

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C, endocarditis, sexually transmitted diseases, psychiatric disorders and obstetric complications on the mothers[1]. Medical problems on the infants include low birth weight (LBW), prematurity, intrauterine growth retardation (IUGR) or small for gestational age (SGA), congenital anomalies and withdrawal syndrome[2]. Although, it is illegal for drug trafficking, the number of drug addicts in Thailand continues to rise[3]. Since February 2003, war against these illicit drugs was declared by the Thai government in order to stop their expansion. It has been known that most of the illegal laboratories, producing amphetamine and heroin are located along the northern border of Thailand, therefore the purity and availability of these drugs in our country must be better than those used in the reports from the USA or western countries where these perinatal effects have been published. So the authors think the true extent of these untoward effects among our patients may be different or more severe. However, reports from Thailand are relatively limited. Therefore, the authors conduct the present study in order to demonstrate the perinatal impacts of these illicit drugs on both mothers and infants.

Material and Method

Data was collected from the medical records of pregnant women who were identified as amphetamine and/or heroin users when they were admitted to the obstetric department at King Chulalongkorn Hospital in Bangkok, Thailand, between January 1997 and December 2002. The medical and demographic characteristics of both mothers and their infants were obtained. The infants were examined by the pediatricians within 6 hours of age and were observed for withdrawal symptoms or other complications for at least 48 hours. Gestational age (GA) was determined according to the Ballard score system[4]. GA equal to or less than 37 weeks was defined as prematurity. Birth weight (BW) and occipito-frontal circumference or head circumference (HC) less than 10th percentile according to the intrauterine growth curve for Thai infants[5] were considered as small for gestational age (SGA) or intrauterine growth retardation and microcephaly respectively. Evaluation of the severity of withdrawal symptoms was based on Lipsitz's neonatal abstinence score[6]. Treatment would be initiated with Phenobarbital if the abstinence score was more than 4 when the infant was not hungry or sleepy. Various indices of neonatal withdrawal were evaluated, including need for treatment, the timing of withdrawal onset and duration of treatment. Initial drug therapy would be changed to opium syrup if the infant experienced diarrhea or vomiting resulting in excessive weight loss or required Phenobarbital > 12 mg/kg/d. For the infants with withdrawal symptoms, hospitalization was continued while they were slowly weaned from treatment. The infant was discharged when remaining free of withdrawal without drug therapy and social evaluation was completed.

Statistical analyses were performed using Chi square, Student-t test and Pearson correlation coefficient where appropriate. P-value < 0.05 was considered statistical significant.

Results

Two hundred and eleven pregnant women were identified among 69,190 women delivered during this 6 year period. There were 178 (84.4%), 28 (13.3%) and 5 (2.4%) women addicted to amphetamine, heroin and both drugs respectively. For comparison of the impacts between these 2 drugs, data of women addicted to both drugs was included in heroin addicted group. Sixty one (28.9%) of them used 2 or more illicit drugs (polydrug users). The largest number was 4 drugs which were found in 2 heroin addicts. Both of them also had received methadone. There was only one woman who used cocaine in addition to heroin, methadone and marihuana. Among the polydrug users, 50 percent were addicted to amphetamine and cigarettes. But the proportion of women with polydrug use among heroin addicts was significantly higher than those with amphetamine addiction, (43.7% vs 27.2%, $p < 0.05$). Nine women who previously used heroin, were able to quit and used amphetamine instead prior to this pregnancy. The number of women used amphetamine was rising with time, as shown in Fig. 1. Only 53 (25.1%) women had attended the prenatal clinic, which occurred during their last trimester of pregnancy. The maximum number of prenatal visits was only 2. Of those women without prenatal care, including 4 women with a history of previous cesarean section, came to the hospital either when they were in late stage of labor or had already delivered the infants at home or in the taxi on the way to the hospital. Sixty eight (32.2%) women were primiparous. Forty seven (22.3%) women had a history of previous abortion with the maximum number of 4 abortions.

All women delivered a live-born singleton except one amphetamine addicted mother who gave birth to a stillbirth. The proportion of normal and abnormal deliveries was 171 to 40. Heroin addicted mothers had a higher percentage of prenatal care and positive HIV serology test. They also had a higher

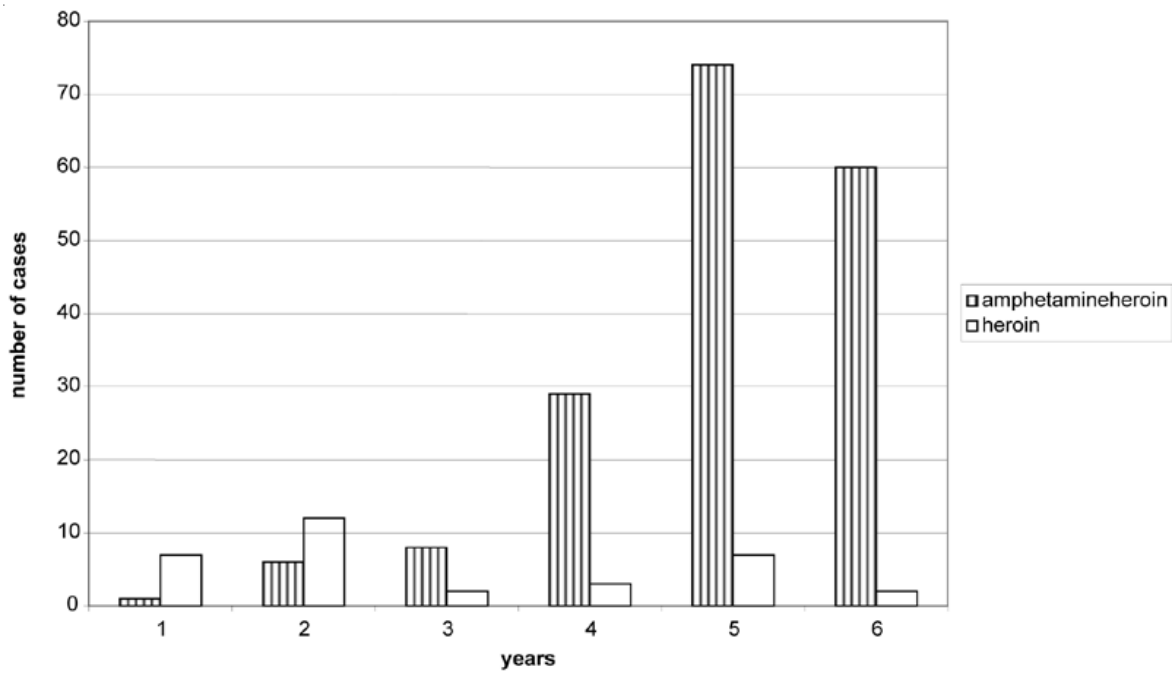

Fig. 1 Number of women addicted to amphetamine and heroin in year 1997-2002

mean frequency of drug use per day and longer mean duration of addiction, in comparison with amphetamine addicts, as shown in Table 1 and Table 2.

Most common obstetric complications were meconium stained amniotic fluid, pre-eclampsia and infection. Varicella-Zoster infection was found in 3 women. On admission to the labor room; among amphetamine addicts, 6 women had psychiatric disorders and hallucination, 3 had non-eclamptic seizures and the other 2 had suicidal attempts. Withdrawal symptoms

Table 1. Characteristics of all addicted mothers

Characters	Amphetamine	Heroin	p-value
Number	178	33	
Age (X ± SD), years	23.4±5.2	23.9±5.0	ns
Primiparous	52 (29.2%)	16 (48.5%)	ns
Previous abortion	37 (20.8%)	10 (30.3%)	ns
Prenatal care	37 (20.8%)	16 (48.5%)	<0.001
Normal delivery	146 (82.0%)	25 (75.7%)	ns
HIV positive mothers	16/175 (9.1%)	7/32 (21.9%)	<0.05

ns = not statistical significant (p > 0.05)

Table 2. Addiction history of the mothers

	Amphetamine		Heroin		p-value
	n	Mean ± SD	n	Mean ± SD	
No. of dose/day	127	2.0±1.5	25	2.8±1.8	<0.05
Duration (yrs)	150	2.3±1.7	32	3.7±3.1	<0.001
Time of last dose (hrs)	136	33.6±44.8	27	17.0±24.8	>0.05

were noted on 2 heroin users during intrapartum and postpartum periods,(Table 3). Both of them were polydrug users, they were addicted to heroin, methadone and amphetamine. Only 2 amphetamine addicts agreed to have tubal resection to prevent subsequent pregnancy, whereas all of the heroin addicts refused to have any birth control measure.

There were 2 neonatal deaths, one each of amphetamine and heroin addicted mothers. In comparison between the group of infants exposed to these drugs, there was no statistical difference in terms of sex ratio, mean birth weight, gestational age, length, head circumference, Apgar score and percentage of prematurity, IUGR or microcephaly, (Table 4). However infants exposed to amphetamine seemed to develop hypoglycemia, infection and respiratory distress more frequently than those heroin exposures (Table 5). All of 5 infants with congenital anomalies were born to amphetamine addicted mothers. There was one each for large nevus flammeus, pigmented nevus, genu recurvatum (vertex presentation infant), Downs' syndrome and congenital heart disease (hypoplastic right ventricle).

Thirty one out of 33 heroin exposed infants (93.9%) had withdrawal symptoms with the mean ± SD onset of 21.5 ± 16.5 hours after birth (range 2-60 hours). One of the 2 infants who had no withdrawal died at age less than 1 hour from severe birth asphyxia and the mother of the other infant had stopped using heroin for approximately 2 months prior to delivery. Withdrawal symptoms of all heroin exposed infants were successfully treated with Phenobarbital with the mean ± SD duration of treatment of 23.7 ± 11.5 days (range 3-42 days). There were 6 heroin addicted women who had been on methadone but irregularly during pregnancy. The severity of withdrawal symptoms on the infants born to these women, determined by the onset and duration of Phenobarbital treatment, were not statistically different compared with those of infants exposed to heroin alone, (30.7 ± 19.3 hours vs 18.0 ± 14.3 hours and 29.0 ± 10.0 days vs 21.8 ± 11.6 days respectively). The duration of heroin addiction was significantly

Table 3. Maternal complications

Complications	Amphetamine	Heroin
Total	178	33
Fetal distress	4	2
Meconium stained amniotic fluid	23	2
Pre-eclampsia	11	0
Antepartum hemorrhage	3	1
Infection	4	3
Psychiatric behavior, hallucination	6	0
Seizures	3	0
Suicidal attempts	2	0
Withdrawals	0	2

Table 5. Complications on the infants

Complications	Amphetamine, n = 178	Heroin, n = 33
Stillbirth	1	0
Neonatal death	1	1
Severe birth asphyxia	1	2
Meconium aspiration syndrome	2	1
Infection	8	1
Respiratory distress	7	0
Hyperbilirubinemia	11	5
Hypoglycemia	7	0
Congenital anomalies	5	0

Table 4. Infants' data

Characters	Amphetamine	Heroin	Total
Number	178	33	211
Male:Female	98:80	15:18	113:98
BW (mean ± SD) g*	2658±451	2561±510	
GA (mean ± SD), wks*	38.1±2.3	37.2±5.6	
Prematurity, n(%)*	55 (30.9)	12 (36.4)	67 (31.7)
LBW, n(%)*	53 (29.8)	14 (42.4)	67 (31.7)
IUGR, n(%)*	19 (10.9)	1 (3.0)	20 (9.5)
Microcephaly, n(%)*	15/155 (9.7)	1/30 (3.3)	16 (8.6)
Duration of hospitalization, days#	7.4±16.3	31.8±37.2	

* p-value > 0.05, # p-value < 0.001

Table 6. Infants' withdrawal symptoms

	Amphetamine (n = 178)	Heroin (n = 33)	p-value
No. of withdrawals, n (%)	4 (2.2)	31 (93.9)	<0.001
Onset, (hour after birth)	10.3±7.5	21.5±16.5	>0.05
Duration of treatment, (d)	6.0±5.3	23.7±11.5	<0.05

correlated with the onset of withdrawal and duration of Phenobarbital treatment, but their correlation coefficient was small, $r = 0.46$, $p < 0.05$ and $r = 0.42$, $p < 0.05$ respectively. However, the time of last heroin dose taken by the mother was not correlated with the onset of withdrawal in the infant.

Among amphetamine exposed infants, only 4 of them (2.2%) developed withdrawal symptoms which did not require specific treatment. Mean ± SD onset of withdrawal symptom was 10.3 ± 7.5 hours (range 3-12 hours). These symptoms included poor feeding, drowsiness and tremor. They were spontaneously subsided by 6 ± 5.3 days (range 2-12 days).

Eighteen mothers, 13 amphetamine and 5 heroin addicts were unable to look after their own infants and left their infants under the custody of their relatives or an orphanage.

Discussion

The authors have shown that the obstetric history of both amphetamine and heroin addicted women in the present study were very poor. Up to 24.2% of them were teenagers and 22.3% had history of previous abortions. Although, there was a higher percentage of heroin addicts seeking prenatal care, the percentage of women with prenatal care in both groups was low, (48.5% and 20.8%). And their prenatal cares was inadequate compared with those of the general population who delivered at our hospital[7] and the other studies[8]. Even 4 amphetamine addicts, who had a history of previous cesarean section, did not have prenatal care. This suggests that most of the addicts have no interest in getting access to the health care system.

Bauer et al[8] found that women who abused drugs during pregnancy were at an increased risk for sexually transmitted diseases and contraction of human immunodeficiency virus (HIV) or viral hepatitis. Serologic tests of the women in the present study have confirmed this observation. Positive HIV antibody was noted on 9.1% and 21.9% of amphetamine and heroin users respectively which were much higher than the national prevalence (1.2%)[9]. All heroin addicts with positive HIV antibody were intravenous drug users. Therefore, they could contact this virus through sharing needles. In contrast, the route of drug use in all HIV positive amphetamine exposures was inhalation. So the authors believe these women must have acquired the virus from their partners via sexual transmission.

Concerning the other sexually transmitted diseases such as syphilis and hepatitis B, it is difficult to tell the true prevalence among the presented patients because only 79.6% and 37.4% of them were tested for these infections with 1.2%and 2.5% positive results respectively.

A report on the obstetric complications on women exposed to amphetamine includes maternal hypertension, tachycardia, proteinuria, premature labor and antepartum hemorrhage[10]. The women in the present study also have increased risk of these complications. Although, heroin addicted women seemed to have more frequent antepartum hemorrhage and infection than amphetamine addicts. In addition, the authors found that both drug intoxication and withdrawal occurred in some of these women during labor which have never been mentioned in previous reports. The authors think it might be due to the stronger drugs the presented women had been exposed to or the other reports did not focus their attention on these effects during labor.

Perinatal effect on the infants in the present study is consistent with the previous studies[11-13]. However, the incidence of heroin withdrawal and duration of treatment in the presented infants seemed to be higher and longer. Again, this could be due to the better quality of drug the presented infants were exposed to. Heroin withdrawal occurred within 2-60 hours after birth. It has been reported that the onset of withdrawal depended on the time of the last dose exposure and the larger maternal methadone dosage in late pregnancy was associated with more severe withdrawal in the infant[14-16]. The present study can not demonstrate these correlations. It could be because the number of women on methadone in the present study was so small and they used this drug irregularly combined with heroin and they might not give the

accurate time of the last dose of drug use. Although, both onset of withdrawal and duration of treatment were correlated with the duration of addiction, the correlation coefficient was small. These findings should have no meaning.

In contrast to heroin, withdrawal symptoms in amphetamine exposed infants has not been clearly defined. Eriksson et al[17] reported the neurologic abnormalities in amphetamine exposed infants including drowsiness, poor feeding and seizures. Oro et al[18] found a wide range of symptoms in infants with intrauterine exposure to cocaine and methamphetamine including abnormal sleep pattern, tremors, poor feeding, hyperactive reflexes, abnormal cry, state of disorganization, vomiting, sneezing and tachypnea but only one of the 28 methamphetamine exposed infants required specific treatment. The presented infants developed less frequent withdrawal symptoms with less severity than heroin exposed infants. Only 4 out of 178 amphetamine-exposed infants (2.2%) developed these symptoms which did not need specific treatment. The authors think that if any infant shows signs or symptoms suggestive of narcotic withdrawal, addiction in the mother should be suspected even in the absence of a history.

Congenital anomalies are found in amphetamine exposed infants only. To date, no clear teratogenic effects of either heroin or amphetamine have been identified. Similar to cocaine, amphetamine cause vasoconstriction via increasing circulating level of nor-epinephrine, serotonin and dopamine[2]. If this effect occurred during the period of organogenesis of the embryo, malformation could be noted. Malformations reported with the use of amphetamine during pregnancy include cleft lip and palate, cardiac defects, biliary atresia and meningomyclocele[3,17,19]. But there is no specific type of malformations associated with this drug. It is difficult to conclude that amphetamine is the cause of anomalies in the presented infants. Since one infant with Downs' syndrome was born to an elderly mother (38 years old). We do not know whether the anomalies in the presented infants were related to the effect of amphetamine or caused by the environment of their mothers or by other confounding factors. This remains to be defined.

The pregnant women in the present study were from a lower socioeconomic background with a complicated social environment. There was a high incidence of neglect and poor parental behavior. Eighteen infants were left in an orphanage or under the custody of their relatives. It is essential to have a social worker who is familiar with these problems and a team approach that can evaluate the maternal infant bonding, social supports and the health status of the infants after discharge. The authors suggest that the infants should not be discharged until they remain free of withdrawal symptoms and all of the treatment team feels comfortable to discharge them.

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ผลกระทบในระยะปริกำเนิดต่อมารดาและทารกจากการที่มารดาเสพยาแอมเฟตามีน และเฮโรอีน ขณะตั้งครรภ์

พิมลรัตน์ ไทยธรรมยานนท์, สมภพ ลิ้มพงศานุรักษ์, ปราโมทย์ ไพรสุวรรณา, สันติ ปุณณะหิตานนท์

ทำการศึกษาย้อนหลังเวชระเบียนของมารดาติดยาแอมเฟตามีนและเฮโรอีนที่มาคลอดบุตรและรับไว้ในโรงพยาบาลจุฬาลงกรณ์ ระหว่างเดือนมกราคม พ.ศ. 2540 ถึงธันวาคม พ.ศ. 2545 เพื่อศึกษาผลกระทบต่อมารดาและทารกจากการใช้ยาเสพติดเหล่านี้ขณะตั้งครรภ์โดยเปรียบเทียบลักษณะมารดาและทารก และเปรียบเทียบผลกระทบที่เกิดขึ้นระหว่างกลุ่มได้รับยาแอมเฟตามีนกับกลุ่มได้รับเฮโรอีน ผลการศึกษาพบว่า มีมารดาติดยาเสพติดเหล่านี้ จำนวน 211 คน แบ่งเป็นกลุ่มติดยาแอมเฟตามีน 178 คน (84.4%) และกลุ่มติดเฮโรอีน 33 คน (15.6%) มีจำนวนผู้ที่ติดยาตั้งแต่ 2 ชนิดขึ้นไป 61 คน (28.9%) ซึ่งสัดส่วนในกลุ่มติดเฮโรอีนสูงกว่ากลุ่มติดยาแอมเฟตามีนอย่างมีนัยสำคัญทางสถิติ (43.7% ต่อ 27.2%, ค่า $p < 0.05$) มารดาเหล่านี้มีการฝากครรภ์เพียงร้อยละ 25.1 มีประวัติแท้งร้อยละ 22.3 มีอุบัติการณ์ติดเชื้อเอชไอวี ร้อยละ 11.1 ครรภ์เป็นพิษร้อยละ 5.2 ติดเชื้ออื่น ๆ ร้อยละ 3.3 และตกเลือดก่อนคลอด ร้อยละ 1.9

มารดา 11 คน เกิดอาการข้างเคียงทางระบบประสาทจากการเสพยาแอมเฟตามีน และอีก 2 คน เกิดอาการถอนยาจากเฮโรอีนในระหว่างคลอด ไม่มีครรภ์แฝด มีทารกตายคลอด 1 คน เสียชีวิตในระยะแรกเกิด 2 คน ลักษณะต่าง ๆ ของมารดาและทารกกลุ่มติดยาแอมเฟตามีนและเฮโรอีนไม่แตกต่างกัน มีทารกเกิดก่อนกำหนด ทารกน้ำหนักแรกเกิดน้อย ทารกโตช้าในครรภ์ และทารกที่มีขนาดศีรษะเล็ก ร้อยละ 31.7, 31.7, 9.7 และ 8.6 ตามลำดับ

มีทารกพิการแต่กำเนิด 5(2.8%) คน ซึ่งทั้งหมดเกิดจากมารดาติดยาแอมเฟตามีน พบอาการถอนยาในทารกเกิดจากมารดาติดเฮโรอีน 31 คน (93.9%) และเกิดจากมารดาติดยาแอมเฟตามีน 4 คน (2.2%) โดยเริ่มเกิดอาการที่อายุเฉลี่ย 21.5 $\pm$ 16.5 ชม. และ 10.3 $\pm$ 7.5 ชม. ($p > 0.05$) ตามลำดับ ทารกทุกคนที่มีอาการถอนยาจากเฮโรอีนได้รับการรักษาหายด้วยยา ฟีโนบาบิตาล ภายในเวลาเฉลี่ย 23.7 $\pm$ 11.5 วัน ส่วนกลุ่มที่มีอาการถอนยาจากยาแอมเฟตามีน อาการหายไปเองโดยไม่ต้องรักษาด้วยยา ภายในเวลาเฉลี่ย 6 $\pm$ 5.3 วัน มารดา 18 คน ทิ้งลูกไว้ในโรงพยาบาล ต้องส่งให้ญาติเลี้ยงหรือส่งสถานสงเคราะห์เด็กกำพร้า

***สรุป**: การศึกษานี้ พบว่าการเสพยาแอมเฟตามีนหรือเฮโรอีนมีผลกระทบอย่างรุนแรงต่อทั้งมารดาและทารก ซึ่งสอดคล้องกับรายงานอื่น ๆ แต่ดูเหมือน มีอุบัติการณ์เกิดขึ้นบ่อยกว่าและรุนแรงกว่า การให้ความรู้และความเข้าใจเกี่ยวกับผลกระทบจากยาเสพติดเหล่านี้ ในด้านการแพทย์ กฎหมาย และสังคมแก่ประชาชน จะช่วยลดการใช้ยาเสพติดและป้องกันการเกิดผลกระทบดังกล่าว*