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Background : *Perinatal use of illicit drug is associated with several medical impacts on both mothers and infants.*

Objective : *To determine the prevalence of perinatal drug abuse, maternal profiles and complications found both in mothers and infants.*

Setting : *Obstetric and Neonatal Unit of King Chulalongkorn Hospital, Bangkok, Thailand*

Research design : *Retrospective and descriptive study*

Subject : *Illicit drug addicted mothers and their infants admitted from January 1997 to December 2002.*

Method : *Data were collected from medical records of the mothers and infants exposed to the substances. The illicit drugs were defined as: heroin, methadone, amphetamine, alcohol, nicotine, marijuana and glue. Statistical analyses were performed by analysis of variance, Chi-square analyses and Student-t test where appropriate. A p-value <0.05 was considered statistical significant.*

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Results : *Out of 69,190 deliveries, 233 (3.4 per 1,000 total births) pregnant women were identified as illicit drug users. High percentage of them had poor obstetric history, including teenage pregnancy (22.2 %), no prenatal care (72.1 %), history of previous abortion (22.7 %) and HIV infection (10.4 %). Amphetamine, cigarette and heroin were the most common drugs use with the incidence of 78.5 %, 27 % and 14.2 %, respectively. Sixty-two (26.6 %) women were polydrug users, and half of them used both amphetamine and cigarette. The major complications on the mothers were amphetamine intoxication (4.7 %), heroin withdrawal (0.9 %), pre-eclampsia (5.6 %), antepartum hemorrhage (1.7 %) and infection (4.3 %). All infants born to these women were singletons except a pair of twins. The proportion of male to female was 124/110. Mean ± SD of birth weight was 2640 ± 469 grams (ranged 420 – 3900 grams). Mean ± SD of gestation age was 38.1 ± 2.3 weeks (ranged 24-42 weeks).*

The major complications of these infants were prematurity (30.3 %), low birth weight (31.6 %), intrauterine growth retardation (11.1 %) and microcephaly (9.2 %). It was found that the incidence of these complications had no statistical difference among the groups of infants exposed to amphetamine, heroin, cigarette and alcohol. There were 4 perinatal deaths (1.7 %). Congenital anomalies were found in 6 infants (2.6 %), thirty-five (15 %) infants developed withdrawal symptoms, 31 from heroin, and 4 from amphetamine.

Keywords : *Illicit drug, Perinatal effects*

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พิมลรัตน์ ไทยธรรมยานนท์, สมภพ ลิ้มพงศานุรักษ์, ปราโมทย์ ไพรสุวรรณา, สันติ ปุณณะหิตานนท์. ผลกระทบจากการใช้ยาเสพติดขณะตั้งครรภ์ต่อมารดาและทารก. จุฬาลงกรณ์เวชสาร 2547 เม.ย; 48(4): 235 - 45

วัตถุประสงค์ : *เพื่อศึกษาความชุกการใช้ยาเสพติดในสตรีตั้งครรภ์และลักษณะของสตรีเหล่านี้ ตลอดจนภาวะแทรกซ้อนที่เกิดขึ้นกับมารดาและทารก*

รูปแบบการวิจัย : *การศึกษาแบบย้อนหลัง*

สถานที่ทำการศึกษา : *หน่วยทารกแรกเกิด โรงพยาบาลจุฬาลงกรณ์*

วิธีการและประชากรศึกษา : *ศึกษาและวิเคราะห์ข้อมูลจากเวชระเบียนสตรีที่มาคลอดบุตรที่โรงพยาบาลจุฬาลงกรณ์ที่มีประวัติการใช้ยาเสพติดและทารกเกิดจากสตรีเหล่านี้ระหว่างเดือนมกราคม พ.ศ.2540 ถึง ธันวาคม พ.ศ.2545 วิเคราะห์ข้อมูลโดยใช้ ANOVA-test, Chi-square test และ Student-t test จากโปรแกรมSPSS-11.0*

ผลการศึกษา : *จากจำนวนสตรีที่มาคลอดบุตรทั้งสิ้น 69,190 คน ในระยะเวลาดังกล่าว พบว่ามีผู้ติดยาเสพติด จำนวน 233 คน คิดเป็นความชุก 3.4 /จำนวนคลอด 1,000 คน ร้อยละ 22.2 มีอายุต่ำกว่า 20 ปี ร้อยละ 72.1 ไม่เคยฝากครรภ์ ร้อยละ 22.7 มีประวัติเคยแท้ง และ ร้อยละ 10.4 ติดเชื้อเอชไอวี มีผู้ติดยาบ้า บุหรี่และเฮโรอีนมากที่สุดถึงร้อยละ 78.5, 27 และ 14.2 ตามลำดับ ร้อยละ 26.6 ติดยามากกว่า 2 ชนิดขึ้นไป ภาวะแทรกซ้อนสำคัญที่พบในมารดาได้แก่ การเกิดผลข้างเคียงจากยาบ้า (4.7 %), อาการถอนยาเฮโรอีน (0.9 %) ครรภ์เป็นพิษแบบ pre-eclampsia (5.6 %) ตกเลือดก่อนคลอด (1.7 %) และติดเชื้อ (3.4 %) มีจำนวนทารกเกิดจากมารดาเหล่านี้ทั้งสิ้น 234 คน ซึ่งเป็นแฝด 1 คู่ มีทารกเพศชาย 124 คน และเพศหญิง 110 คน น้ำหนักแรกเกิดโดยเฉลี่ย 2,640 $\pm$ 469 กรัม (พิสัย 420 – 3,900 กรัม) อายุครรภ์โดยเฉลี่ย 38.1 $\pm$ 2.3 สัปดาห์ (พิสัย 24 – 42 สัปดาห์) ภาวะแทรกซ้อนที่สำคัญที่เกิดขึ้นกับทารกได้แก่ เกิดก่อนกำหนด (30.3 %) น้ำหนักแรกเกิดต่ำกว่า 2,500 กรัม (31.6 %) โตช้าในครรภ์(11.1 %)และศีรษะเล็ก (9.2 %) อุบัติการณ์เกิดภาวะแทรกซ้อนดังกล่าวไม่แตกต่างกันระหว่างกลุ่มทารกที่เกิดจากมารดาติดยาบ้า บุหรี่ เฮโรอีน หรือเหล้า ทารกเสียชีวิตระยะปริกำเนิด 4 คน (1.7 %) นอกจากนี้ยังพบทารกพิการแต่กำเนิด 5 คน (2.1 %) และ35 คน (15 %) เกิดอาการถอนยา 31 คน ถอนยาจากเฮโรอีน อีก 4 คนจากยาบ้า*

คำสำคัญ : *ยาเสพติด,ผลกระทบต่อการตั้งครรภ์, ผลกระทบต่อทารกแรกเกิด*

Prenatal illicit drug use is a serious public health problem with enormous financial and social burdens. Several medical impacts on both mother and infants have been reported. Pregnant and drug-exposed women have high risk of contacting HIV, hepatitis B and C, endocarditis, sexually transmitted diseases and psychiatric disorders. In addition, they also have increased risk of obstetric complications including abortion, intrauterine death, placental insufficiency, pre-eclampsia, premature labor, premature rupture of membrane and post partum hemorrhage.[1] It is well established that illicit drugs can cross the placenta and cause a severe impact, not only on the development of the fetus but also on the infant during its later stage of life. More than 75 % of the infants exposed to these substances have major medical problems when compared to 27 % in the unexposed infants.[2] Medical problems in infants that may be associated with maternal drug use which include low birth weight (LBW), prematurity, unexplained intrauterine growth retardation (IUGR), congenital anomalies and withdrawal symptoms.[3] In addition, they also have an increased risk for altered neurodevelopment and long term health status including some psychosocial problems such as child negligence and child abuse. During the past decade, we have observed that the number of pregnant women abused by one or more drugs has been increasing among those who were admitted to our hospital for delivery. However, the number of reports on the impact of prenatal drug exposure on both mother and infant in our country is still limited. Therefore, we conduct a study on these women and their offspring in order to determine the prevalence of various kinds of drug use and demonstrate their impacts during the perinatal and neonatal periods.

Materials and Methods

Information was collected from medical records of all pregnant women who were identified as illicit drug users when they were admitted to the Department of Obstetrics of King Chulalongkorn Memorial Hospital in Bangkok, Thailand, from January 1997 to December 2002. The illicit drugs were defined as heroin, methadone, amphetamine, alcohol, nicotine, marijuana and glue. The medical and demographic characteristics of both mothers and their offspring were obtained. The infants were examined by pediatricians within 6 hours after delivery and were observed for withdrawal symptoms or other complications for at least 48 hours. Gestational age (GA) was determined according to Ballard score system.[4] GA of 37 weeks or less was defined as prematurity. Birth weight (BW) and head circumference (HC) less than 10^{th} 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 system.[6] Treatment would be initiated with phenobarbital if the abstinence score was more than 4 when the infant was not hungry or sleepy. The infants were discharged when they were free of withdrawal.

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

Results

Two hundred and thirty-three substance-abuse pregnant women were identified among 69,190 women who delivered during this 6 year period. The prevalence was 3.4 per 1,000 births. All of them delivered live-born singleton except one women delivered a set of stillbirth premature infants. Mean ± SD of maternal age was 23.8 ± 5.3 years, (ranged 15-41 years). There were seventy-one (30.5 %) primiparous women. Fifty-two (22.2 %) women aged less than 20 years. It was difficult to define their marital status or occupation, because almost all of these women were not married and had no permanent job. Sixty-five (27.6 %) women acquired prenatal care just during their last trimester. There were only 1-2 visits per person for the whole course of pregnancy. Those women who had no prenatal care came to the hospital either when they were in late labor or when they had already delivered at home or in the taxi on the way to the hospital. The proportion of normal and abnormal deliveries was 187 to 46 cases. Twenty-four out of 46 abnormal deliveries were cesarean section. Previous cesarean section was the indication in 6 women. However, only 2 of them had prenatal registration. Fifty-three (22.7 %) women had history of previous abortion with the maximum number of 4. Screening for HIV antibody, VDRL titer and hepatitis B antigen were performed on 230, 184 and 94 women with positive result of 24 (10.4 %), 2 (1.1 %) and 3 (3.2 %) cases, respectively (Table 1).

Table 1. Characteristics of prenatal illicit drug use mothers.

Characters	Number (%) of mothers
Total number	233
Age, mean ± SD (range)	23.8 ± 5.3 (15-41) years
Primiparous	71 (30.5)
History of previous abortion	53 (22.7)
Mothers with prenatal care	65 (27.9)
Polydrug users	62 (26.6)
Mode of delivery:	
Normal	187 (80.2)
Cesarean section	24 (10.3)
Others	22 (9.5)
No. of positive serology test	
HIV	24/230 (10.4)
VDRL	2/184 (1.1)
HBsAg	3/94 (3.2)

Amphetamine, cigarette and heroin were the most common substances used by these women with the incidence of 78.5 %, 27 % and 14.2 % respectively. Sixty-two (26.6 %) of them used 2 or more substances, (Figure 1). Among these polydrug users, 50 percent were addicted to amphetamine and cigarette. The largest number of drug use was 4 substances which were found in 2 women. Both of them were addicted to heroin and one of them also used cocaine, the only one who used cocaine in this study.

Obstetric complication occurred quite common. Meconium stained amniotic fluid and pre-eclampsia were the 2 most common associated findings. Four women had antepartum hemorrhage, 2 cases with placenta abruption and the other 2 cases with *placenta previa*. Infection was found in 10 (4.3 %) women. These infections were, namely: 2 herpes zoster, 2 syphilis, 3 acute pyelonephritis; and 1 each of varicella, pneumonia, and infected wound. Two heroin addicts developed withdrawal symptoms during their postpartum period. Drug intoxication or adverse drug reaction was noted in 11 (6 %) amphetamine addicts. There were 6 women with hallucination and psychotic behavior, 3 with non-eclamptic seizures and 2 with suicidal attempts (Table 2).

Only 4 women agreed to have birth control either by hormonal injection or tubal resection. The rest of them had no interest in the prevention of subsequent pregnancy.

There were 234 infants born to these women. The proportion between male and female infants the study was 124 to 110 cases. Mean $\pm$ SD of birth weight and gestational age were 2640 $\pm$ 469 grams and 38.1 $\pm$ 2.3 weeks, respectively. Seventy-one (30.3 %) of them were premature, 74 (31.6 %) had low

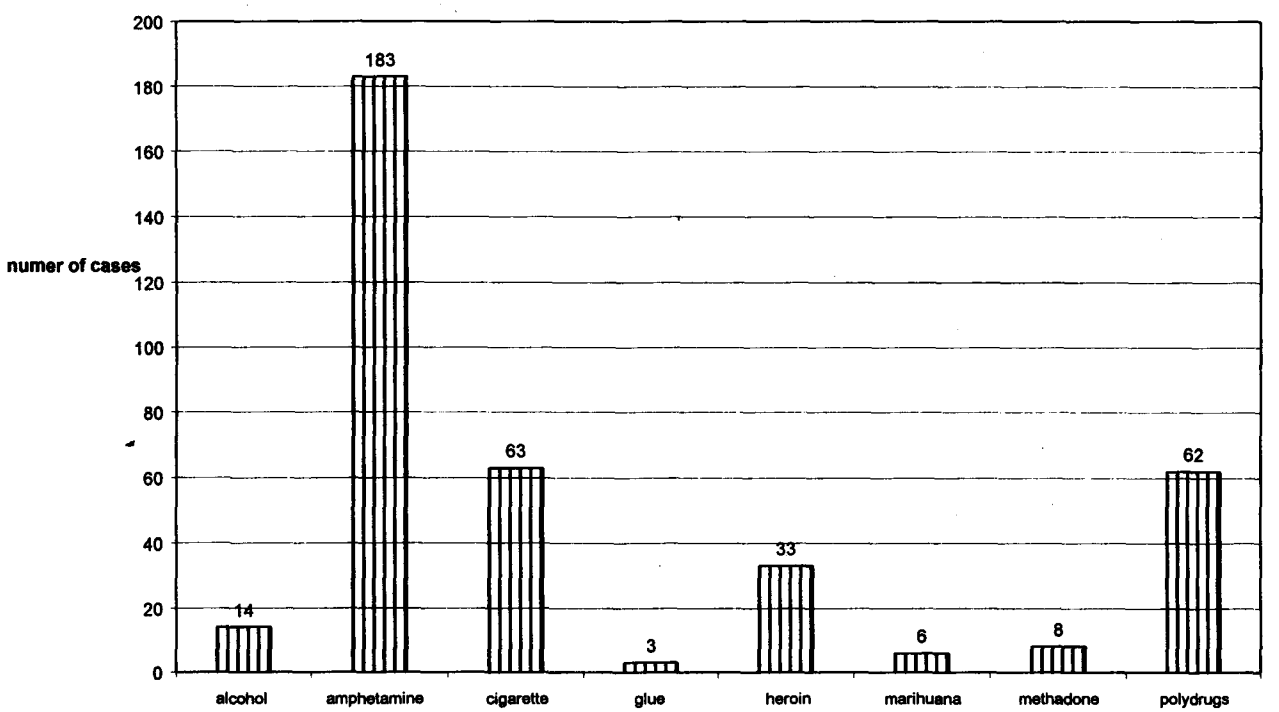

Figure 1. Type of drug addictions.

Table 2. Incidence of complications in the mothers.

Complications	Incidence, n (%)
Meconium stained amniotic fluid	29 (12.4)
Pre-eclampsia	13 (5.6)
Antepartum hemorrhage	4 (1.7)
Infection	10 (4.3)
Hallucination & psychotic behavior	6 (2.6)
Non-eclamptic seizures	3 (1.3)
Suicidal attempts	2 (0.9)
Withdrawal symptom	2 (0.9)

birth weight and 25 out of 226 infants (11.1 %) whose gestational age were recorded were small for their gestational age (Table 3). One out of 5 infants had severe birth asphyxia (Apgar score at 1st min $\leq$ 3) and had prolapsed cord. There were 2 early neonatal deaths. In comparison of the infants' characteristics stratified by type of drug exposure, there was no statistical difference in terms of mean birth weight, mean gestational age and mean Apgar score, (ANOVA test, $p > 0.05$). In addition, the percentage of prematurity, low birth weight, intrauterine growth retardation or small for gestational age and microcephaly were also not statistical different (Chi'square test, $p > 0.05$) (Table 4). Although, the percentage of microcephalic infants seemed to be higher in those born to alcoholic mothers, most of their mothers also used amphetamine. Infants exposed to heroin had significant longer mean $\pm$ SD hospitalization when compared with those without heroin exposure (31.8 $\pm$ 37.2 days vs. 7.3 $\pm$ 15.2 days; $p < 0.0001$). This was due to the need of prolonged hospitalization for the treatment of neonatal withdrawal symptoms.

Table 3. Infants' data.

	Number (%)
Total number	234
Male : Female	124 : 110
BW, mean $\pm$ SD (range)	2640 $\pm$ 469 (420 - 3900) grams
GA, mean $\pm$ SD (range)	38.1 $\pm$ 2.3 (24 - 42) weeks
Prematurity	71 (30.3)
Low birth weight	74 (31.6)
Intrauterine growth retardation	25/226 (11.1)
Microcephaly	16/173 (9.2)

Table 4. Infants' characteristics stratified by type of maternal drug abuse.

	Type of drug abuse			
	Amphetamine	**Heroin**	**Smoking**	**Alcohol**
Number*	183	33	63	14
Mean ± SD of BW, g.	2653 ± 452	2550 ± 517	2698 ± 456	2730 ± 533
Mean ± SD of GA, wk	38.0 ± 2.3	38.2 ± 2.5	38.0 ± 1.2	38.1 ± 1.7
Mean ± SD of 1-min Apgar score	8.6 ± 1.4	8.5 ± 1.7	8.7 ± 1.3	8.8 ± 0.6
Prematurity, n (%)	55 (29.9)	9 (28.1)	18 (28.6)	4 (28.6)
LBW, n (%)	53 (28.8)	12 (37.5)	15 (23.8)	5 (35.7)
IUGR, n (%)	20/180 (11.1)	2/31 (6.4)	8/62 (12.9)	1/14 (7.1)
Microcephaly, n (%)	15/153 (9.8)	1/24 (4.2)	6/54 (11.1)	3/12 (25)

* Infants exposed to polydrug will be counted repeatedly according to the type of prenatal drug use.
All items, p-value > 0.05

Withdrawal symptoms were found in 31 (93.9 %) heroin exposed infants and in 4 (2.2 %) of amphetamine group. Twenty-nine out of 31 infants with heroin withdrawal symptoms needed specific treatment. They were successfully treated with phenobarbital. The mean ± SD duration of treatment was 23.7 ± 11.5 days (range 3-42 days). Withdrawal symptoms occurred in amphetamine exposed infants were characterized by poor feeding, drowsiness and tremor which spontaneously subsided within 6 ± 5.3 days (range 2-12 days).

The major illness of these infants were hyperbilirubinemia (11 cases), respiratory distress (6 cases), hypoglycemia (6 cases), and infection

Table 5. Neonatal complications.

Complications	**Number (%) of infants (Total = 234)**
Still birth	2 (0.85)
Neonatal death	2 (0.85)
Severe birth asphyxia, (Apgar score ≤ 3 at 1 min)	5 (2.1)
Hyperbilirubinemia	11 (4.7)
Respiratory distress	13 (5.5)
Hypoglycemia	6 (2.6)
Infection	9 (3.8)
Withdrawal symptom	35 (15) (Heroin 31, Amphetamine 4)
Congenital anomalies	6 (2.6)

(9 cases). Congenital anomalies were found in 6 infants (2.6 %). They were one each for Downs' syndrome, hypoplastic right ventricle, club foot, *genu-recurvatum*, *nevus flammeus* and large pigmented nevi. All of them were born to amphetamine addicted mothers, except for one born with club foot whose mother was a heavy smoker (Table 5). Nineteen infants were not discharged with their mothers, 10 of them were transferred to an orphanage and 9 were under the custody of their relatives.

Discussion

The prevalence of prenatal illicit drug use in this study is 3.4 per 1000 births. The figure is probably an underestimation. Some of the asymptomatic women who denied illicit drug use were not included; therefore we estimate that the real figure must be higher. We realize that this prevalence does not represent the national statistic, since the data is only collected from our hospital. Our hospital serves every ethnic communities including one of the high risk population, one of the largest slum in Bangkok (Klong Toey). This slum area has been long term recognized as endemic for illicit drug use and the majority of the women (28.7 %) lived in this area. So the overall prevalence may be higher than the national figure. It is also higher than that reported in Singapore, [7] a country in the same region. The prevalence of prenatal drug use in the U.S.A. is varied between 4 and 270 per 1000 birth [8] depending upon whether the study is performed in a low or high risk population. A study in pregnant American women in 1992 showed that 5.5 % of them reported using an illicit drug during gestation. The highest rates of use were found for marijuana (2.9 %), cocaine (1.1 %) and heroin (0.1 %). Cigarette and alcohol were considered as recreation substances, which were found in 20.4 % and 18.8 % of pregnant woman, respectively.[8] Heroin was the most common drug use in Hong Kong and Singapore.[7,10] In contrast to our study in which the commonest drug use was amphetamine and we also included smoking and alcohol drinking as illicit drug use. There was only 6 (2.6 %) women used marijuana in our study. Cocaine is not famous among the women in our study. We believe it is because of its high price and the difficulty in getting this drug in Thailand. Bauer et al.[11] found that 93 % of the mothers in their study in the US used a combination of alcohol, cigarette and marijuana. Since it is not the common practice for women in Thailand to smoke or drink as in the US; therefore, the prevalence of polydrug use in our study is much smaller, (26.6 %).

Only 65 (27.9 %) of addicted women in our study had prenatal care, all of which were in their last trimester. This poor access to medical care is probably due to their ignorance or poverty or because they are afraid of facing the social stigmatization associated with illicit drug use and the potential legal consequences.

We have shown that prenatal illicit drug use can cause many serious medical impacts on both mothers and infants which are consistent with the other studies. [12-14] Poor obstetric history as well as many perinatal complications are quite common in our study. Withdrawal symptoms can be found in infants exposed to either heroin or amphetamine. But it is more common and more severe in heroin withdrawal. Amphetamine withdrawal symptoms occurred in only 4 infants and the symptoms were mild and spontaneously subsided within 2-12 days after birth.

Poor feeding is the pertinent amphetamine withdrawal symptoms. Incidence of congenital anomalies is higher than that of overall population of infants delivered in our hospital (2.6 % vs 1.7 %).[15] Although most of the complications are associated with intrauterine amphetamine exposure, it is not known whether they are caused by the chemical effect of the drug, environmental effect or a combination of both factors. Low socioeconomic status, lack of prenatal care and polydrug use may be the confounding factors that make identification of specific effects of individual drug very difficult. Further extensive epidemiological study on prenatal illicit drug use is still needed. Drug abuse by pregnant women is an important, complex and growing problem. Maternal self-reporting frequently downsizes the figure of drug exposure. Detailed maternal drug history should be obtained. Increasing awareness our improving and understanding of drug abuse in the medical, legal and social aspects will enable us to reduce the barriers of treatment for this population. Prenatal illicit drug use should be suspected in high risk women with poor obstetric history. Drug screening during pregnancy can also be helpful in identifying mothers and infants who are at risk. It may facilitate early counseling and decrease infant drug exposure. Because infants are victims of this circumstance; they definitely need to be protected.

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