

Maternal and Neonatal Complications of Substance Abuse in Iranian Pregnant Women

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Abstract- There is an increased prevalence of maternal substance abuse during pregnancy in younger women in all socioeconomic classes and races. Our aim was to determine the prevalence and correlates of self-reported substance abuse among pregnant women and obstetric complications or neonatal outcomes in Iran. This retrospective cohort study is covering a five year period on medical records of pregnant women attending the maternity unit of four major hospitals (Mahdiah, Taleghani, Imam Hossein and Akbarabadi Hospitals). Women who reported using opium, heroin, crack, cannabis or methamphetamine were compared with women with no reported history of drug abuse for obstetric complications and prenatal morbidity and neonatal mortality. From 100,620 deliveries substance abuse was recorded for 519 women giving a prevalence of 0.5%. Opium was the most prevalent substance abused followed by crack (a mix of heroin and amphetamines). The exposed group had significantly more obstetric complications including preterm low birth weight and postpartum hemorrhage than the non-exposed group. The exposed group had significantly worse prenatal outcomes including more admissions to intensive care unit and higher infant mortality than the non-exposed group. None of the women in the exposed group was on methadone treatment at time of delivery. Risks of maternal and neonatal complications were increased in substance using pregnant women, especially preterm birth and low birth weight. We recommend a multidisciplinary team to provide methadone maintenance therapy for substance using pregnant women and urinary screen of all pregnant women presenting to hospital.

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Introduction

Substance abuse is a complex public health problem with social and economic health implications (1,2). Although maternal substance abuse during pregnancy occurs in all socioeconomic classes, ages, and races, there is an increased prevalence in younger women (3-6). Nearly 90% of drug-using women are of childbearing age (7). In the US, the reported prevalence of substance abuse among non-pregnant and pregnant women aged 15-44 was 10% and 4% respectively, but this level increased to 15.5% among pregnant women aged 15-17 years (8,9). Sexually transmitted diseases, domestic

violence, poverty and depression are more common in substance using women than non-substance using women (1,9). The coexistence of substance abuse with social problems such as poor nutrition and hygiene, social deprivation, psychological problems and high risk lifestyle may increase these complications in pregnant women leading to morbidity in neonates (10-14). Monitoring intrauterine exposure to drugs is important for the development of suitable interventions for maternal and neonatal health. It has been suggested that prenatal care should include drug testing (15).

Opium is the most drug type abused in Iran (16). This is due in part to Iran being on the opium trafficking

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route from Afghanistan to western countries and its large population of youth. Also Iranians use a drug called crack a combination of heroin and amphetamines that is not found elsewhere. The extent of substance abuse among Iranian pregnant women is unknown and studies carried out in the west may not be applicable to Iran. Therefore this study aimed to examine the prevalence and correlates of substance abuse during pregnancy, and obstetric and the perinatal outcomes of babies in comparison with non-substance using pregnant women in Iran.

Materials and Methods

This was a retrospective cohort study of medical records of women who had attended the obstetric ward at one of four major hospitals affiliated to Shahid Beheshti and Tehran Universities of Medical Sciences (Mahdieh, Taleghani, Imam Hossein and Akbarabadi Hospitals) from April 1, 2004 to March 31, 2009. Inclusion criteria were having a singleton pregnancy and having delivered a live or stillborn infant after 20 weeks' gestation. Substance abuse was self-reported by mothers and recorded in their medical files. Exclusion criteria were having incomplete data in their medical files or if their history of substance abuse was unclear. The exposed group comprised all women who reported using opium, heroin, crack, cannabis, methamphetamines or methadone during pregnancy. The non-exposed group comprised women who denied any illegal drug use during their current pregnancy. This group was selected in a simple random method and the number of women in the non exposed group was equal to the number in the exposed group for each hospital and for each year. Demographic characteristics including age, gravidity, medical history, and clinical information regarding antenatal care, gestational age at delivery, obstetric and postpartum complications, mode of delivery, immediate neonatal outcomes and 5-minute apgar score were

retrieved from the medical records. Gestational age was based on the last menstrual period (LMP), ultrasound or both. Preterm delivery was defined as delivery before complete 37 weeks' gestation. Premature rupture of membranes (PROM) was defined as rupture of the amniotic membranes before the onset of labor.

Fetal growth restriction or small for gestational age (SGA) was diagnosed if actual birth weight was below the 10th percentile for gestational age. Prenatal data including neonatal birth weight, intrauterine fetal death, still birth, neonatal intensive care unit (NICU) admission and neonatal abstinence syndrome (NAS) were extracted from the neonatal medical records. The signs and symptoms of NAS included high pitched crying, irritability, convulsion, tremor and respiratory distress.

Statistical analysis was performed with SPSS-16 (Statistical Package for the Social Science, for Windows, Chicago). Univariate analysis was performed using Chi-square and Fisher exact test. Student's t-test and ANOVA were used to compare group means. *P*-values less than 0.05 were defined as statistical significance. The study was approved by the Ethics Committee at Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Results

During the five year study period there were 100,620 deliveries in the four hospitals. Substance abuse was reported by 519 cases, giving a prevalence of substance abuse by pregnant women of 0.5%. 439 women with substance abuse and complete medical records and correct inclusion criteria were entered into the study. The most common substance abused was opium (62.6%), followed by crack (20.3%), polydrugs (7.5%), heroin (3.9%), methamphetamines (3.9%) and marijuana (1.7%).

Table 1. Characteristics of pregnant women.

Variables	Types of drugs abused during pregnancy						non-exposed n=519
	Crack n=89	Opioid n=293	Crystal n=17	Cannabis n=7	Polydrug n=33	Total n=439	
Mean Age (SD)	25.5 (6)	30 (6.4) ^ψ	25.8 (3.5)	26.2 (4.9)	27.3 (5.5)	28.7 (6.4)	26.5 (5.6)
Prime gravid (%)	67.9	33.7 ^φ	77.8	50	50	43	54.5
Prenatal care (%)	12.4 ^φ	30.5 ^ψ	23.5	28.6	9.1 ^ψ	19.6 ^π	28.9
Anemia (%)	15.6 ^ψ	17.9 ^φ	25 ^ψ	0	15.2 ^ψ	17.2 [*]	5.2
Cesarean (%)	37.1 ^φ	38.2 ^φ	41.2	14.3 ^ψ	39.4	37.8 [¥]	44.3

^ψ *P*<0.05, ^φ *P*<0.001, ^π *P*=0.001 and RR=1.24 (95% CI: 1.1-1.4), ^{*} *P*<0.001 and RR=1.75 (95% CI: 1.51-2.04), [¥] *P*=0.048 and RR=1.15 (95% CI: 1.01-1.3).

Table 2. Intra and post-partum complications

Variables	Types of drugs abused during pregnancy						Non-exposed n=519
	Crack n=89	Opioid n=293	Crystal n=17	Cannabis n=7	Polydrug n=33	Total n=439	
Preterm birth (%)	19.6 ^Φ	39.2 ^Φ	75 ^Ψ	18.2	30.4	39.5 ^Π	22.3
Gestational age Weeks (SD)	35.5 (4.4) ^Φ	36.7 (3.5) ^Φ	34.2 (4.7) ^Ψ	37.5 (3.5)	37 (2.8)	36.5 (3.8) ^Φ	37.9 (2.3)
Weeks of gestational age at preterm birth (SD)	31.7 (4.2) ^Φ	33.3 (3.4) ^Φ	32.3 (3.5)	32 (5.6)	33.8 (0)	32.9 (3.5) ^Φ	34.3 (1.9)
Premature Rupture Of Membrane (%)	22.5	30.7	28.6	41.2	33.3	29.6	28.9
Maternal Withdrawal syndrome (%)	5 (5.6)	6 (2)	0	0	3 (9.1)	----	----
Postpartum Hemorrhage (%)	3.5 ^Ψ	8.5 ^Φ	28.6 ^Ψ	0	9.1	7.5*	2.5
Mean duration of hospital admission (SD)	2.6 (1.7)	2.9 (1.8)	2.8 (0.9)	2.9 (2.2)	3.5 (1.7)	2.8 (1.8)	2.9 (1.8)

Ψ $P < 0.05$, Φ $P < 0.001$, Π $P < 0.001$ and RR=1.61 (95% CI: 1.35-1.92), * $P < 0.001$ and RR=1.61 (95% CI: 1.32-1.95).

There was no significant difference for maternal age between groups (28.7 vs. 26.5 years) except opiate using women were older than non-exposed group (30 vs. 26.5 years, $P < 0.05$). The exposed group was significantly less likely to have had prenatal care (19.6% vs. 28.9%) and was significantly more likely suffer anemia at admission (17.2% vs. 5.2%) than the non-exposed group (Table 1).

Intra and post-partum complications

The exposed group experienced a significant higher prevalence of preterm births than the non-exposed group

(39.5% vs. 22.3%; $P < 0.001$, RR=1.61, 95%CI: 1.35-1.92). Babies born to those in the exposed group had a significantly younger gestational age (36.51 vs. 37.95; $P < 0.001$) and in preterm birth group gestational age at birth was 32.97 vs. 34.35 weeks. Postpartum hemorrhage was significantly more common among the exposed group than the non exposed group (7.5% vs. 2.5%; $P < 0.001$ RR=1.61 (1.32-1.95). The groups did not differ on premature rupture of membrane (29.6% vs. 28.9%) and duration of stay in hospital (2.8 vs. 2.9 days) (Table 2).

Table 3. Neonatal outcomes.

Variables	Types of drugs abused during pregnancy						Non-exposed n=519
	Crack n=89	Opioid n=293	Crystal n=17	Cannabis n=7	Polydrug n=33	Total n=439	
5 th min Apgar score(SD)	9.6 (1)	9.7 (0.7)	10 (0)	9.3 (1.9)	9.7 (0.4)	9.6 (0.8)	9.8 (0.5)
Birth weight (SD)	2560 (654) ^Φ	2673 (598) ^Φ	2224 (589) ^Φ	2763 (829) ^Ψ	2502 (518) ^Φ	2634 (617) ^Φ	3001 (608)
Birth length (SD)	48.6 (2.3)	47.3 (4.4) ^Φ	48 (5.2)	48.2 (8.1)	45.9 (4.4) ^Φ	47.5 (4.2) ^Φ	49.2 (3)
Head circumference(SD)	33.6 (2.2) ^Ψ	32.9 (2.3) ^Φ	31.2 (3.7) ^Ψ	31.2 (6.8) ^Ψ	33.6 (3.4)	33.1 (2.6) ^Φ	34.3 (1.9)
SGA (%)	28.3 ^Ψ	26.8 ^Φ	25	9.1	37.5 ^Ψ	27.3 ^Π	12.1
NICU admission (%)	67.4 ^Φ	57 ^Φ	28.6	64.7 ^Ψ	72.7 ^Φ	60.2*	31.7
NICU admission days(SD)	4.6 (4.9) ^Φ	4.3 (5.3) ^Ψ	6.2 (8.7) ^Φ	3 (3.1)	4.8 (6.8) ^Φ	4.9 (5.7) ^Φ	3 (2.7)
Neonatal abstinence (%)	36 (40.4)	113 (38.6)	0	6 (35.3)	15 (45.5)	----	----
Neonatal death (%)	10.1 ^Φ	5.8 ^Ψ	0	5.9	6.1	6.6 [¥]	1.9
Anomaly (%)	5 (5.6) ^Ψ	11 (3.8)	1 (5.9)	0	1 (3)	18 (4.1) ^μ	8 (1.5)

SGA: Small for Gestational Age, NICU: Neonatal Intensive Care Unit.

Ψ $P < 0.05$, Φ $P < 0.001$, Π $P < 0.001$ and RR=2.25 (95% CI: 1.65-3.06), * $P < 0.001$ and RR=1.75 (95% CI: 1.53-2.01), ¥ $P < 0.001$ and RR=1.66 (95% CI: 1.36-2.03). μ $P = 0.017$ and RR=2.66 (95% CI: 1.16-6.05).

Neonatal outcomes

In terms neonatal results, the groups did not differ on the 5th minute apgar score. Babies born to mothers in the exposed group had significantly lower birth weights (2633.8 vs. 3000.94; $P<0.001$), and smaller birth lengths (47.5 vs. 49.25; $P<0.001$) and head circumference (33.1 vs. 34.35; $P<0.001$) and a larger percentage were small for their gestational age (27.3 vs. 12.1; $P<0.001$). Babies born to mothers in the exposed group were almost twice as likely to be admitted to neonatal ICU (60.2 vs. 31.7; $P<0.001$), require a longer stay in ICU (4.98 days vs. 3.03; $P<0.001$) and to die than those born to mothers in the non-exposed group (6.6% vs. 1.9%; $P<0.001$) (Table 3). Neonatal abstinence syndrome developed in 170 infants (38.7%) born to mothers in the exposed group (40.4% of crack abusers, 38.6% of opiate abusers, 35.3% of crystal abusers and 45.5% of poly drug abusers) with no significant difference between them.

Neonatal anomalies were reported in 4.1% of exposed and 1.5% of non-exposed groups ($P<0.05$, RR=2.66, CI: 1.16-6.05). In the exposed group the following anomalies were reported; club foot, micropenis, macrocephaly, cardiac anomaly, large tongue, anomalies of limbs, hypospadias and polydactyly (Table 3).

Discussion

This is the first large scale study to document maternal drug abuse and neonatal short term complications in Iran. Several key findings were the prevalence of substance abuse was 0.5% among women at four major hospitals; the majority reported using opium or heroin. This trend in maternal drug abuse indicated a growing problem for obstetrics to address. Drug abuse by pregnant women appears higher in the West (4), in America (5.5%), United Kingdom (5%) and Australia (6%) (17-19), but lower in countries such as Croatia where a prevalence of 0.2% was reported (20).

In our study, the types of drugs abused by pregnant women differed to other studies. For example, the majority of our women used opium (62.6%), whereas most frequent substance abused by pregnant women in south London was heroin (38%), followed by cocaine (24%) (21). Likewise our study found a very low level of marijuana use 1.7% which was in stark contrast to 39% of pregnant women in Australia using marijuana (17). These differences are to be expected due to geographical locations and different drug using patterns.

In this study diagnosis of substance abuse was based on maternal self-reporting to the attending physician. There may have been some under reporting due to the stigma of being a female substance abuser in our society (22) or physicians omitting to ask specifically about substance abuse. As the diagnosis of a patient with substance abuse is significant to outcomes, it is critically important to refer such patients to appropriate treatment for drug abuse. Pregnancy is an ideal opportunity for substance using women to access addiction treatment (23). Such services will need to be non-judgmental and easy for these women to access. Our higher level of anemia at admission and inadequate prenatal care among substance using mothers were similar to other studies in Australia and Croatia (20,24). Also our findings on preterm birth, postpartum hemorrhage, size for gestational age and admission to NICU were similar to results of other studies (17,20,24-27).

Neonatal abstinence syndrome (NAS) developed in 38.7% of infants born to women in the exposed group which was low in comparison to 71% reported by Vucinovic *et al.* (20) in Croatia. The difference may be due to low experience of detecting or recording non significant symptoms. Standard charts for the assessment of neonatal abstinence syndrome are required for early detection and appropriate treatment of infants complicated by neonatal abstinence syndrome. Our finding of a low prevalence of NAS may also be due to mothers were not on methadone as they were in many other studies (23,24). The mean length of hospitalization for the neonates of women in the exposed group was approximately 50% more than for the non-exposed group, which was similar to other studies (20,24,26).

Iran has a large number of methadone maintenance programs and substance abusers are encouraged to enroll in methadone treatment. Despite the existence of minimal charge treatment none of the studied cases used these facilities during pregnancy. As a consequence the women in our exposed group differed from women in studies in Australia (21) where over 80% of heroin using mothers were enrolled in methadone therapy program. Low uptake of methadone treatment among substance using women in Iran may be due to judgmental and hostile attitudes of medical staff or clinics may be inundated with male clients and thus be unwelcoming for female clients. Dedicated methadone clinics, or at least daily sessions, for women have been shown to draw women into treatment, many for the first time (28). Pregnant substance abusers need the services of a

multidisciplinary team specially trained to provide proper support and treatment for this at risk group. As our study demonstrated, a high proportion of substance using women admitted just at the time of delivery, make management of these groups more difficult. Reaching out to these women through mass media could be one way to facilitate their entry into prenatal care. Prenatal care should include drug testing to improve detection and management of women who abuse substances (15). It has been recommended to perform testing at the first prenatal visit or at least at delivery if access to prenatal care was poor. Active follow and care of these cases can be helpful as demonstrated in South London in 2007 (21).

A limitation to our study was the reliance on self report to determine substance abuse and we were unable to ascertain duration of substance abuse before delivery. Another limitation was the lack of a proper measure of socio-economical status. Maternal education could similarly affect the risk of preterm birth and birth weight, while poor nutrition may restrict fetal growth in substance using women (29). A more detailed and prospective study is required to define and eliminate the confounders such as the underlying causes of preterm delivery and low infant birth weight in this group of pregnancy. In conclusion risks of maternal and neonatal complications were increased in substance using pregnant women. Substance abuse during pregnancy increased the risk of preterm birth, postpartum hemorrhage, low birth weight, admission to ICU and neonatal death. We recommend a multidisciplinary team specially trained to provide proper support and treatment for this at risk group, and urinary screen of all pregnant women presenting to hospital.

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