



## Epidemiology of perinatal substance use: Exploring trends in maternal substance use



Jennifer J. Rodriguez<sup>a</sup>, Vincent C. Smith<sup>b,\*</sup>

<sup>a</sup> Beth Israel Deaconess Medical Center, Boston, MA, USA

<sup>b</sup> Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA

### ABSTRACT

Over the last two decades, the prevalence of substance use among women of childbearing age has risen dramatically in the United States making substance use during pregnancy a significant public health concern. This article offers a general overview of the epidemiology of perinatal substance use focusing primarily on the United States but when available international trends will be presented as well.

### 1. Introduction

Substance abuse and alcohol use during pregnancy are significant and growing public health concerns [1,2]. The total annual societal cost of substance use in terms of lost goods, lost productivity, treatment, and medical services in the United States is estimated to be \$510.8 billion [3]. Over the last two decades, the prevalence of opioid use among women of childbearing age has risen dramatically in the United States [4]. According to the WHO, women account for approximately 40% of the substance-using population. Specifically, women are most at risk of substance use during their reproductive years between the ages of 18–29 [5].

In the 1970s, public concern regarding potential teratogens intensified when researchers in France observed fetal alcohol syndrome in women who drank large amounts of alcohol during pregnancy [2]. By the 1980s, widespread use of crack cocaine in the United States fueled public concern and outrage [6]. Perinatal substance use remains a significant public health concern associated with adverse consequences for a mother and her developing fetus. Epigenetics and teratogenicity add further considerations related to maternal obstetrics and fetal outcome [5]. In the United States, the trends of substance use during pregnancy are similar to those observed worldwide [5]. According to a U.S. National Survey in 2012, 5.9% of pregnant women use illicit drugs, 8.5% drink alcohol, and 15.9% smoke cigarettes, with as many as 50% of pregnant women reporting polysubstance use [7].

Trends in substance use are similar among developed high-income countries, and comparable with observations made in the United States, Europe, and Australia [5]. In South Australia, for example, approximately 7.9 infants per 1000 live births are born to mothers who reported substance use [8]. Similarly, a 2001 study in England reported

7.5 infants per 1000 live births born to substance-using mothers in the northern Yorkshire region, a nearly 40-fold increase to its 0.19 per 1000 deliveries estimate in 1993 [5]. Of the substance-using mothers in Australia, 86% also smoked and 10.3% endorsed psychiatric conditions [8]. In the United States and Australia, the three most commonly used substances during pregnancy are tobacco, alcohol, and cannabis [6]. This article offers a general overview of the epidemiology of perinatal substance use focusing primarily on the United States but when available international trends will be presented as well.

### 2. Tobacco

Tobacco is the product of cured leaves of the tobacco plant resulting in products that include cigarettes, electronic cigarettes, and smokeless tobacco. Because of the frequency of its use, tobacco has an effect of a huge magnitude because of the number of pregnancies affected. Tobacco is the most commonly used substance in pregnancy, followed by alcohol and illicit substances [7]. Among women aged 18–30, the prevalence of cigarette use is highest at age 18 when approximately 36% of women report cigarette use [9]. Furthermore, cigarette use among women is unique compared to alcohol and marijuana use in that cigarette use initiation rates are very low in the mid- and late-20s; almost all current cigarette users (88%) initiate use at or before age 26 [10]. In Australia, 12% of women report smoking during the first 20 weeks of pregnancy, and 9% continue to do so after 20 weeks [6]. In a 2010 United Kingdom study, as many as 97.4% of pregnant known substance users reported tobacco smoking [11].

Tobacco use during pregnancy is a significant public health issue for women everywhere because it is associated with higher infant mortality rates and poor birth outcomes such as preterm birth, small for

\* Corresponding author.

E-mail address: [vsmith1@bidmc.harvard.edu](mailto:vsmith1@bidmc.harvard.edu) (V.C. Smith).

gestational age, and low birth weight.<sup>12,6,7</sup> Furthermore, although about one third [13] to one half [7] of women stop tobacco use during pregnancy, about 16% of women will resume after delivery [6]. Currently there is a strong public interest in illicit drug use during pregnancy, but the health, social, and economic costs related to tobacco use during pregnancy are higher than those for illicit drug use [6,12]

### 3. Alcohol

Next to tobacco, alcohol is the most commonly used substance in pregnancy [7]. There is no amount of alcohol that can be considered safe during pregnancy. Binge drinking (having 4 or more drinks at one time) is the most dangerous pattern of alcohol consumption during pregnancy [2]. In the general population, binge alcohol use is highest among Millennials (defined as people who reached young adulthood in the early 21st century) and lowest among Baby Boomers (defined as people born worldwide between 1946 and 1964) with Gen X (defined as the demographic cohort following the Baby Boomers and preceding the Millennials) in the middle [14]. Among women aged 18–30, the highest prevalence of binge drinking occurs at age 22 (34%) [9].

In a survey conducted between 2011 and 2013, approximately 1 in 10 pregnant women in the United States reported drinking alcohol in the past 30 days, and about 1 in 33 pregnant women report binge drinking in the past 30 days [15,16]. In a 2010 United Kingdom study, 43.8% of pregnant women reported alcohol use [11]. Some women report decreasing or eliminating alcohol use during pregnancy, but 7.6% of pregnant women report continued alcohol use with 1.4% binge drinking [17]. A prospective study on perinatal abstinence and relapse found that among women with alcohol use prior to pregnancy, 96% of women with heavy drinking achieved abstinence in pregnancy but by three months postpartum, 51% of abstinent women relapsed [7].

Fetal Alcohol Spectrum Disorder (FASD) is an overarching term that encompasses a range of possible conditions associated with prenatal alcohol exposure, including fetal alcohol syndrome (FAS), partial fetal alcohol syndrome (pFAS), alcohol-related birth defects (ARBD), alcohol-related neurodevelopmental disorder (ARND), and neurobehavioral disorder associated with prenatal alcohol exposure (ND-PAE) [2]. FASDs are the leading cause of preventable intellectual and developmental disabilities in the Western world. If a fetus is not exposed to alcohol during gestation he or she cannot develop an FASD. Children with FASDs have a constellation of physical, behavioral, and cognitive abnormalities resulting from prenatal alcohol exposure [2]. Studies of grade school children suggest that the rate of an FASD is estimated at 24 to 48 per 1000 children [18].

### 4. Cannabis

With regional legalization and medical indications, cannabis has become one of the most commonly used substances during pregnancy. Among women aged 18–30, marijuana use peaks at age 18 (23%) [9]. Prevalence estimates of perinatal cannabis use range from 10% [19] to 43% [20].

Among past-year marijuana users ( $n = 17,934$ ), use almost daily was reported by 16.2% of pregnant women of whom 18.1% met criteria for abuse and/or dependence [19]. Among pregnant women who were admitted to substance use treatment for the first time ( $n = 489,796$ ), 40.6% reported any level of cannabis use, and 40.8% reported cannabis use as the primary drug of choice at treatment admission [21]. This could partly be due to a perception that marijuana is “safe”. Approximately 70% of pregnant women believe there is slight or no risk of harm from using marijuana once or twice a week [19].

The demographic characteristics of pregnant women who used marijuana have changed over time, with white non-Hispanic women, criminal justice referrals, and those with a psychiatric comorbidity becoming more common [20].

While pregnant women reporting cannabis use as the primary drug

of choice were significantly less likely to co-use other substances, those involved in the criminal justice system were significantly more likely to co-use cocaine and opioids, but significantly less likely to co-use alcohol [21]. Smokers of tobacco, alcohol users, and other illicit drug users were 2–3 times more likely to use marijuana in the past year than respective nonusers, adjusting for sociodemographic characteristics [19].

A prospective study on perinatal abstinence and relapse found that among women with substance use prior to pregnancy, 76% of women with marijuana use achieved abstinence in pregnancy but by three months postpartum, 41% of abstinent women relapsed [7].

### 5. Opioids

Opioids are narcotics that act on opioid receptors that are medically used primarily for pain relief and commonly abused. Among all people surveyed from the 2003–2014 National Surveys on Drug Use and Health age 18 and older, opioid use from 2013 to 2014 showed that non-medical prescription opioid (NMPO) only is the most common type of opioid use with prevalence among adults of 3.76%, compared to 0.10% for heroin-only and 0.23% for co-use [22].

Of those reporting past year opioid use, the proportion by type of opioid used changed from 2003 to 2014 with NMPO having a relative decline of 4.65% to 91.95% in 2013–2014 [22]. Among all opioid users in 2013–2014, the highest prevalence of co-use was seen among those who were aged 26–34 (9.76%), unemployed (12.08%), and reported abusing (16.81%) and using (11.87%) illicit drugs, or psychological distress (11.87%) [22].

Heroin-only use increased from 1.69% of all opioid use in 2003–2004 to 2.37% in 2013–2014 [22]. The annual average rate of past-year heroin use in 2011–2013 was 2.6 per 1000 persons aged  $\geq 12$  years [23]. The largest increase in heroin use was among those who had previously reported NMPO use, suggesting NMPO use may be a gateway to heroin use and subsequent co-use [23]. NMPO and heroin co-use is growing at a rate that is cause for concern [22]. When studied, Millennials exhibited statistically significant higher risk of substance use with especially worrisome patterns of increase in heroin and OxyContin use [14].

The rate of past-year heroin use in 2011–2013 for women was 1.6 per 1000 [23]. This rate is, however, rapidly increasing with trends in heroin alone and heroin co-use among females growing at a rate double that of males [23].

Opioid use during pregnancy has risen sharply with maternal opioid use increasing from 1.19 to 5.63 per 1000 hospital births per year [24]. Part of this increase is because the prevalence of pregnant women being prescribed opioids has increased. A study showed that among 112, 029 pregnant women, 28% were prescribed at least one opioid during pregnancy in the context of an increasing misuse of prescription pain medication increasing among pregnant women [25]. Women prescribed opioid pain relievers were more likely than those not prescribed opioids to have depression, anxiety disorder, and to smoke tobacco [25]. By 2014, over 41% of pregnant women admitted to publically funded substance use disorder treatment programs reported a primary opioid use disorder [26].

Neonatal abstinence syndrome (NAS) is the collective group of issues that neonates may experience in the days after birth when exposed to opioids in the womb. The incidence rates for NAS and maternal opioid use increased nearly 5-fold in the United States between 2000 and 2012 [24]. Rural areas of the United States have been disproportionately affected by the opioid crisis with the incidence of NAS per 1000 births in hospitals increasing from 1.2 to 7.5 in rural areas compared with 1.4–4.8 in cities [27]. Furthermore, the proportion of newborns with NAS in rural parts of the country increased from 12.9% in 2004 to 21.2% in 2013 [27]. The frequency of hospital deliveries related to maternal opioid use increased from 1.3 to 8.1 per 1000 deliveries in rural areas compared with 1.6–4.8 in urban areas [27].

Internationally in 2012, average annual prevalence of opioid abuse

among adults in Europe was around 0.4% (approximately 1.3 million people) with heroin being the most frequently used opioid in Europe [28]. The estimated prevalence of opioid use ranges from less than 0.1% to around 0.8% among 15–64 year olds, 20% of which women of childbearing age [28].

Ontario Canada noted a 16-fold increase in the number of mother-infant pairs affected by opioid dependence from 46 in 2002 to almost 800 in 2014 [29]. The percent of infants with NAS remained around 58% during this same period of time [29]. Methadone was the most frequently used treatment for prenatal opioid dependence; there was little buprenorphine or buprenorphine + naloxone use. Rates of pre-term birth and low birth weight were high [29]. Opioid Maintenance Treatment (OMT) has become the mainstream treatment modality for people with opioid use disorder. In Norway, a higher proportion of women in OMT use prescription drugs prior to, and during, pregnancy than pregnant women in the general population [30].

Opioid use by pregnant women is a growing concern that will need to be addressed at both a prescriber and policy level.

## 6. Cocaine

Cocaine, a strong central nervous system stimulant used by 14–21 million people each year [31], is one of the most frequently used illegal drugs globally. Cocaine comes in forms that can be used either by nasal insufflation (e.g. snorted), smoked, or dissolved and injected. Use is highest in North America followed by Europe and South America [31]. Despite its popularity, cocaine use is less frequently used currently than it has been in the past and the demographics of who is using cocaine have also changed [14].

Cocaine use from 2007–2016 was highest among Millennials (1.31%; 95% CI = 1.24%–1.40%) and lowest among Baby Boomers (0.27%; 95% CI = 0.23%–0.32%), with Gen X (0.70%; 95% CI = 0.64%–0.77%) in the middle [14]. The rates of alkaloidal (crack) cocaine use have declined since the 1980s [32]. Use of alkaloidal cocaine is notably higher among Gen X (0.28%; 95% CI = 0.23%–0.33%) as compared with Millennials (0.15%; 95% CI = 0.13%–0.17%) and Baby Boomers (0.12%; 95% CI = 0.10%–0.16%), particularly in 2007 [14].

There is limited current data on how many pregnant women use cocaine making it hard to know how exactly frequently it is used by pregnant women, but it is estimated to be 1.1% at any point in pregnancy [32]. It has been suggested that there is a high prevalence of cocaine use during pregnancy [33]. A study by Pereira et al. [34], found that the 17% of pregnant women used licit or illicit drugs and 9.2% of them used some version of cocaine [34]. A prospective study on perinatal abstinence and relapse found that among women with substance use prior to pregnancy, 73% of women with cocaine use achieved abstinence in pregnancy, but by three months postpartum, 27% of abstinent women who used cocaine relapsed [7].

Cocaine is a very frequently used illicit substance. Given the prevalence of cocaine use, it is reasonable to presume that some pregnant women use cocaine. Based on the difficulty to find recent data, likely underreporting of use due to concerns about criminal consequences, and lack of universal screening, it is not clear how often pregnant women use cocaine.

## 7. Methamphetamine

Methamphetamines are synthetic stimulant drugs that are highly addictive and becoming increasingly popular. In 2002, 5.3% of the adult population ages 12 and older, corresponding to approximately 12 million people, had used methamphetamines at least once in their lifetime and there were 323,000 new users of methamphetamines [35]. In 2006, nearly 40% of all female substance users (i.e. more than 400,000 reproductive-aged women) stated they had used methamphetamine in the prior month [36]. There is only limited data on

methamphetamine use during pregnancy because few systematic studies have estimated the prevalence of methamphetamine use by pregnant women [35]. Despite limited national data and the substantial regional use variability, the overall use of methamphetamine by pregnant women seems to have increased since the 1990s mirroring the increased use by the general population [33,37] (Terplan, Smith, Kozloski, & Pollack, 2009) (Terplan, Smith, Kozloski, & Pollack, 2009) (Terplan, Smith, Kozloski, & Pollack, 2009) (Terplan, Smith, Kozloski, & Pollack, 2009).

Most of the data about use in pregnant women is derived from specifically selected populations. Coming from an enriched sample that is not nationally representative, the population studied by Arria et al. [35], was chosen from “heavy use” regions of the United States where methamphetamine use during pregnancy is a notable concern. Arria et al. found that methamphetamine was used by 5.2% participants at some point during the pregnancy [35]. Similarly, of the 245,970 pregnant women admitted to treatment programs between 1994 and 2006, methamphetamine was the primary substance used for 8% in 1994 and 24% in 2006 [37]. Methamphetamine disorders now account for one quarter of all admissions of pregnant women into substance-abuse treatment [33]. This means that methamphetamine has become a leading substance compelling treatment during pregnancy [37].

There is some evidence to suggest the population of pregnant women using methamphetamine is also changing from an initial concentration of predominantly white women in the West to increasing numbers in the Midwest and Southeast, including an increasing proportion of Hispanic or Latina women [37]. In the United States and New Zealand, compared to other substance using populations the methamphetamine using groups had lower socioeconomic status, increased single parenting, were more likely to present for their first prenatal visit later in pregnancy than comparison mothers, and had increased poly substance use [38].

Despite the limited availability of data, methamphetamine use during pregnancy seems to be a significant and increasing issue.

## 8. Polypharmacy

Despite discussing each substance individually, many people use multiple substances—polypharmacy. Yang et al. [14], found the use of at least two substances excluding binge alcohol, was highest among Gen X, followed by Millennials and lowest among Baby Boomers [14]. There is some variability in those who use multiple substances. Jones et al. [23] found that 96% of past-year heroin users reported use of at least one other drug during the past year, and 61% reported using at least three different drugs [23]. The percentage of heroin users with past-year marijuana, cocaine, or alcohol abuse or dependence remained stable between 2002 and 2013, but the percentage of heroin users with opioid pain reliever abuse or dependence more than doubled during that same time period [23].

Pregnant women reporting cannabis use as the primary drug of choice were significantly less likely to co-use other substances unless they were involved with the criminal justice system where they were significantly more likely to co-use cocaine and opioids, but significantly less likely to co-use alcohol [21].

## 9. Conclusions

Because substance use during pregnancy is very widespread, substance use during pregnancy continues to be a significant public health concern. Most of the substances used during pregnancy are legal. It is hard for one to know the full extent of the substance use during pregnancy because of underreporting. Substance use in pregnancy can lead to a number of deleterious effects in mother and her offspring that varies depending upon the drug, point of exposure, and extent of use. Pregnancy is a time when women can be very motivated to change patterns of substance use. Comprehensive treatment programs should

be made available to help women with substance use disorders during the motivating period of pregnancy.

## 10. Practice points

- Perinatal substance use is a prevalent problem and a big public health issue
- Substance use crosses every demographic, geographic, and socio-economic characteristic
- Pregnancy is a time when women can be very motivated to change patterns of substance use
- Comprehensive treatment programs should be made available to help women with substance use disorders during the motivating period of pregnancy

## 11. Research directions

- Epidemiological results are skewed towards developed countries that have a systemic method of data collection from their population, such as Canada and Australia.
- Drug use occurs in almost every country and data are lacking from those many regions
- There is limited data on treatment programs that are effective in areas with varying resources
- To better characterize the full effects of perinatal substance use, there needs to be more comprehensive data on substance usage and linkage with outcomes for the families and the child, as well as long-term follow up

## Conflicts of interest

None.

## References

- [1] Krans EE, Patrick SW. Opioid use disorder in pregnancy. *Obstet Gynecol* 2016;128(1):4–10.
- [2] Williams JF, Smith VC, Committee On Substance, Abuse. Fetal alcohol spectrum disorders. *Pediatrics* 2015;136(5):e1395–406. <https://doi.org/10.1542/peds.2015-3113>.
- [3] Miller TR, Hendrie D. Substance abuse prevention dollars and cents: a cost-benefit analysis. Rockville, MD: US Department of Health and Human Services, Substance Abuse and Mental Health Services Administration, Center for Substance Abuse Prevention; 2009.
- [4] Lind JN, Petersen EE, Lederer PA, Phillips-Bell GS, Perrine CG, Li R, et al. Infant and maternal characteristics in neonatal abstinence syndrome - selected hospitals in Florida, 2010-2011. *MMWR Morb Mortal Wkly Rep* 2015;64(8):213–6.
- [5] Cook JL, et al. Epidemiology and effects of substance use in pregnancy. *J Obstet Gynaecol Can* 2017;39(10):906–15.
- [6] Burns L, Coleman-Cowger VH, Breen C. Managing maternal substance use in the perinatal period: current concerns and treatment approaches in the United States and Australia. *Subst Abuse* 2016;10(Suppl 1):55–61.
- [7] Forray A, Foster D. Substance use in the perinatal period. *Curr Psychiatr Rep* 2015;17(11):91. <https://doi.org/10.1007/s11920-015-0626-5>.
- [8] Kennare R. Substance use during pregnancy: risk factors and obstetric and perinatal outcomes in South Australia. *Aust N Z J Obstet Gynaecol* 2005;45:220–5.
- [9] Evans-Polce RJ, Schuler MS, Schulenberg JE, Patrick ME. Gender- and age-varying associations of sensation seeking and substance use across young adulthood. *Addict Behav* 2018;84:271–7. <https://doi.org/10.1016/j.addbeh.2018.05.003>.
- [10] U.S. Department of Health and Human Services. The health consequences of smoking—50 Years of progress: a report of the surgeon general. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2014.
- [11] Goel N, Beasley D, Rajkumar V, Banerjee S. Perinatal outcome of illicit substance use in pregnancy—comparative and contemporary socio-clinical profile in the UK. *Eur J Pediatr* 2011;170(2):199–205. <https://doi.org/10.1007/s00431-010-1284-6>.
- [12] Gadsby D. Alcohol, substance use and pregnancy: health Behaviors joint strategic needs assessment literature review. Lancashire County Council; 2014. *JSNA [pdf]*, Lancashire County Council.
- [13] Forray A, Merry B, Lin H, Ruger JP, Yonkers KA. Perinatal substance use: a prospective evaluation of abstinence and relapse. *Drug Alcohol Depend* 2015;150:147–55. <https://doi.org/10.1016/j.drugalcdep.2015.02.027>.
- [14] Yang Justin Christopher, Roman-Urrestarazu Andres, Brayne Carol. Binge alcohol and substance use across birth cohorts and the global financial crisis in the United States. *PLoS One* 2018;13(6):e0199741. <https://doi.org/10.1371/journal.pone.0199741>.
- [15] Green PP, McKnight-Eily LR, Tan CH, Mejia R, Denny CH. Vital signs: alcohol-exposed pregnancies—United States, 2011-2013. *MMWR Morb Mortal Wkly Rep* 2016;65(4):91–7. <https://doi.org/10.15585/mmwr.mm6504a6>.
- [16] Tan CH, Denny CH, Cheal NE, Sniezek JE, Kanny D. Alcohol use and binge drinking among women of childbearing age - United States, 2011-2013. *MMWR Morb Mortal Wkly Rep* 2015;64(37):1042–6. <https://doi.org/10.15585/mmwr.mm6437a3>.
- [17] US surgeon general releases advisory on alcohol use in pregnancy. February 21, 2005 Available at: <http://come-over.to/FAS/SurGenAdvisory.htm>, Accessed date: 20 August 2018.
- [18] May PA, Baete A, Russo J, Elliott AJ, Blankenship J, Kalberg WO, et al. Prevalence and characteristics of fetal alcohol spectrum disorders. *Pediatrics* 2014;134(5):855–66. <https://doi.org/10.1542/peds.2013-3319>.
- [19] Ko JY, Farr SL, Tong VT, Creanga AA, Callaghan WM. Prevalence and patterns of marijuana use among pregnant and nonpregnant women of reproductive age. *Am J Obstet Gynecol* 2015;213(2):201. <https://doi.org/10.1016/j.ajog.2015.03.021>.
- [20] Martin CE, Longinaker N, Mark K, Chisolm MS, Terplan M. Recent trends in treatment admissions for marijuana use during pregnancy. *J Addiction Med* 2015;9(2):99–104. <https://doi.org/10.1097/adm.0000000000000095>.
- [21] Washio Y, Mark K, Terplan M. Characteristics of pregnant women reporting cannabis use disorder at substance use treatment entry. *J Addiction Med* 2018. <https://doi.org/10.1097/adm.0000000000000424>.
- [22] Mital S, Windle M, Cooper HLF, Crawford ND. Trends in non-medical prescription opioids and heroin co-use among adults, 2003-2014. *Addict Behav*; 2018. <https://doi.org/10.1016/j.addbeh.2018.05.005>.
- [23] Jones CM, Logan J, Gladden RM, Bohm MK. Vital signs: demographic and substance use trends among heroin users - United States, 2002-2013. *MMWR Morb Mortal Wkly Rep* 2015;64(26):719–25.
- [24] Patrick SW, Schumacher RE, Benneyworth BD, Krans EE, McAllister JM, Davis MM. Neonatal abstinence syndrome and associated health care expenditures: United States, 2000-2009. *J Am Med Assoc* 2012;307(18):1934–40. <https://doi.org/10.1001/jama.2012.3951>.
- [25] Patrick Stephen W, Dudley Judith, Martin Peter R, Harrell Frank E, Warren Michael D, Hartmann Katherine E, et al. Prescription opioid epidemic and infant outcomes. *Pediatrics* 2015;135(5):842–50. <https://doi.org/10.1542/peds.2014-3299>.
- [26] Short VL, Hand DJ, MacAfee L, Abatemarco DJ, Terplan M. Trends and disparities in receipt of pharmacotherapy among pregnant women in publically funded treatment programs for opioid use disorder in the United States. *J Subst Abuse Treat* 2018;89:67–74. <https://doi.org/10.1016/j.jsat.2018.04.003>.
- [27] Villapiano NLG, Winkelman TNA, Kozhimannil KB, Davis MM, Patrick SW. Rural and urban differences in neonatal abstinence syndrome and maternal opioid use, 2004 to 2013. *JAMA Pediatr* 2017;171(2):194–6. <https://doi.org/10.1001/jamapediatrics.2016.3750>.
- [28] European Monitoring Centre for Drugs and Drug Addiction. European drug report 2014: trends and developments [internet]. Lisboa: EMCDDA 2014 Available from: <http://www.emcdda.europa.eu/publications/edr/trends-developments/2014>, Accessed date: 11 January 2019.
- [29] Brogly SB, Turner S, Lajkosz K, Davies G, Newman A, Johnson A, Dow K. Infants born to opioid-dependent women in ontario, 2002-2014. *J Obstet Gynaecol Can* 2017 Mar;39(3):157–65.
- [30] Lund IO, Skurtveit S, Engeland A, Furu K, Ravndal E, Handal M. Prescription drug use among pregnant women in opioid Maintenance Treatment. *Addiction* 2013 Feb;108(2):367–76.
- [31] Pomara C, Cassano T, D'Errico S, Bello S, Romano AD, Riezzo I, Serviddio G. Data available on the extent of cocaine use and dependence: biochemistry, pharmacologic effects and global burden of disease of cocaine abusers. *Curr Med Chem* 2012;19(33):5647–57.
- [32] Bhuvanewar CG, Chang G, Epstein LA, Stern TA. Cocaine and opioid use during pregnancy: prevalence and management. *Prim Care Companion J Clin Psychiatry* 2008;10(1):59–65.
- [33] Gouin K, Murphy K, Shah PS. Effects of cocaine use during pregnancy on low birthweight and preterm birth: systematic review and metaanalyses. *Am J Obstet Gynecol* 2011;204(4):340. <https://doi.org/10.1016/j.ajog.2010.11.013>. e341-312.
- [34] Pereira CM, Pacagnella RC, Parpinelli MA, Andreucci CB, Zanardi DM, Souza R, et al. Drug use during pregnancy and its consequences: a nested case control study on severe maternal morbidity. *Rev Bras Ginecol Obstet* 2018. <https://doi.org/10.1055/s-0038-1667291>.
- [35] Arria AM, Derauf C, Lagasse LL, Grant P, Shah R, Smith L, et al. Methamphetamine and other substance use during pregnancy: preliminary estimates from the Infant Development, Environment, and Lifestyle (IDEAL) study. *Matern Child Health J* 2006;10(3):293–302. <https://doi.org/10.1007/s10995-005-0052-0>.
- [36] Substance Abuse and Mental Health Services Administration. 2007.
- [37] Terplan M, Smith EJ, Kozloski MJ, Pollack HA. Methamphetamine use among pregnant women. *Obstet Gynecol* 2009;113(6):1285–91. <https://doi.org/10.1097/AOG.0b013e3181a5ec6f>.
- [38] Woules TA, LaGasse LL, Derauf C, Newman E, Shah R, Smith LM, et al. Co-morbidity of substance use disorder and psychopathology in women who use methamphetamine during pregnancy in the US and New Zealand. *Drug Alcohol Depend* 2013;127(1–3):101–7. <https://doi.org/10.1016/j.drugalcdep.2012.06.016>.