

SUBSTANCE USE DURING PREGNANCY

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SUMMARY

Pregnancy is a period of transition with physical changes in the maternal body but also mental and psychological ones. This phase may be accompanied by symptoms of anxiety, depression or irritability, which are part of non-pathological adaptation mechanisms. These symptoms can, however, be intense and constitute real psychiatric syndromes, particularly when the woman presents vulnerability factors. While fetal exposure to alcohol and other drugs is one of the leading preventable causes of developmental delay and birth defects in newborns, substance use during pregnancy is common, particularly in Europe. There is no amount and no time during pregnancy where consuming alcohol and other substances of abuse is safe. This narrative review reflects the point of view of the obstetrician, the constraints of his therapeutic framework with its limitations of time, training and tools to detect and manage substance-related disorders. Validated detection questionnaires are poorly adapted to obstetric practice; detection and first brief interventions can be delegated to save time but at the risk of reducing the involvement of the obstetrician. The combined management of pregnancy and addictions by a psychiatrist and an obstetrician comes up against different frameworks and working deadlines in the two disciplines.

Key words: pregnancy - alcohol, drugs - mental health - vulnerability

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INTRODUCTION

Pregnancy is a period of transition with physical changes in the maternal body but also psychological and sometimes psychiatric changes. Although mental disorders are often associated with substance use (Jané-Llopis & Matytsina 2006), it is recommended to abstain from alcohol and other substances of abuse during pregnancy. Fetal alcohol exposure is one of the leading preventable causes of developmental delay and birth defects in newborns. There is no time or period during pregnancy when the use of alcohol and other substances is safe. This narrative review reflects the obstetrician's perspective, the constraints of their therapeutic framework with its limitations of time, training, and tools to detect and manage substance-related disorders. Obstetrics is a screening medicine. Supervision of care is limited to the 9 months of pregnancy. The temporality of psychiatrists and that of obstetricians is not the same. This results in communication difficulties and some misunderstandings about the expectations of the two professions. In general, the patients are in good health, and obstetric monitoring aims to detect pathological events that influence the successful continuation of the pregnancy. The monitoring framework is precise and can be intensified at any time (KCE 248BS 2015).

Pregnancy monitoring in Belgium includes:

- 7 to 10 prenatal consultations lasting 15 to 20 minutes with systematic data collection: History, additional examinations and clinical examination:

weight gain, urine dipstick, blood pressure, doptone (device that allows you to listen to the heartbeat of the fetus) / ultrasound;

- 3 ultrasounds lasting 20 to 30 minutes.

A lot needs to be done, and on top of that, there is a demand to detect mental illness and vulnerabilities. The search for mental disorders, great social insecurity, mental retardation or age (Coenen 2019) are part of the anamnesis. Detecting substance use can be a challenge. Consumers can remain discreet or minimize consumption. Validated detection tools or questionnaires for obstetricians are lacking. In this review, we will identify the frequencies of exposure to substances and their consequences during pregnancy. Suggestions for possible improvements will be made.

METHOD

This is a narrative analysis whose reasoning and justification are the obstetrician's point of view. The obstetrician is confronted on the front line with the vulnerability of the pregnant patient. In an integrative medicine framework, our hypothesis is that if the obstetrician's work framework is well known, other health professionals will be able to better position themselves. Narrative reviews include a non-complete and non-exhaustive sample of the literature. Different researchers may take different approaches depending on the purpose of the review. The authors searched for references until the viewpoint discussed was covered.

Table 1. Prevalence of drinking among women 15 to 49 years of age (in 2016)

Region	Per capita consumption (liters)	Prevalence (%)			
		Current drinking	Former drinking	Lifetime abstinence	Heavy episode drinking
Europe	4.6	53.9	30.3	15.9	18.7
Low-Income economies	1.2	17.4	73.8	8.8	5.5
Lower-middle-Income economies	1.5	20.6	71.3	8.1	5.0
Upper-middle-Income economies	2.7	37.6	50.7	11.8	10.4
High-Income economies	4.5	60.7	18.4	20.9	17.3

RESULTS

Alcohol

Epidemiology

Alcohol consumption is higher in developed countries. 53.9% of European women of childbearing age drink alcoholic beverages. The average consumption is 4.6 liters of pure alcohol per year per woman (Povova 2021) (Table 1).

In 2016, the global incidence of alcohol consumption during pregnancy was 9.8%. The incidence in Europe is 25%, with Ireland in first position with a consumption rate of 60.4% (Popova 2017, 2018). In 2018, in Belgium, one in three women declared having drunk during their pregnancy. 43% consume alcohol while breastfeeding (SPF) (Table 2).

Table 2. Global prevalence of any alcohol use during pregnancy. Fetal alcohol syndrome (fas) and fetal alcohol spectrum disorder among the general population

Region	Alcohol use during pregnancy %	FAS per 10,000	FASD per 10,000
Globally	9.8	9.4	77.3
Europe	25.2	24.7	198.2
Ireland	60.4		
Denmark	45.8		
UK	41.3		

Obstetrical / maternal Impact

Alcohol consumption increases the risk of intrauterine fetal death, late miscarriage, prematurity, growth restriction and low birth weight. (Kesmodel 2000, 2002, Albertsen 2004, Broccia 2023). First trimester miscarriages occur with a frequency of 15% in the general population and are increased by alcohol consumption. With consumption of less than or equal to 5 drinks per week, each additional drink per week is associated with a 6% increase in the risk of miscarriage (Sundermann 2019). In a meta-analysis (Bandoni 2023), bringing together 36 studies conducted in nine countries, including samples of 500 to 40,000 participants, cognitive, academic, socio-emotional and behavioral outcomes were assessed from early childhood to the age of 19. It was not possible to determine a precise threshold for alcohol consumption by the mother inducing a neurodevelopmental disorder in

her child. Two other studies carried out by a Danish team (Broccia 2023) recorded all the births between 1996 and 2018 of their population located third in the world for alcohol consumption during pregnancy (1,191,295 births of which 4,823 had been considered as heavily exposed to alcohol). There is an increased risk for many obstetric parameters (small for gestational age, prematurity, hemorrhage during pregnancy). The maternal profile of users compared to the control group was more likely to have individuals suffering from a psychiatric illness (49.8% versus 9.6%), drug use (22% versus 0.4%), and tobacco use (64.3% versus 15.8%) with a low level of education (64.1% versus 17.6%). Tracking children from birth to age 18 shows many negative associations.

Fetal/neonatal impact

The placenta acts as a filter for molecules according to their weight. The placenta does not provide a barrier for alcohol and exposes the fetus to the effects of consumption. Not only, the dose of alcohol is proportionally greater on the fetal body volume compared to the maternal body volume, but there is also an amplified effect of exposure due to the system specific to intra-uterine life. Alcohol passes from maternal blood to fetal blood, and then the fetal kidney filters and eliminates it in the form of urine in the amniotic fluid. Which the fetus swallows and ingests again, thus prolonging exposure (Brien 1983, Underwood 2005). The global prevalence of alcohol use during pregnancy has been estimated at 9.8% (95% CI 8.9-11.1). The prevalence of fetal alcohol syndrome (FAS) is estimated at 9.4 per 10,000 people (95% CI 9.4-23.3) (Popova 2016). FAS is rare but fetal alcohol spectrum disorders are more numerous with an incidence of 77.3 per 10,000 for the world population and 198.2 per 10,000 for the European population.

The difficulties of screening for fetal alcohol syndrome

First described more than 50 years ago (Lemoine 1968, Jones 1973), it is always determined after birth. There is a combination of physical and cognitive elements: the lips are thin, the philtrum is long, the wings of the nose are spread with a more flattened nose and there is an intellectual disability of varying depth.

It is impossible to confirm the diagnosis of FAS on ultrasound and a puncture of amniotic fluid would not allow us to say to what degree the fetus is affected. If we

compare two images, seeking to show a longer and rounded philtrum, it is almost impossible to make the diagnosis of one fetus exposed (right) and the other not (Figure 1).

The combination of alcohol and other substances

Alcohol is often associated with other substances of abuse, nutritional deficiencies as well as environmental and psychosocial stressors such as domestic violence, precariousness or psychiatric comorbidities. Co-exposure models are observed to be more harmful, particularly the consumption of alcohol and tobacco or

alcohol and cannabis (Odendaal 2009, Shuffrey 2020, Boa-Amponsem 2019, Levitt 2009).

Screening tools: questionnaires

A survey carried out among American obstetric practitioners, shows that between 2000 and 2010, systematic screening for addictions fell from 92% at the first prenatal consultation to 82%. The screening tool during this first consultation was the history in 80% of cases. 51% of obstetricians used a questionnaire of which only 11% were scientifically validated (Ko 2020) (Figure 2).

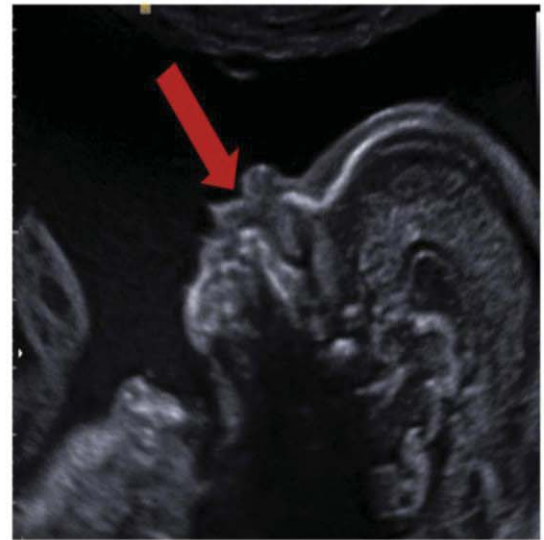


Figure 1. Diagnosis of FAS

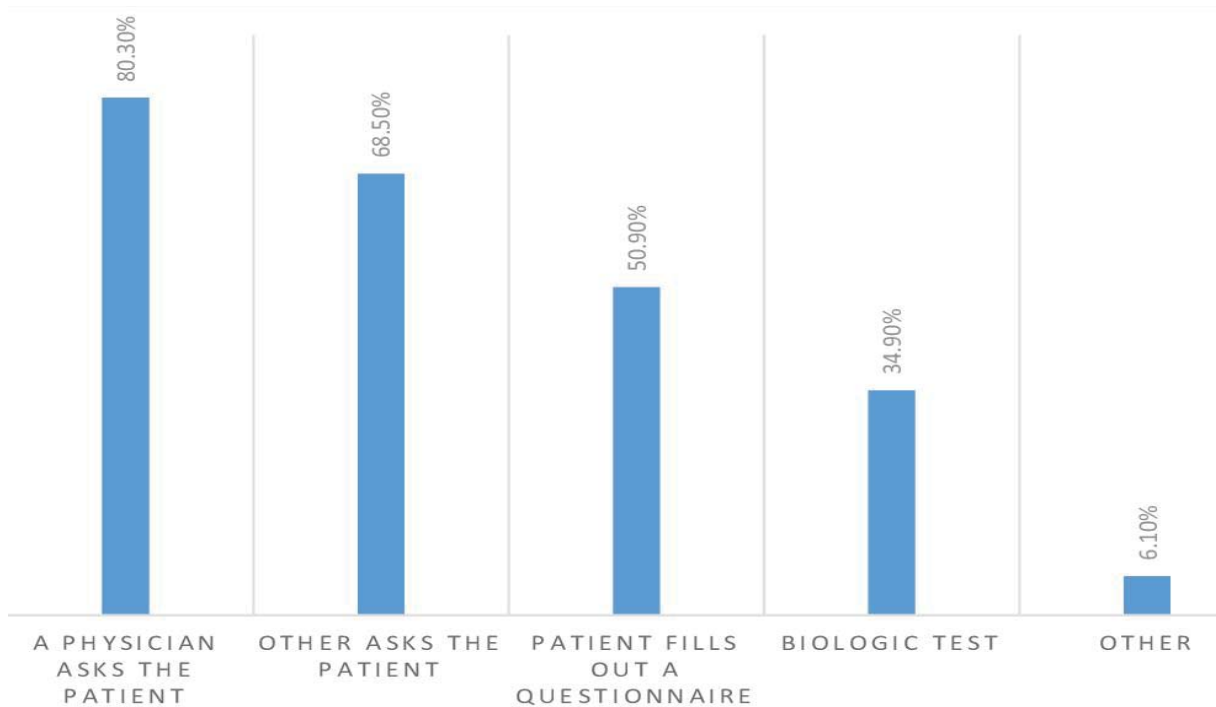


Figure 2. How practice obtains information about pregnant patient substance use

A study carried out between 2007 and 2008, at the Jeanne De Flandre University Hospital in Lille, France, evaluated the effectiveness of a systematic self-questionnaire distributed in the waiting room, to screen for substance consumption (alcohol, drugs and tobacco) during pregnancy. Over a period of 10 months of observation, 34% of patients received the self-questionnaire (n = 1974) with 89.4% of analyzable responses, comparing the answers given by the questionnaire to the information collected in the medical file (n = 1600). For alcohol consumption, the self-questionnaire allowed a screening of 4% while traditional consultations showed screening scores of 0.1%. Results were similar for tobacco: 9.8% VS 4.9%. The self-questionnaire could be a more effective tool than the anamnesis (Fline-Barthes 2015).

Tobacco

Epidemiology

The overall prevalence of active smoking stood at 22.3% in 2020 and 7.8% among women. A meta-analysis reports an overall prevalence of tobacco consumption during pregnancy of 1.7%. The prevalence is higher in European countries (8.1%), and lower in African countries (0.8%). Globally, 72.5% of women who smoked during pregnancy used tobacco daily and 27.5% occasionally (Lange 2018). In the United States, only 1% of female smokers of childbearing age abstained during pregnancy (Kendrick 1996).

Obstetric/maternal impact

Smoking is associated with an increased risk of early miscarriage (RR = 1.23) (Layoun 2022) and premature birth (McDonald 1992). In utero exposure to tobacco was found in 11% of cases of premature birth (McDonald 1992). Stopping smoking, particularly at the start of pregnancy, would be associated with a reduction of up to 20% in this risk. A study was carried out on a sample of 25 million patients to establish a minimum threshold for cigarette consumption that could increase the risk of premature birth. The data was collected in the United States National Vital Statistics System, between the years 2011 and 2018. All adult women who gave birth to babies alive, without hypertensive disease or pre-existing diabetes, and with complete data on smoking and gestational age at delivery were included. Participants reported their smoking status (yes or no) and the daily number of cigarettes consumed before and during each trimester of pregnancy. This study demonstrated that cigarette consumption as low as one to two cigarettes per day is associated with an increased risk of premature birth (Liu 2020). Smoking is associated with Preterm Premature Rupture of Membranes (PPROM) (Harger 1990, Hadley 1990) and an increased risk of placental abruption (Salihu 2007). This association

appears to be independent of the presence of PPRM, which in itself is an established risk factor for placental abruption (Layoun 2022). A meta-analysis conducted on 21 studies established a positive correlation between smoking and the risk of placenta previa (Shobeiri 2017). The link between smoking and placenta accreta has not yet been well established (Layoun 2022).

Fetal / neonatal impact

Low birth weight (<2500g) is the best-studied complication linked to smoking during pregnancy (Layoun 2022). Smoking during pregnancy was found in 35% of mothers of children born alive with low birth weight (McDonald 1992). Stopping tobacco consumption, especially at the start of pregnancy, is associated with a reduction in this risk, which becomes equal to that of non-smoking patients (Layoun 2022). In utero exposure to tobacco also appears to be associated with a higher risk of intrauterine growth restriction (IUGR). A retrospective study carried out on 927,424 births with a 25% rate of in utero exposure to tobacco in any trimester established an Odds Ratio of 2.26 for an IUGR below the 10th percentile and an OR of 2.44 (CI 2.37–2.51) for an IUGR below the 5th percentile (Blatt 2015). This risk is reduced even more the earlier you stop smoking during pregnancy (Blatt 2015). A meta-analysis of 142 articles evaluates the relationship between passive or active smoking with perinatal mortality (Pineles 2016). Maternal smoking during pregnancy is associated with an increased risk of stillbirth with a relative risk of 1.46 (CI 1.38-1.54 [n = 57 studies]), neonatal death with a relative risk of 1.22 (CI 1.14–1.30 [n = 28 studies]) and death perinatal with a relative risk of 1.33 (CI 1.25-1.41 [n = 46 studies]). This risk of perinatal mortality tends to increase if exposure to tobacco in utero occurs throughout the pregnancy (Qu 2020). In 3284 births with congenital malformations, when smoking was present during pregnancy, higher relative risks of microcephaly, clubfoot and cleft lip and palate were observed (Van den Eeden 1990). In a retrospective study comparing a group of 2207 births with cleft lip and palate to 4414 births without congenital malformations, in utero exposure to tobacco increased the risk of cleft lip and palate, with an Odds Ratio of 1.34 (Chung 2000). Tobacco use during the first trimester is associated with a greater prevalence of congenital heart disease, independent of demographic characteristics and established heart disease risk factors (OR = 1.16). These heart diseases mainly include abnormalities of the pulmonary valve (OR = 1.48), abnormalities of the pulmonary arteries (OR = 1.71) and isolated damage to the interatrial septum (OR = 1.22). This risk increases with the number of daily cigarettes consumed and the maternal age particularly from the age of 35 (Sullivan 2015).

Illicit drugs

In the United States, a NIDA survey conducted among a nationally representative sample of 2,613 women who gave birth in 1992 (Mathias 1995) shows that 5% of women used illicit drugs during pregnancy: 2.9% used cannabis and 1.1% cocaine.

Cannabis

It is the third psychoactive substance consumed after alcohol and tobacco. Tetrahydrocannabinol (THC) is lipophilic and accumulates rapidly in the brain and fatty tissues. THC metabolites can be detected in urine 1 to 3 days after a single consumption and after more than 30 days in case of chronic consumption (Verstraete 2004). From 14 weeks of pregnancy, THC receptors are present in the placenta. Exposure is observed mainly during the first trimester and the effects are rather reassuring on the risk of malformation. Obstetric and neonatal impacts are observed for regular consumption (> 6 times per week). These include prematurity, intrauterine growth restriction, small for gestational age, neonatal tremors regressing in approximately one month. The role of tobacco smoked with cannabis is difficult to distinguish from that of cannabis alone (CRAT).

Cocaine

Cocaine is the fourth most used substance by pregnant women in the United States. Cocaine use during pregnancy is associated with a risk of premature birth, low birth weight and a younger gestational age at delivery (Gouin 2011). The main obstetric risk is placental abruption. There is a correlation between sudden infant death and drug use in the broad sense, which includes opioids, methadone and cocaine. Calculated on a sample of 4 million births, the risk of sudden death increases up to nine times compared to those patients not exposed to drugs. (Makariuos 2022).

Opioids

Epidémiology. Opioids include a wide range of natural or opiate alkaloid derivatives (heroin, codeine and morphine) and synthetic (fentanyl and oxycodone (Wouldes 2023)). According to the EMCDDA (European Monitoring Center for Drugs and Drug Addictions), the global prevalence of opioid use in 2021 was estimated at 0.6%. Approximately 60.4 million people were involved in non-medical use of opioids worldwide, including 31.5 million were users of opiates, primarily heroin. In addition to non-medical use, approximately 14 to 22% of pregnant women in the United States are prescribed opioids for pain relief during their pregnancies (Bateman 2014, Desai 2014).

Fetal and neonatal impact. Opioids cross the placental barrier and cause dependence in the fetus. The clinical picture is marked by excessive crying, fever, irritability, seizures, slow weight gain, tremors, diarrhea,

vomiting, and eventually death (NIDA). A study carried out over 10 years shows a prevalence of Neonatal Abstinence Syndrome (NAS) of 76.5%, for 51 heroin users during pregnancy (Vucinovici 2008).

A metaanalysis of 68 studies of which 46 had an unexposed comparison group, 30 performed statistical tests to measure associations between maternal opioid use during pregnancy and birth defects. 17 documented statistically significant positive associations. Oral clefts and ventricular septal defects/atrial septal defects and clubfoot were the most commonly reported specific malformations. However, due to the methodological limitations of the studies, uncertainty remains regarding the extent of opioid teratogenicity. On the other hand, cognitive and psychomotor deficiencies, as well as behavioral disorders, are significantly reported in preschool children with prolonged exposure to opioids in utero (Baldacchino 2015).

Maternal and obstetrical impact. Opioid abuse or dependence during pregnancy significantly increases the risk of obstetric morbidity and mortality (Ayumi 2014). In a sample of 113,105 pregnant patients consuming or dependent on opioids during their pregnancies in the United States, a significant increase in the risk of maternal cardiac arrest, intrauterine growth restriction, placental abruption, and Preterm Premature Rupture of Membranes (PPROM) and oligohydramnios was demonstrated. An increased risk of premature labor and cesarean section has been established (Ayumi 2014). Between the years 2004 and 2017 in the United States, the prevalence of heroin use among women of reproductive age was 0.12% (Vanderziel 2020). It has been clearly established that intrauterine exposure to heroin and methadone is associated with an increased risk of perinatal mortality, premature births and low birth weight (Boer 1994, Hulse 1997, 1998, Behnke 1993, Fajemirokun-Odudeyi 2004). Substituting heroin for methadone during pregnancy could theoretically improve the neonatal prognosis (Fajemirokun-Odudeyi 2004). However, these benefits could be canceled if high doses of methadone are used, or on the contrary, insufficient doses but with persistence of heroin use (Fajemirokun-Odudeyi 2004).

Ecstasy

N-methyl-3,4-methylenedioxyamphetamine; 3,4-methylenedioxymethamphetamine (MDMA), better known as ecstasy, is an illicit drug that is a vasoconstrictor, along with amphetamines and cocaine (Draper 2008). MDMA is a powerful stimulant of the central nervous system, acting particularly on the serotonergic axis by significantly increasing the release of serotonin (Draper 2007) thus creating neurotoxicity. Ecstasy crosses the placental barrier (CRAT) and is associated with a higher prevalence of birth defects and neurodevelopmental disorders. A survey carried out by the

NTIS (The UK national Teratology Information Service) (McElhatton 1999) on 136 children exposed to ecstasy in-utero revealed a significantly increased risk of congenital malformations (15.4%) with a predominance of congenital heart disease and musculo-skeletal malformations. An increase in the prevalence of gastroschisis has also been described, especially when consumption occurs during the first trimester (Smid 2019, Parrott 2014). In-utero exposure to ecstasy is associated with dose-dependent neurodevelopmental delay, mainly during the first trimester. This delay is particularly observed in the acquisition of fine and gross motor gestures, with persistence at 24 months of life and seems to be linked to the serotonergic neurotoxicity caused by ecstasy (Smid 2019, Draper 2007). Ecstasy consumption increases cortisol levels with levels up to 800% of the initial value (Draper 2007). As cortisol also passes the placental barrier, ecstasy use during pregnancy has a fetal and neonatal impact caused by the drug itself and by the increase in cortisol. The neonatal consequences of hypercortisolism include low birth weight, reduced head circumference and reduced Apgar score. Neurodevelopmental impacts include cognitive, behavioral and emotional disorders. The latter seem to be linked in part to the fact that increased cortisol levels further accentuate the neurotoxicity caused by ecstasy.

Solvents

Solvent abuse involves the intentional inhalation of volatile substances (Baydala 2010). These substances include a varied range of pharmacologically active products including aliphatic, aromatic or halogenated hydrocarbons, nitrous oxide and volatile alkyl nitrites (Williams 2007, Lorenc 2003). The substances most frequently reported to U.S. poison control centers between 1996 and 2001 include gasoline (41%), paint (13%), propane or butane (6%), air fresheners (6%), % and formalin (5%) (Spiller 2004). A Canadian study was carried out on 56 pregnant patients consuming volatile substances. 46.4% of these women consumed only solvents while 53.6% were multiple consumers. A rate of 21.4% premature birth was recorded. Concerning fetal impacts, intrauterine growth restriction was diagnosed in 16.1% of cases. In addition, major congenital malformations were observed in 16.1% of cases. Seven of 56 children had facial features of fetal alcohol syndrome and two of 51 were born with cleft lip and palate. Neonatal metabolic acidosis was diagnosed in 17.8% (Scheeres 2002). Another investigation found that pregnant women exposed to organic solvents were four times more likely to have a child with central nervous system (CNS) defects compared to women who were not exposed during pregnancy (Holmberg 1980). There is no recent literature available on this issue. Further research would therefore be imperative to obtain more up-to-date data.

DISCUSSION

Narrative reviews offer a flexible but rigorous approach to knowledge synthesis, which is useful to many educators and researchers. This approach has limitations; they are not often reproducible due to the influence of authors and context on selection, sampling and analysis. We did this review from the obstetrician's point of view. The obstetrician must be considered a front-line worker in the care of pregnant women. Because substance-induced fetal mortality and morbidity is significant, with potentially major consequences on development and adult life, the consumption of alcohol and drugs is discouraged during all stages of pregnancy. However, substance use during pregnancy, particularly alcohol, is common in Europe. Screening, management of substance use during pregnancy and, where applicable, referral to a treatment program is a challenge for front-line workers; they cannot all be trained and do not have the time to do everything. The use of questionnaires can be recommended, but this proposal is hampered by the scarcity of validated assessment tools and screenings that are brief enough to be used in primary care. The complexity linked to the multitude of substances consumed, sometimes in combination, probably contributes to the relative lack of research (Saitz 2010, Squires 2010, Lanier & Ko 2008). If consumption is detected, the obstetrician can provide a brief intervention such as communicating information on the effects of substances and giving advice on specialized care. Collaborative care in which staff other than the obstetrician screen and counsel patients is certainly a way to ease the burden of multiple tasks. However, delegation risks leading to low involvement of the obstetrician (Squires 2010). Timing is also an issue if the patient needs to be referred for specialist care. Psychiatrists and treatment programs for substance users do not treat substance use on an emergency basis. While the effects of toxic substances on the fetus are measured in days, psychiatric treatment may not be available for weeks, sometimes months. For patients to benefit from pregnancy monitoring and substance use management, an integrative approach must be considered between the two specialties.

CONCLUSION

Many factors (genetic, sociocultural, environmental...) can contribute to the vulnerability of women, particularly in terms of the consumption of psychoactive products. Consumption of alcohol and other substances during pregnancy is more common in the most economically developed countries. Any woman who is pregnant or wishes to become pregnant must be informed about the risks associated with the consumption of psychoactive substances during pregnancy. This

consisted above all, of offering them care like all high-risk pregnancies, with the same protocols and the same professionals. Valid screening tools are poorly suited to obstetric practice. Interactions between obstetricians and substance professionals such as psychiatrists can be complicated: identification, assessment, and the way of acting over time can present considerable differences depending on the field in which one is located.

Ethics:

The present study was conducted in accordance with the Declaration of Helsinki guidelines.

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Contribution of individual authors:

Maylis Desiron & Caroline Kadji were responsible for the design.

Caroline Kadji provided most of the literature searches and analyses.

Maylis Desiron, Clara Saad, Juan Martin Tecco & Caroline Kadji contributed interpretation of data, manuscript writing.

The final version was written by Caroline Kadji & Juan Martin Tecco.

The manuscript was approved by all authors.

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