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Prevalence of Illicit Drug Use During Pregnancy: A Global Perspective

RONAN A. TAVELLA, VICTÓRIA O.M. DE ABREU, ANA LUIZA MUCCILLO-BAISCH & FLÁVIO M.R. DA SILVA JÚNIOR

Abstract: The World Drug Report 2019 presented an alarming figure to the world: more than 5% of the world's population has been using some type of illicit drug, and that number is growing every year. While its use increases, its abuse during pregnancy has become a global public health problem, resulting in medical and social challenges related to maternal and child health. In this context, the objective of this review was to determine the prevalence of illicit drug use during gestation across the globe, alongside with a critical review of the evaluated studies. Research was performed by simultaneously searching terms ("pregnant woman OR pregnant" OR "gestation" OR "pregnancy" AND "illicit drugs" OR "street drugs") in the databases of the Scientific Electronic Library Online, PubMed, and Web of Science. Comparisons between studies were performed in software Statistica 10.0. The data presented worrying results in relation to the variation in prevalence of illicit drug use during pregnancy, when comparing studies based on interviews or questionnaires (self-reported) (1.65%) and studies based on toxicological analysis (12.28%). In addition, we emphasize the high prevalence (5.16%) of illicit drug use among adolescent pregnant women and the low number of studies on this population. This study reveals worrying data about pregnant drug-user population, mainly the underestimation of prevalence in studies that use only questionnaires or similar methods in comparison to studies that use toxicological analysis of biological matrices. This scenario reveals necessity for health systems in different countries to establish specific public health policies for this population.

Key words: pregnant women, drugs, gestation, substance use disorder, adolescent pregnancy.

INTRODUCTION

The World Drug Report 2019 presented by the United Nations Office on Drugs and Crime (UNODC) reported that, in 2017, about 271 million people were using illicit drugs around the globe, which is 5.5% of the world population (UNODC 2019). The same report shows that, from 2010 to 2017, the number of drug users rose from 226 million (5% of the world population) to 271 million (5.5% of the world population) (UNODC 2019). It is a cause for concern that illicit drug use in the world is increasing every year.

In the 1971 United Nations Convention on Psychotropic Substances the expression "psychotropic substance" was the term used to refer to those natural or synthetic substances or any natural material listed in the four schedules of the convention, which have been prohibited from commercialization except for prescribed use (UNODC 1971). Thus, as Asimakopoulos et al. (2016) stated in his review, licit drugs are those for which the prescription for medical use is permitted by law, while illicit drugs are those for which non-medical use is prohibited by law.

However, it is important to note that depending on the region, there may be permissive legislation for the use of illicit substances in different scenarios.

Substance use disorder is a medical condition in which the use of one or more substances leads to a clinically significant impairment or distress (APA 2013). Drug dependence has been considered an important issue in recent decades, but its history stretches back for millennia and it is now identified by the World Health Organization (WHO) to be among the 20 highest risk factors for health problems (WHO 2009).

The use of illicit drugs is expanding and has reached major proportions. Their use and abuse during pregnancy has become a global public health problem in the last two decades, generating several medical and social challenges related to illicit drug use and maternal and child health (WHO 2009). Pregnancy combined with the use of psychotropic substances, whether legal or illicit, may cause obstetric complications, including placental abruption and increased incidence of premature rupture of membranes, as well as abortion, increased maternal mortality, stillbirth and neonatal mortality (Schempf 2007, Kassada et al. 2013). Despite knowing the risks, illicit drug use among women has increased. Among drug users, 90% are of childbearing age, between 15 and 40 years old, and 30% started using illicit drugs before the age of 20 (Melo et al. 2014).

An accurate estimate of the prevalence of illicit drug use during pregnancy is difficult given the abuse of polysubstances and the overlapping of social factors (Melo et al. 2014). However, it is known that the illicit substances most used in pregnancy include cocaine, opioids, and marijuana (Kassada et al. 2013).

Gestation is a period of great transformation in a woman's life, causing significant changes to her body, her psyche, and her socio-familial role (Rocha et al. 2016). The use of illicit drugs during pregnancy can lead to insufficient nutrition in the mother and fetus. In addition, the risk of infection and body fluid transmitted diseases increases if non-sterile needles are used (Slamberova 2012). More frequent occurrences of anemia, hepatitis, and preeclampsia, and an increased tendency for hypertension, have been demonstrated in women who abuse drugs during pregnancy (Slamberova 2012). Therefore, the risk of miscarriage, stillbirth, preterm birth, low birth weight, and decreased head circumference is increased (Rocha et al. 2016).

Some illicit drugs can act on the maternal cardiovascular system, causing adrenergic hyperstimulation and vasoconstriction. In this case, there is an increase in heart rate and maternal blood pressure, with a consequent decrease in blood flow to the uterus and a risk of intrauterine growth restriction (Oliveira et al. 2016). Other illicit drugs can act on the central nervous system and its use during pregnancy may increase the risk of a congenital malformation and may be associated with preterm birth, intrauterine growth disturbances and neonatal morbidity. There is also a possibility that drug exposure can affect brain development with long-term neuropsychological harm as a result (Källén et al. 2013). As can be seen, the complications of illicit drug use are not restricted to pregnant women, but also affect their fetuses.

As stated by Slamberova (2012), the number of babies with congenital defects due to drugs has been increasing over the years. This is due not only to an increase in the prevalence of drug abuse among pregnant women, but also to an increase in behavioral disorders, such as smoking and alcohol consumption, and social aspects, such as lack of prenatal care and low socioeconomic status (Oliveira et al. 2016). The diagnosis of drug-related problems

must be made during anamnesis in prenatal consultation, where a non-judgmental approach is prerequisite for obtaining the necessary details (Wright & Walker 2001, Rocha et al. 2016). Although it is a growing problem in the world population, there are few published studies on the use of illicit drugs during pregnancy and it is a public health problem that is little discussed. It should also be noted that clinical trials are generally restricted to statistical comparisons because scientific research on pregnant women is performed carefully. The absence of epidemiological studies addressing the use of, and dependence on, illicit drugs during pregnancy, limits the analysis of their effects on the mother and newborn (Slamberova 2012).

In this context, use, abuse, and dependence on psychotropic substances represents a great concern for different institutions and spheres of society, as it is a behavior capable of causing potentially serious physical and psychological consequences for both mother and child (Rocha et al. 2016). Faced with this new challenge in obstetric care, we aimed to determine the prevalence of illicit drug use during gestation across the globe, alongside with a critical review of the evaluated studies.

MATERIALS AND METHODS

This study presents a critical review of the literature on the topic of illicit drug use during pregnancy, highlighting the prevalence of use pointed out in the studies, and considering differences in subject age, geographic position (continent), and type of study (interviews/questionnaires or toxicological analysis).

The search strategy aimed to find published studies from any country and language. The following computerized databases were searched in August 2019: PubMed, Web of Science, and Scientific Eletronic Library Online (SciELO). The search terms used were: "*pregnant woman OR pregnant" OR "gestation" OR "pregnancy" AND "illicit drugs" OR "street drugs".*

To delimit the study, the following inclusion criteria were used to select articles: published since 2000; presenting data regarding pregnant women who used illicit drugs during pregnancy or within a period of 3 months prior to pregnancy. As exclusion criteria: be a review article, monograph, dissertation or thesis; be an article that addresses the use of two or less illicit drugs among the individuals surveyed; be a comparative study of biological matrices and/or analytical methods; article in case study; article on animal experimentation. The exclusion of studies that addressed only one or two types of illicit drugs was performed in order to minimize overestimations in prevalence caused when including researches were all participants used illicit drugs. Furthermore, there were no restrictions on language.

Two reviewers, working independently and in duplicate screened abstracts and titles for eligibility using standardized instructions. Articles included by at least one reviewer were retrieved. Following abstract screening, eligibility of reports was assessed through full-text screening. We assessed the eligibility of each study using the criteria that were previously described. To find additional relevant articles, the reference lists of all of the retrieved studies were examined. Authors were contacted when it was unclear whether full-text manuscripts were eligible for inclusion in this review and if the necessary data was missing. Authors were contacted by an email to the corresponding author. At the level of full-text screening, any disagreements were resolved by consensus between the two reviewers (R.A.T. and V.O.M.A.) with a third reviewer acting as the arbiter (F.M.R.S-J.). The flowchart of the review process

can be found in the Supplementary Material - Flowchart.

Reviewers rated the quality of each study based on established criteria and a modified version of the Newcastle-Ottawa Scale (NOS) (modified to meet the needs of this study) including 9 items divided in selection, comparability and exposure (Wells et al. 2019). Each item could score one time. Then, the studies were classified as high risk (1-3 points), intermediate risk (4-5 points) and low risk of bias (6-9 points). Only studies classified as low risk of bias were included in the review. The modified NOS are presented in the Supplementary Material - Modified Newcastle - Ottawa Quality Assessment Scale.

Data extraction was performed independently using a standardized form. The following outcomes were recorded from each selected article: year of publication; total number of study participants (n); prevalence of illicit drug users, either reported in interviews or found by toxicological analysis; the illicit drug most found in the study; mean age or the age interval with the largest number of study participants (the median age was used where neither of these were available); the method of obtaining information on illicit drug use; and the place where the study was conducted. It is worth mentioning that the percentage presented for the most commonly reported drug is related to the prevalence of its use during pregnancy.

Presentation and analysis of data

Prevalence data were presented individually and the weighted arithmetic averages were calculated. Comparisons between studies were performed in software Statistica 10.0 using means of comparison tests (ANOVAs, t-test for dependent or independent samples, or their non-parametric equivalents). It is important to emphasize that when there were two ways of obtaining information (interview versus toxicological analysis) the highest prevalence among the different forms was considered to calculate the weighted arithmetic average.

RESULTS AND DISCUSSION

Using the descriptors presented, 719 articles were found in the platforms database. Of these, 589 were excluded after abstract and title screening, 41 were duplicates, 21 were excluded for not meeting the criteria and 2 did not meet the quality assessment score. In addition, 4 articles were added through reference lists. Thus, 70 articles were included in the review.

Prior to the 2000s, few studies have investigated the use of different illicit drugs by pregnant woman. Here is possible to emphasize the research by National Institute on Drug Abuse perfomed in 1992 and published in 1996, found that 5.5% of pregnant women surveyed used an illicit drug. Despite this, most studies at that time sought to verify the use of some specific drugs and their outcomes, and thus did not add the other drugs to their conclusions. As a result, in this review we chose to only add the published articles from the 2000s.

Table I shows the list of studies included in this review, revealing the state of art at this date. The total number of studies published between 2000 and 2019, addressing the selected topic, was 70, representing a total of 689553 participants from 14 different countries. The prevalence found when we considered the sample size of each study was 1.83%. The illicit drug reported as the most frequent in the studies was marijuana (42.85% of studies), followed by cocaine (14.29%). We emphasize that marijuana is the most commonly used illicit drug around the world (UNODC 2016).

Table I. Review of the literature from the years 2000 to 2019 on the subject of pregnant women and use of illicit drugs.

Year	N	Prevalence of illicit drug use from interview (%)	Prevalence of illicit drug use found in the analysis (%)	Most reported drug	Mean age ± SD, Interval with higher prevalence of age or median	Way of obtaining the information	Country	Reference
2001	2002	4.6	-	The author did not specify	20 - 25 (40.3 %)	Interview	USA	(Chasnoff et al. 2001)
2002	456	20.4	-	Marijuana (100 %)	12 - 17 (100 %)	Interview	Australia	(Quinlivan & Evans 2002)
2002	3118	0.96	-	The author did not specify	20 - 34 (69.8 %)	Interview	Brazil	(Gama et al. 2002)
2003	432	1.2	-	Marijuana (100 %)	25 - 34 (76 %)	Interview	Denmark	(Kesmodel et al. 2003)
2003	1249	2.8	-	Marijuana (64 %)	21 - 30 (61 %)	Interview	USA	(Ebrahim & Gfroerer 2003)
2003	5159	23	-	The author did not specify	The author did not specify	Interview	USA	(Peters et al. 2003)
2004	1083	11.7	-	Cocaine (34.5)	19-29 (70%)	Interview	USA	(Kerker et al. 2004)
2005	549	2.5	10.9	Opioids (79.8 %)	28.9 ± 6.2	Interview and meconium	Spain	(Pichini et al. 2005)
2005	145	6.2	-	The author did not specify	15 - 18 (100 %)	Interview	USA	(Kaiser & Hays 2005)
2005	160	6	-	Marijuana (100%)	23.4 ± 5.2	Interview	USA	(Bernstein et al. 2005)
2005	1812	16.3	-	The author did not specify	27.9*	Interview	Europe	(Hankin et al. 2005)
2006	1000	-	6	Marijuana (66%)	11 - 19 (100 %)	Hair	Brazil	(Mitsuhiro et al. 2006)
2006	413	0.5	-	Marijuana (100%)	25.20 ± 5.52	Interview	Russia	(Chambers et al. 2006)
2006	1632	11	-	Marijuana (54%)	25 - 34 (47 %)	Interview	USA	(Arria et al. 2006)
2007	1000	1.7	-	Marijuana and cocaine (100%)	11 - 19 (100 %)	Interview	Brazil	(Chalem et al. 2007)
2007	1013	12	-	The author did not specify	25.1 ± 5.4	Interview	USA	(Blake et al. 2007)
2007	976	6	-	Marijuana (83%)	26-39 (74%)	Interview	Australia	(Wallace et al. 2007)
2007	244	-	18.9	The author did not specify	31.6*	Urine or serum	USA	(Kunins et al. 2007)
2008	218	6	-	Marijuana (50%)	27 ± 6.6	Interview	Puerto Rico	(Vélez et al. 2008)
2008	913	16	-	Cocaine (67. 8%)	23.7 ± 5	Interview	USA	(Orr et al. 2008)
2008	498	-	32	Opioids (53.5 %)	The author did not specify	Umbilical cord	EUA	(Montgomery et al. 2008)

Table I. Continuation

2008	416834	1.1	-	Marijuana (50%)	The author did not specify	Interview	Australia	(Burns et al. 2008)
2009	1209	2.9	10.9	Marijuana (64 %)	28.8 ± 5.6	Interview and meconium	Spain	(Garcia-Algar et al. 2009)
2009	623	18.8	-	The author did not specify	32 ± 3	Interview	Spain	(Ibieta et al. 2009)
2010	5871	3.6	-	Marijuana (90 %)	>= 30 (40.15 %)	Interview	USA	(Van Gelder et al. 2010)
2010	4094	5.3	-	The author did not specify	20 - 34 (78.7 %)	Interview	USA	(Dott et al. 2010)
2010	142	-	30.3	Marijuana (67.4 %)	26 ± 6.5	Hair and blood serum	Spain	(Falcon et al. 2010)
2010	154924	1.1	-	The author did not specify	The author did not specify	Interview	Canada	(Burstyn et al. 2010)
2010	194	-	12	Methamphetamine (70%)	23.35*	Meconium	Uruguay	(Hutson et al. 2010)
2010	1476	7	-	Marijuana (82%)	24 ± 6	Interview	USA	(Chung et al. 2010)
2010	868	3.4	-	Methamphetamine (70%)	26.9 ± 6.2	Interview	USA	(Wright & Tam 2010)
2011	25049	3.2	-	Marijuana (78.8 %)	20 - 24 (37.79 %)	Interview	Australia	(Hayatbakhsh et al. 2011)
2011	503	0.4	-	Marijuana (100 %)	32.9 ± 5.1	Interview	Italy	(De Santis et al. 2011)
2011	23	35	-	The author did not specify	29.8 ± 5.1	Interview	Brazil	(Gardenal et al. 2011)
2011	248	33.3	-	Marijuana (94 %)	25 ± 5.8	Interview	Canada	(Muckle et al. 2011)
2011	36	30.5	-	Cocaine (45.5 %)	26.1 ± 5.4	Interview	Brazil	(Manenti et al. 2011)
2011	500	20.2	-	The author did not specify	23.6 ± 4.5	Interview	USA	(El-Mohandes et al. 2011)
2011	11852	0.1	-	The author did not specify	30.2 ± 4.8	Interview	Canada	(Crane et al. 2011)
2012	347	-	2.6	Cocaine (100 %)	28.6 ± 6	Hair	Spain	(Joya et al. 2012)
2012	107	-	16	Marijuana (64.7 %)	31 (Median)	Hair	Spain	(Friguls et al. 2012)
2012	811	4.1	-	The author did not specify	20 - 35 (68.3%)	Interviews	Brazil	(Lobato et al. 2012)
2012	280	-	28.9	Marijuana (74.1 %)	26 ± 3.5	Hair	EUA	(Falcon et al. 2012)
2013	115	-	34.8	Marijuana (90 %)	23.6 ± 0.7	Urine	USA	(Gaalema et al. 2012)
2013	209	4.3	15.4	Cocaine (80.5 %)	31.9 ± 18.4	Interview and hair	Spain	(Lendoiro et al. 2013)
2013	394	1.5	-	Crack, marijuana and cocaine (33 % cada)	25.28	Interview	Brazil	(Kassada et al. 2013)

Table I. Continuation

2013	415	-	18.8	Cocaine (78 %)	Pregnant women who died soon after birth	Blood and urine	USA	(Hardt et al. 2013)
2013	8961	0.5	-	The author did not specify	20 - 34 (78 %)	Interview	Brazil	(Viellas et al. 2013)
2013	1040	11.8	-	The author did not specify	24.6*	Interview	USA	(Shneyderman & Kiely 2013)
2013	175	-	13.7	Cocaine (87.5 %)	The author did not specify	Hair	Spain	(Concheiro et al. 2013)
2013	898	6.9	-	The author did not specify	24.8 ± 5.9	Interview	USA	(Masho et al. 2013)
2014	845	7.6	-	Crack (59.9 %)	>= 25 (57.8 %)	Interview	Brazil	(Melo et al. 2014)
2014	200	-	13	Marijuana (83.8 %)	26 (Median)	Urine	USA	(Schauberger et al. 2014)
2014	1367	1.2	-	The author did not specify	11 - 19 (100%)	Interview	Brazil	(Jorge et al. 2014)
2014	299	10	-	The author did not specify	20 - 24 (52.8 %)	Interview	Brazil	(Miranda et al. 2014)
2014	1240	1.3	-	The author did not specify	20 - 24 (45 %)	Interview	Brazil	(Ribeiro et al. 2014)
2014	13545	1.2	-	Marijuana (100%)	25 – 34 (63.6%)	Interview	France	(Saurel-Cubizolles et al. 2014)
2015	451	1.9	-	Marijuana (100 %)	31.4 ± 5.2	Interview	Spain	(Blasco-Alonso et al. 2015)
2015	1085	-	2.2	The author did not specify	31 (Median)	Interview and urine	China	(Lam et al. 2015)
2015	165	10.9	-	The author did not specify	10 - 16 (100 %)	Interview	Mexico	(Sam-Soto et al. 2015)
2016	166	1.9	-	Crack (55.4 %)	26.6 ± 6.7	Interview	Brazil	(Oliveira et al. 2016)
2016	1447	1.5	-	Crack (35 %)	20 - 34 (81 %)	Interview	Brazil	(Rocha et al. 2016)
2016	314	12.1	-	Marijuana (65.8%)	The author did not specify	Interview	Brazil	(Renner et al. 2016)
2016	727	-	17.1	(Cocaine 50 %)	The author did not specify	Hair and Meconium	Spain	(Concheiro et al. 2016)
2016	295	-	8.5	Marijuana (53%)	33 (Median)	Urine	USA	(Kreshak et al. 2016)
2017	422	19.7	34	Marijuana (77%)	25 (Median)	Interview and urine	USA	(Chang et al. 2017)

Table I. Continuation

2017	3578	0.8	7.7**	Marijuana ***	24 - 35 (87.4%)	Interview and urine	Thailand	(Assanangkornchai et al. 2017)
2018	436	-	0,9	Marijuana	The author did not specify	Blood	Denmark	(Aagaard et al. 2018)
2018	494	-	27.4	Marijuana (81.39%)	28 ± 4.8	Urine	USA	(Oga et al. 2018)
2019	174	15.8	-	The author did not specify	28,1 ± 5.9	Interview	USA	(Wisner et al. 2019)
2019	33	66.2	-	Heroin (37.5)	27.8 ± 4.48	Interview	USA	(Sanjuan et al. 2019)

*** Mean without the presence of the standard deviation.**
**** Prevalence of a sample of 488 women within the study population in which urine sample was obtained for evaluation.**
***** From the data of the article it was not possible to define the percentage of users of illicit drugs that used marijuana.**

According to the previously stated about the difference of licit and illicit drugs, a drug may fall under both categories of licit drug or illicit drug, depending on its usage. The presence of this distinction makes it possible to reduce possible overestimations of drug use values in some studies, especially in those that contain toxicological analyses, since in the studies with interviews the question makes it clearer as to which illicit drug was used. The main illicit drug that could end up having its values overestimated in toxicological analyses is the opioids, because their use during pregnancy can be commonly associated with prescribed drugs used to alleviate the pain. However, almost all the selected studies, which performed analyses in biological matrices, stated that the women may not have reported drug use (when using opioids) because they were unaware of the constituintes of the medication they have taken legitimately (Kreshak et al. 2016, Assanangkornchai et al. 2017). Only Pichini et al. (2005) and Montgomery et al. (2008) do not mention this fact in their studies, but their research included an interview in which a question about the use of illicit drug was presented. Furthermore, these studies were the only ones in this review in which the majority of the population evaluated used opioids.

Most of the studies presented in this review (91.43%) were performed with adult pregnant women (older than 20 years), whereas only 8.57% focused on adolescents. In 68.57% of the studies, only questionnaires or interviews were used, whereas 31.43% of the studies evaluated the presence of illicit drugs in biological materials collected from the mother and/or child. Different biological matrices were used in toxicological analysis present in the studies in this review. Among these matrices are: hair, urine, serum, whole blood, umbilical cord and meconium. Most used matrix were urine and hair, being present in 40.9% and 36.36% of the studies that used toxicological analysis, respectively. Hair and urine are biological matrices characteristic for use in toxicological analyzes that seek to verify the presence of illicit drugs. Hair is mainly used due to its high window of detection, being possible to find substances up to 3 months after its use. However, in this matrix, the concentrations of substances are remarkably low. Thus, these hair techniques require methods and equipment that have low limits of quantification (Concheiro et al. 2013).

The reported prevalence of illicit drug use in pregnant women was 7.4 times higher in studies that used toxicological examination compared to those that used only questionnaires or

interviews to obtain data. In the latter form of data collection, the weighted prevalence (considering the sample size) was 1.65%. On the other hand, studies that used toxicological analysis the weighted prevalence was 12.28%.

Figure 1 shows the prevalence of illicit drug use in pregnancy in studies that compared the two forms of data collection (Pichini et al. 2005, Garcia-Algar et al. 2009, Hardt et al. 2013, Chang et al. 2017, Assanangkornchai et al. 2017). In these studies, there was a significant increase in prevalence when the data were obtained by toxicological analysis (3.8 times higher; weighted average 2.84% versus 10.77%). Among these studies, we highlight two that presented 9.6 (Assanangkornchai et al. 2017) and 4.4 (Pichini et al. 2005) times more pregnant women using illicit drugs than the data reported in interviews or questionnaires. It can also be observed that this is a recurrent behavior in studies on pregnant women because, over the years from 2001 to 2019, there seems to be consistent underestimation regarding the use of illicit drugs during gestation.

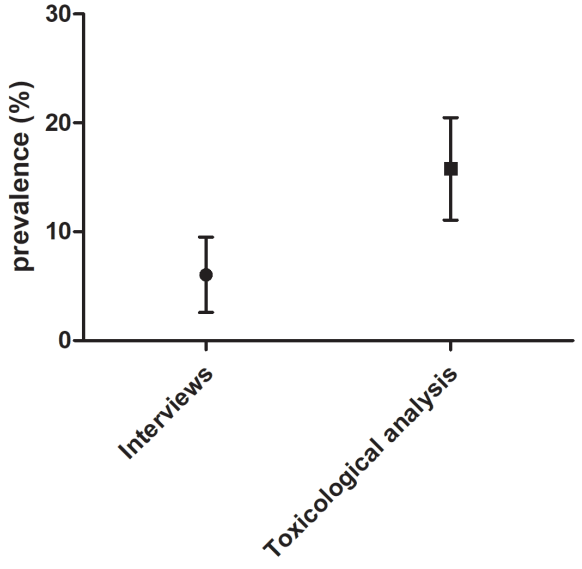

Figure 1. Distribution of prevalence of illicit drug use by pregnant women in studies comparing the two forms of data collection.*

These underestimated rates when the outcome is obtained through interview or questionnaire can be attributed to the mother's feelings of fear, shame, and guilt at the possibility of harming the fetus, and also to their fear of being judged, rather than supported, by the professionals who attend them (Kassada et al. 2014). Along with it, there are different laws and programs in many countries that determine procedures for the evaluation and subsequent notification to child protection agencies when there is a newborn exposed to illicit substances. As an example, we can quote "The Child Abuse Prevention and Treatment Act" (CAPTA), present in multiple states of the USA (Child Welfare Information Gateway 2016). After this notification, different actions can be taken by child protection services, they can offer direct assistance to the family of the newborn, including them in different government programs, or sending the mother to a referral treatment. But if this does not work, they can issue the request to the state to take legal custody over the child reporting maltreatment to the health and well-being of the newborn (Child Welfare Information Gateway 2014). From this information it is possible to imply that the underestimated rates may, also, be attributed to the mother's feeling of fear at the possibility of losing their child to the State.

Moreover, a recent study by Ondersma et al. (2019) compared five existing instruments for ability to identify illicit drug, opioid and alcohol use, under privacy expectations consistent with applied practice and using a gold standard incorporating toxicological analysis, showed that all screening instruments (interviews) for substance use in pregnancy tested (Substance Use Risk Profile—Pregnancy (SURP-P), CRAFFT, 5Ps, Wayne Indirect Drug Use Screener (WIDUS) and the National Institute on Drug Abuse (Quick Screen)) did not presented both high sensitivity and high specificity, and area under the curve

was low for nearly all measures, demonstrating a clear failure of the self-report screening instruments used to obtaining this information.

From these data, it is evident that toxicological analysis is the more reliable method of determining the actual prevalence of illicit drug use during pregnancy. On the other hand, we stress that this technique is costly and not always economically viable in less wealthy or underdeveloped regions. In addition, biological sampling is challenging due to the fact that it does not address windows of detection and does not make diagnosis of substance use disorders, only providing a point prevalence on day of testing.

The stratified results for continent and age group are presented in Table II. The total prevalence (using the weighted average of the 70 studies) was 1.83%, and the studies were carried out on all continents except Africa. The prevalence of illicit drug use during pregnancy is similar across continents (Figure 2: Europe, North America, and South America), but the small number of studies in Oceania and Asia hinders a better understanding. Another important point is the high prevalence of illicit drug use during pregnancy in adolescents, though the number of studies is extremely low. The weighted average prevalence among adolescents is three times higher than among women over 20 (Table II).

As a limitation of this research, multiple studies included in this review were screening women who were at high risk for substance use. Therefore, the statistics derived for usage rate presented in this study can be an overestimate since there is a wide variation between the prevalence found in the studies in this review. However, the use of the weighted average allows to minimize, even a little, this overestimation through calculations that give greater influence to the prevalence of studies with larger sample numbers. Moreover, multiple risk factors associated with illicit drug use and abuse are described in the literature. Among them, some social and demographic characteristics, such as: young women, especially adolescents, under 18 years; single women; low schooling, with less than 8 years of completed studies (U.S Department of Health and Human Services 2013, Rocha et al. 2016). Other social factors include: family history of substance use disorder, user partner, risky sexual behavior, victims of domestic violence (U.S Department of Health and Human Services 2013, Melo et al. 2014, Rocha et al. 2016). Some factors were related to health care, more specifically to prenatal care. The late prenatal start and the large number of absences at consultations were considered a risk factor (U.S Department of Health and Human Services 2013, Rocha et al. 2016).

It is also important to highlight that the studies that presented prevalence of illicit drug use above 30% in interviews, were performed in populations with characteristics that predispose them to a greater consumption of illicit drugs (Gardenal et al. 2011, Muckle et al. 2011, Manenti et al. 2011, Sanjuan et al. 2019). The study by Gardenal et al. (2011) presented a prevalence of 35%, however, it included only pregnant women with hepatitis C and marginalized population characteristics. The study by Muckle et al. (2011) presented a prevalence of 33.3% for drug use during pregnancy, although this study was carried out in an Inuit population (Eskimo) from a region of Canada already known for its high percentage (30%) of illicit drug use (mostly marijuana) (Jetté 1994). The study by Manenti et al. (2011) had a prevalence of 30.5% for the use of illicit drugs during pregnancy. However, it concerned a population of pregnant women who were HIV-positive, and also displaying marginalized population characteristics. The study by Sanjuan et al. (2019) had a prevalence of 66.2% (the higher prevalence found in this

Table II. Weighted average prevalence of illicit drug use in different continents and age group.

N° of studies	Continent	Prevalence (from the weighted average)	Range of prevalence (%)
4	Oceania	1.25%	1.05 - 20.4
17	South America	2.03%	0.5 - 35
31	North America	2.7%	0.1 - 66.2
15	Europe	4.87%	0.4 - 30.3
3	Asia	5.94%	0.5 - 7.7
70	All articles	1.83%	0.1 - 66.2
	Age group*		
6	Adolescents (10-19 years)	5.16%	1.2 - 20.4
64	Older than 20 years	1.81%	0.1 - 66.2

*** The studies that did not specify any data about the age of the participants were included in the section "older than 20 years".**

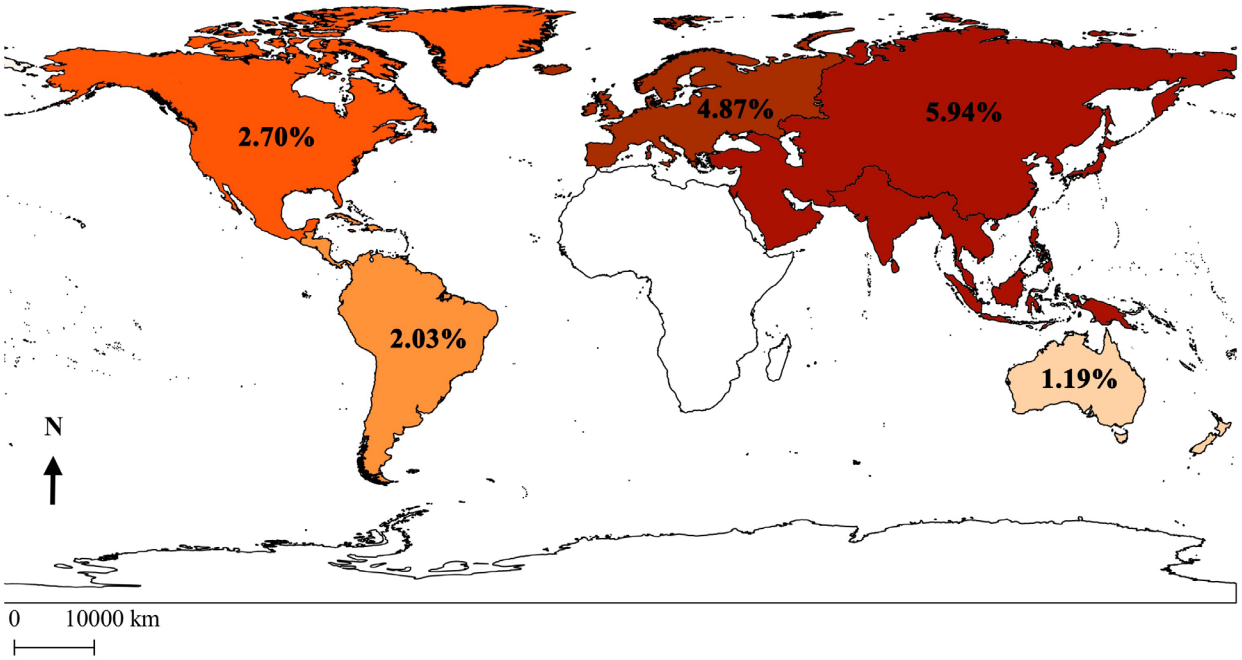

Figure 2. Prevalence of illicit drug use across continents (weighted mean of the studies).

review), mainly because it was performed in pregnant women with substance use disorder and prior trauma exposure. It is noteworthy that the other studies that presented prevalences above 30%, were studies which used toxicological analytical techniques (Montgomery et al. 2008, Falcon et al. 2010, Gaalema et al. 2012, Chang et al. 2017), which, as previously described, usually present higher prevalence.

As stated before, the most frequent illicit drug reported was marijuana and cocaine, and both may cause deleterious effects on the foetus. Pollard (2007) allege that illicit drugs affect the fetus by crossing the placenta in varying amounts and may permanently affect brain structure and function. Marijuana exposure may modify neuronal structure and function via endocannabinoid receptors, which are widely distributed in the fetal brain (Behnke & Smith 2013). Cocaine, on the other hand, by interacting with monoaminergic transmitters, alters neuronal growth, development, and cytoarchitecture (Ackerman et al. 2010). The neonatal effects of prenatal drug exposure range from deficits in growth to acute withdrawal symptoms (Shankaran et al. 2004). One review reported that marijuana is not generally associated with growth reduction, but is accompanied by an increased startle response and tremors (Behnke & Smith 2013). Abnormal neurobehavior is commonly described in cocaine exposed infants, who also demonstrate irritability, poor alertness, and orientation (Behnke & Smith 2013).

From this review, it is possible to verify that the most commonly consumed illicit drug worldwide among pregnant women is marijuana, followed by cocaine, and crack cocaine. It is also possible to verify that the use of illicit drugs during pregnancy is carried out by women of all ages, in all regions of the world, and with only a few regional changes in the type of drug consumed or the life habits in some populations.

It is important to make health professionals aware of the importance of comprehensive, humanized and qualified care for pregnant women, with a view to promoting health, preventing harm, diagnosis of drug abuse, early treatment and social reintegration. These support actions are efficient, since they reduce the level of stress, anxiety and depression among pregnant women, creating an environment less prone to the use of psychotropic substances (Schempf 2007, Kassada et al. 2014).

Furthermore, early detection of illicit drug use during pregnancy using toxicological analysis in biological matrices or effective screening programs, combined with the participation of qualified professionals and the development of further studies on the subject, possibly will help find the correct direction of the necessary measures to improve quality in pregnancy. Moreover, these actions may contribute to the reduction of obstetric complications and, consequently, reduce health costs.

CONCLUSION

This study reveals worrying data about the pregnant drug-user population. We particularly emphasize two points: the underestimation of prevalence in studies that use only questionnaires, interviews, or similar methods in comparison to studies that use the toxicological analysis of biological matrices; and the high prevalence of illicit drug use among adolescent pregnant women. The average prevalence of illicit drug use in pregnant women, among the studies that conducted questionnaires or interviews, was 1.65%, whereas in studies that performed toxicological analysis it was 12.28% (7.4 times higher).

However, the high costs, complexity of techniques, and need for specialized equipment and personnel make toxicological analysis an unattractive option in routine examinations on pregnant women. In order to reduce the serious effects of illicit drug use during pregnancy, the development of different approaches should be encouraged. These could include cheaper techniques to detect compounds or social inclusion techniques in basic care that reduce the omission of information by pregnant women to health professionals. Health professionals can improve on two fronts: by implementing policies and actions to reduce drug use during pregnancy, and by reducing underestimations of drug use in this context.

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SUPPLEMENTARY MATERIAL

Flowchart
Modified Newcastle - Ottawa Quality Assessment Scale

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RONAN A. TAVELLA[1]
https://orcid.org/0000-0003-2436-4186

VICTÓRIA O.M. DE ABREU [2]
https://orcid.org/0000-0002-0350-0081

ANA LUIZA MUCCILLO-BAISCH [3]
https://orcid.org/0000-0002-9475-6698

FLÁVIO M.R. DA SILVA JÚNIOR [1]
https://orcid.org/0000-0002-7344-4679

[1] Universidade Federal do Rio Grande, Instituto de Ciências Biológicas, Campus Carreiros, Av. Itália, Km 8, 96203-900 Rio Grande, RS, Brazil

[2]Universidade Federal do Rio Grande, Faculdade de Medicina, Campus Saúde, Rua General Osório, s/n, 96201-900 Rio Grande, RS, Brazil

[3]Universidade Federal do Rio Grande, Centro Regional para Estudos, Prevenção e Recuperação de Dependentes Químicos, Campus Saúde, Rua General Osório, s/n, 96201-900 Rio Grande, RS, Brazil

Correspondence to: **Flávio Manoel Rodrigues da Silva Júnior**
E-mail: f.m.r.silvajunior@gmail.com

Author contributions

The author Ronan Adler Tavella is responsible for the development and execution of the research, as well as for the writing of the article. Victória Oliveira Melo de Abreu is responsible for the second review and verification of the agreement of the obtained data. Authors Ana Luiza Muccillo-Baisch and Flávio Manoel Rodrigues da Silva Júnior are advisor of the research project and are responsible for reviewing the article.