v. 3, n. 49, 2023

International Journal of Health Science

PREVALENCE OF THE USE OF RISK DRUGS DURING PREGNANCY AND LACTATION IN BASIC HEALTH UNITS IN THE FEDERAL DISTRICT

Maria Carolina Jorge Albernaz
Medicine Course
Centro Universitário de BrasíliaBrasília-Federal District- Brazil
http://lattes.cnpq.br/9239582019057983

Carolina da Mata Oliveira
Medicine Course
Centro Universitário de BrasíliaBrasília-Federal District- Brazil
http://lattes.cnpq.br/8357282698729215

Emanuel Guimarães Cardoso
Medicine Course
Centro Universitário de BrasíliaBrasília-Federal District- Brazil
http://lattes.cnpq.br/4610235840503773

Maria Fernanda Araujo Barbosa Lima
Medicine Course
Centro Universitário de BrasíliaBrasília-Federal District- Brazil
http://lattes.cnpq.br/6321970057743842

Leticia Saldanha Camargos Aires
Medicine Course Centro Universitário de Brasília
Federal District - Brazil
https://orcid.org/0000-0002-7819-121X

All content in this magazine is licensed under a Creative Commons Attribution License. Attribution-Non-Commercial-Non-Derivatives 4.0 International (CC BY-NC-ND 4.0).

Rafaella Oliveira Dias
Medicine Course
Centro Universitário de BrasíliaBrasília-Federal District- Brazil
https://lattes.cnpq.br/1503032033668710

Luiza Novaes Carvalho
Medicine Course
Centro Universitário de BrasíliaBrasília-Federal District- Brazil
http://lattes.cnpq.br/1548043040894514

Laryssa Ramos Pino de Souza
Medicine Course
Centro Universitário de BrasíliaBrasília-Federal District- Brazil
https://lattes.cnpq.br/1603761287395941

Ana Luiza Briere
Medicine Course
Centro Universitário de BrasíliaBrasília-Federal District- Brazil
http://lattes.cnpq.br/5236262303133788

Larissa Rodrigues de Almeida Rego de Oliveira
Medicine Course
Centro Universitário de Brasília Brasília–Federal District- Brazil http://lattes.cnpq.br/4141876520486389

Júlia Oliveira Silva
Medicine Course
Centro Universitário de Brasília
Brasília- Federal District- Brazil http://lattes.cnpq.br/8628024772483683

Maria Eduarda Jorge Albernaz
Medicine Course
Centro Universitário do Planalto Central Aparecido dos SantosBrasília- Federal District- Brazil
https://orcid.org/0009-0006-0336-4303

Abstract: The use of medication during pregnancy and lactation is a subject of extreme relevance, since the scarcity of research with these groups makes it difficult to access data on the possible effects and risks of drugs.
The objective of the current study seeks to analyze the use of drugs in pregnant and breastfeeding women attended at the Basic Health Units in the central region of the Federal District and classify the risk of such drugs according to the Food and Drug Administration. In this research, data were collected through a questionnaire using Google Forms. The research took place between August 2020 and July 2021, through bibliographic analysis and data collection from the questionnaire. The results showed that 34% of the women were lactating and 66% were pregnant and 100% had some medical prescription, including folic acid, ferrous sulfate and multivitamins. The rate of self-medication was high, 22%, with analgesics, antipyretics and antiemetics being the most used therapeutic classes. The use of drugs by these women was predominant in the first trimester, followed by the second and third, and they were being monitored by medical assistance. Given these results, we concluded that health professionals were cautious when prescribing medications, demonstrating a rational prescription. However, the relevance of the production of campaigns by the Basic Units is highlighted, alerting and guiding professionals in the area to pay attention to the care in drug prescriptions, as well as the women in this group about the possible effects, in addition to emphasizing the risks of self-medication. This way, we will avoid prescription errors and, consequently, damage to the health of the pregnant woman, fetus and child.
Keywords: pregnant women; nursing mothers; medicines; risk; teratogenic.

INTRODUCTION

Information on the safety of drug use in pregnant and lactating women is usually insufficient for robust data analysis, considering that these categories of patients are not included in clinical studies performed during the development of most drugs (FDA, 2002). Thus, it is necessary to assess the prevalence of the use of drugs consumed during pregnancy and breastfeeding, as they may be related to direct damage to the fetus, such as low weight, malformations and changes in development or indirect consequences for the infant. (KASSADA, D.S et al, 2015; BALLONE GJ, 2011). Prescribers must ensure that maternal treatment is indicated when necessary, and then select the medication compatible with breastfeeding (Ministry of health, 2000), or, if the cost-benefit ratio justifies it, interrupt breastfeeding and guarantee the treatment of the lactating woman. (World Health Organization, 2002).

This concern about the effects of drugs on pregnancy resulted in the development of an internationally adopted system, which classifies drugs into five categories: A, B, C, D and X (Table 1, Annex), based on the risk to the development of the fetus. According to FDA data, about two-thirds of approved drugs are classified in category C because there are no data on human pregnancies and animal studies either revealed adverse effects or were not performed. Less than 1% of drugs are registered in category A, indicating that they are safe in pregnancy based on controlled studies in pregnant women (FDA, 2000a; FDA, 2000b). In general, information about the effects on human pregnancy becomes available after the products are marketed, through individual reports of congenital anomalies, clinical case reports, epidemiological studies and adverse event reporting systems (FDA, 1999).

It can be noted that the main researchers in this area of interest are linked to academic and university health centers and also to national and international agencies that finance research. Since, analysis of data about the drugs used by pregnant and breastfeeding women is extremely important in the scope of primary care, in view of the large amount of prenatal care and follow-ups performed by such units. Thus, the prescription of drugs must be done cautiously, always seeking to assess the risk/benefit ratio and this study aimed to evaluate the use and risk of using drugs during pregnancy and breastfeeding among women assisted in basic units. of the central region of the Health System of the Federal District.

THEORETICAL FOUNDATION

Pregnant women may need to use medication either because of pre-existing health problems, or because of conditions that arise during this period, or because of complications related to the pregnancy itself.

Studies carried out in Brazil on the use of medication during pregnancy (MENGUE et al, 2001; FONSECA et al, 2002; CARMO; NITRINI, 2004;

OSORIO-DE-CASTRO et al, 2004) pointed to a high prevalence of use of at least one medication during pregnancy which ranged from 82.9% to 97.6%, an average of 2.3 to 4.2 medications per pregnant women, a significant percentage of women reporting drug use without medical indication (31.2% to 33.5%) and a worrying use of prescribed drugs with little information about the risks in pregnancy. In Paraná, studies showed that 94.67% of the women interviewed claimed to use at least one drug during the gestational period, a figure close to those indicated in national (83.8% to 94.58%) and international (81.2%) surveys. % to 85.2%) (KASSADA et al, 2015). In Tayside, Scotland, it was analyzed that primary care prescribers prescribe

potentially dangerous drugs in pregnancy appropriately and cautiously, but many drugs do not have safety data (IRVINE et al, 2010).

In the study carried out by Costa, Coelho and Santos (2017), a comparative analysis was carried out between the use of medicines in pregnant women before and during pregnancy in municipalities in the interior of Bahia. Before pregnancy, it was found that more than half of pregnant women (52.1%, n = 567) used some medication. During the first trimester of pregnancy, it was found that 75.5% of pregnant women started using some medication and in subsequent trimesters these prevalences dropped to 44.1% and 6.4%. Knowing that the first trimester of pregnancy is the one with the highest risk of teratogenic effects, the prevalence of drug use in this period without proper knowledge is a serious problem.

According to another study carried out in a primary care environment with pregnant women in Ireland, Dillon et al, (2015) found that 46.8% (n = 1,104) of these used some medication during pregnancy, except for folic acid. Furthermore, it showed that according to the FDA pregnancy risk categories, excluding oral contraceptives, progestogens, and infertility treatments, category D drugs were prescribed in 4.7% (n = 110) and category X drugs in 3.1% (n = 72) of pregnancies. It was observed that after the initial prenatal consultation, prescriptions for drugs in these classes were reduced, but there is still room for further reduction, which is limited by the lack of data related to the effects of such drugs on pregnancy.

In a study in the Dutch population (DE WAARD et al., 2019) it was confirmed that about 95.5% of the participants also used medication during the gestational period. One-third of these used at least one drug with unknown risk to the fetus. Those considered to be teratogenic were used by 6.5% of the participants, while 29.5% used medication with a (suspected) pharmacological effect on the fetus. Among the most frequent are non-opioid analgesics, antacids and vitamins.

In another study (HENG et al., 2020), the effects on children were compared after the use of different antibiotics by mothers during pregnancy. It was observed that of these, Penicillins (69%) and macrolides (10%) were the most prescribed, with an average of 62% as single therapy during pregnancy. It was found that macrolide antibiotics have greater risks than penicillin and can generate cardiovascular malformations, if used in first quarters. Genital deformities at any time of pregnancy. And there are also assumptions about neurological changes.

In Italy between 2008-2012, Ventura et al (2018) found that excluding vitamins and minerals, 80.6% (n = 153,079) of women used at least one medication, with an average of 4.6 per pregnancy. Among these, the most commonly prescribed were those related to blood and hematopoietic organs (53.0%), followed by anti-infectives for systemic use (50.7%). As for those considered inadequate, progestogen supplementation was administered in 20.1% of pregnancies; teratogenic drugs were prescribed in 0.8%, especially those related to the treatment of heart failure. It was also possible to analyze that the fact of going through more than one delivery and the high level of education were significant protective aspects for all potential inappropriate and teratogenic prescriptions investigated.

There are few studies on the use of drugs in lactation. In the study carried out in maternity hospitals in Belo Horizonte (LAMOUNIER, 2002), a wide use of medication was observed in the immediate postpartum period, with most drugs being compatible with breastfeeding. However, in the study carried out in Denmark (OLESEN, 1999), a high exposure to drugs

with unknown or potentially harmful effects on neonates was observed (35.8% and 4.8%, respectively). The use of contraindicated drugs during lactation (about 10%) or with insufficient studies (about 50%) was also observed in the study carried out in the city of Londrina/PR (DALLA COSTA, 1999). In an American study by Stultz et al. (2007) showed that up to 96% of lactating women used some medication during breastfeeding. In addition, it also noted that more than a third of the drugs used were classified as possibly or probably unsafe or of unknown safety. Those frequently used are among analgesics, anesthetics, sedatives and antibiotics, and according to Verstergen, Ito (2019) for the use of such, one must analyze the potential risks of interrupting the medication, continuing the medication while interrupting breastfeeding and continuing breastfeeding.

In relation to the test with a portion of Dutch women, De Waard et al. (2019), lactation was initiated by 88.7% of participants, of which 84.2% used medication during breastfeeding. In a similar study in Australia, some of the mothers - afraid of harming the baby - either decided or were advised to stop breastfeeding, or stopped taking medication during this phase (HUSSAINY; DERMELE, 2011 apud DE WAARD et al., 2019). 3.8% of participants used unsafe teratogenic drugs even though they were aware of their possible risks.

METHOD

This is a descriptive, observational, quantitative, cross-sectional study that was carried out from August 2020 to July 2021, in health units in the central region of the Federal District health system, where pregnant and lactating patients who were followed up were interviewed. in Basic Health Units (UBS's). The sample was of convenience (n= 100), and all pregnant women/nursing mothers assisted during the study period in the chosen basic units and who agreed to participate in the surveys attended. The inclusion criteria for participants in the study are as follows: pregnant or breastfeeding women attended at basic health units in the central region of the Federal District who agree to participate in the study. Exclusion criteria were women who did not meet the inclusion criteria. The interviews were carried out in person using a questionnaire, structured and validated, at the UBS's, with 26 questions. The following were recorded: sociodemographic data (age, marital status, education and occupation); obstetric and contraceptive history; prenatal care data; data on medication use during pregnancy through symptom-oriented questions (name, indication for use, whether prescribed or not, trimester of pregnancy in which they were used, dose and duration of use).

Concomitant with data analysis, a survey was carried out of the drugs and corresponding pharmaceutical specialties prescribed with known risk classification in pregnancy and lactation, based on the list published by the FDA, which orders them into five risk categories (Tables 1), and updated by Briggs (1998). The participants were informed about the study's objectives, procedures, possible risks, as well as the benefits of the study, and were included in the experimental procedures after signing the Free and Informed Consent Form (TCLE). The study was approved by the Ethics Committee of UniCEUB, and the Health Department of the Federal District in accordance with Resolution nº 466/12 of the National Health Council. The data obtained were calculated and tabulated using Microsoft Office Excel.

RESULTS AND DISCUSSION

The use of drugs during pregnancy and lactation involves several risks, since most of them have the ability to cross the placenta, reaching the fetal circulation. Some of these

substances can also be passed to the infant through breastfeeding. Unfortunately, studies about these possible adverse effects are scarce, so it becomes difficult to prescribe correctly. When recommending any medication to this group of women, attention must be paid to the risk classification based on the *Food and Drug Administration – (FDA)*. The FDA has proposed a classification of drugs according to the risk associated with their use during pregnancy. This classification divides drugs into five categories (A, B, C, D and X) according to the danger they pose during pregnancy. Controlled studies have shown that category A drugs pose no risk to the fetus in the first trimester of pregnancy, there is no evidence of risk in later trimesters, and the possibility of fetal harm seems remote. With regard to drugs classified in B, there are no studies carried out with these drugs in pregnant women, however, animal studies have not shown fetal risk, but some of them have shown some adverse effect of animal reproduction on the fetus (other than a decrease in fertility), however, not confirmed in controlled studies in women during the first trimester and without evidence of risk in later trimesters. In category C, studies in animals have shown adverse effects on the fetus such as teratogenicity, fetal death or other, but there are no controlled studies available in women, thus these drugs must only be administered if the benefit justifies the potential risk to the fetus. In category D, there is positive evidence of human fetal risk, but the benefits of use in pregnant women may justify the use despite the risk, for example, if the drug is needed in a life-threatening situation for a serious illness, to which safer agents cannot be used or are not effective. Finally, in category X, studies in animals and humans have demonstrated fetal anomalies, evidence of fetal risk based on human experience, or both. The risk of using the drug in pregnant women in this case is clearly above the possible benefit. The drug is contraindicated in women who are or may become pregnant. Therefore, another important factor to be analyzed is the issue of self-medication, which despite good rates of guidance and correct prescriptions regarding drugs, many women still practice it.

In this study, a questionnaire was applied to pregnant women (66%) and lactating women (34%) aged 15 to 42 years, in which the majority had completed high school and paid work with an average family income of 2 minimum wages. Of these volunteers, 44% are married, 31% are single and 25% are in a stable relationship. Regarding prenatal care, 91% of pregnant women started in the first trimester, and the vast majority were advised on the use of medication during this period. These results show the effective participation of health professionals in providing guidance on the risks of self-medication during pregnancy, with greater medical participation. All women in the study received some medical prescription, including folic acid, ferrous sulfate and multivitamins. On the other hand, 22% of them performed self-medication, which is worrying, since there are medications that pose risks to the fetus, infant and even the mother. Such results are similar to the studies by Mengue et al. (2001); Fonseca et al. (2002); Carmo; Nitrini, 2004; Osorio-de-Castro et al. (2004) pointed to a high prevalence of use of at least one medication during pregnancy, which ranged from 82.9% to 97.6%. Likewise, studies have shown an average of 2 to 4 drugs per pregnant woman and a significant percentage of women reporting drug use without medical indication (22% to 35.5%) and a worrying use of prescribed drugs with little information about the risks in pregnancy.

Both in the current study and Irvine et al (2010) it was found that the use of potentially dangerous drugs was used appropriately and cautiously, aiming at the risk-benefit ratio,

although many drugs still do not have enough studies directed at these groups.

The first quarter had the highest rates of drug use, as well as in the study by Costa, Coelho and Santos (2017) whose this period also had the highest rate (75.5%) of drug use. medicines, followed by 44.1% and 6.4% in the second and third quarters.

In the current study, it was pointed out that the most used drugs during pregnancy were: ferrous sulfate (81%), paracetamol (30%), scopolamine bromide (10%), dimenhydrinate (7%), methyldopa (4%), dipyrone (3 %) and nystatin (1%), anti-inflammatories (7%). Like Verstergen, Ito (2019) and De Waard et al (2019) also found that analgesics, antibiotics and vitamins were the most frequently used drugs. As for antibiotics, there was a 17% prescription rate. In addition to prescribed medications, it was possible to identify self-medication of the following therapeutic classes: analgesics, antiemetics and antipyretics, so that 22% of pregnant women used medications without the necessary instructions and that could expose the fetus to risks.

Regarding the classification of drugs (Table 1), the multivitamin and mineral supplements Folic Acid, ferrous sulfate and magnesium hydroxide fall into the class of antianemics, framed in risk category A. These drugs play an important role during the first weeks of pregnancy, because it is a prophylactic procedure against neural tube defects and helps to form white and red blood cells, not presenting contraindications during pregnancy (FUCHS, 2010). At least one of these was used by all women in the current study. Along with this class is also the antifungal Nystatin B.

In risk category B, there are the antiemetic Dimenhydrinate (Dramin B6), the analgesic Paracetamol, the non-steroidal anti-inflammatory drug Ibuprofen, the antispasmodic N-Butylscopolamine bromide with Paracetamol (BuscoDuo) and N-Butylscopolamine bromide (Buscopan). In addition to these, antihistamines such as Loratadine, the H2 receptor antagonist Ranitidine, the antiflatulent Dimethicone and the antifibrinolytic Tranexamic Acid are also in this class. Studies with drugs from this group are still being carried out to clarify their adverse effects in humans, but those that already exist have not shown confirmed fetal risk. Therefore, the drug must only be used in patients when other safer alternatives are not available.

The antibiotics used by the women in the current study were: Amoxicillin, Azithromycin, Benzylpenicillin Benzathine (Benzetacil), Cephalexin, Nitrofurantoin (Macrodantin), which are also considered in group B, in which care must be taken when prescribing and must only be used in patients when other safer alternatives are not available. Regarding the type C classification, there is no research in pregnant women or even in animals, therefore the drugs in this group are of judicious risk, that is, they can lead to teratogenic or toxic effects. The antifungal Miconazole, the antiemetics Dimenhydrinate (Dramin B6), Ondansetron Hydrochloride (Vonau) and Metoclopramide Hydrochloride (Plasil), the antipyretic Dipyrone, the anticoagulant Enoxaparin sodium, the oral hypoglycemic agent Metformin Hydrochloride, the antimicrobial Tinidazole, the antihypertensive Methyldopa, antiseptic, hemostatic, anti-hemorrhoidal (Polycresulen, Cinchocaine Hydrochloride (Proctyl), antiparasitic Ivermectin, antacid Aluminum Hydroxide and antiviral Oseltamivir Phosphate fall into this group. usual, it is contraindicated during pregnancy (BRASIL, 2010).

Antidepressants (Sertraline and Fluoxetine) and the steroidal anti-inflammatory

Therapeutic Class	Active principle	Risk rating
Supplements, Multivitamins and Minerals	Folic acid, Ferrous Sulfate, Multivitamin and Mineral (Materna, Suplevit, Natele and Damater),	A
Antifungal	Nystatin B, Miconazole	A/ C
Antiemetic	Dimenhydrinate (Dramin B6), Ondansetron Hydrochloride (Vonau) and Metoclopramide Hydrochloride (Plasil)	B/ C
Analgesic and Antipyretic	Paracetamol and dipyrone*	B/ C * must not be used during pregnancy
Non-steroidal anti-inflammatory	Ibuprofen, Acetylsalicylic Acid (ASA)	B (D if used in the 3rd quarter)/ D
Steroidal anti-inflammatory	Dexamethasone	C (D if used in the 1st half of pregnancy)
Antispasmodic and analgesic	N-Butylscopolamine Bromide and Acetaminophen (BuscoDuo) Antispasmodic N-Butylscopolamine Bromide (Buscopan)	B
H2 receptor antagonist	Ranitidine	B
Antibiotic	Amoxicillin, Azithromycin, Benzylpenicillin Benzathine (Benzetacil), Cephalexin, Nitrofurantoin (Macrodantin)	B
Anticoagulant	Sodium Enoxaparin	C
Oral hypoglycemic	Metformin Hydrochloride	C
Proton Pump Inhibitor	Pantoprazole (Pantozol)	D
Antimicrobial	Tinidazole	C
Antihypertensive	Methyldopa	C
Antihistamine	Loratadine	B
Sex hormone	Progesterone (Utrogestan)	D
Hormonal contraceptive	Drospirenone + Ethinylestradiol/(Yasmin), Estradiol Enanthate+Algestone Acetophenide (Perlutan)	X
Antiseptic, hemostatic, anti-hemorrhoidal	Polycresulen, Cinchocaine Hydrochloride (Proctyl)	C
Antidepressants	Sertraline, fluoxetine	C (D if used in the 2nd half of pregnancy)
Antiparasitic	Ivermectin	C
Anxiolytic	Clonazepam	D
Antiacid	Aluminum Hydroxide + Magnesium Hydroxide	C / A
Antiflatulent	Dimethicone (luftal)	B
Antifibrinolytic	Tranexamic Acid (transamine)	B
Antiviral	Oseltamivir phosphate (tamifllu)	C

Table 1. Relationship by risk classification of prescription drugs.

Classification legend according to the American FDA classification: A - No evidence of risk, B - There are still no adequate studies in women, animal studies have not shown risk, C - Animal studies have shown some adverse effects on the fetus, D - Studies reveal evidence of risk in humans, used only if the potential benefit justifies the potential risk, X – Studies prove that there are fetal abnormalities or evidence of risk for the same. Do not use under any circumstances, as the risks outweigh the potential benefits

Dexamethasone are also classified as risk C, and the former, if used during the second half of pregnancy, become risk D, while dexamethasone, if used in the first half, also becomes risk D. - if you are part of this group. With regard to antidepressants, the study by Costa, Reis and Coelho (2010) concluded that they are not related to an increased risk of malformations in the fetus or risks when used during breastfeeding.

As for category D, the drugs showed signs of teratogenic risk, however, the potential benefits for the mother may outweigh the possible consequences, for example, in cases of life-threatening illnesses, and for which there are no other safer drugs; and in the current study, the proton pump inhibitor (Pantoprazole), the sex hormone progesterone (Ultrogestan) and the anxiolytic Clonazepan were used by the volunteers, all grouped in this class (BRASIL, 2010).

In risk category X, we found two lactating women who used hormonal contraceptives - Drospirenone + Ethinylestradiol (Yasmin) and Estradiol Enanthate + Algestone Acetophenide (Perlutan) - in which studies prove that if used during pregnancy there are chances of fetal abnormalities and there are also strong contraindications during the breastfeeding period. (BRASIL, 2010)

The research shows good results in relation to the risk classification, but we emphasize that this study has limitations, since in the interviews some pregnant women had difficulty in informing the name of the medication used.

FINAL CONSIDERATIONS

Based on the research carried out and the results found regarding the prevalence of medication use during pregnancy and lactation and its risks, it was possible to verify that the inappropriate use of these is of great risk to the fetus, and may lead to teratogenic effects. Due to the scarcity of studies with this group, those responsible for prescribing drugs must be aware of the risks, especially in the first trimester of pregnancy, since it is in this phase that neurological development occurs and makes the fetus more susceptible to complications. In addition, there is also the danger of passing toxic substances to the infant through breast milk, which may trigger problems in its development.

Therefore, it is extremely important for health professionals to update themselves on the possible risks, according to the FDA table, so that they can conscientiously make prescriptions, warn women about the dangers of self-medication and inform them of the possible adverse effects both for them, as well as for the fetus and for the child.

Thus, it is important that Health Units carry out campaigns to expand the community's knowledge about the dangers of self-medication during this period, in addition to encouraging health professionals to seek information, contributing to the reduction of inappropriate prescriptions. Thus, it is hoped that more research will be carried out with this group, since it is an area little explored in order to obtain greater insight on the subject.

REFERENCES

ALLONE, GJ. **Gravidez e Medicamentos.** In: Psiqweb. [S. l.], 2002. Revisado em 2011. Disponível em: <http://www.psiqweb.med.br/site/?area=NO/LerNoticia&idNoticia=140>. Acessoem 8 mai 2020.

BRASIL. Ministério da Saúde. **Secretaria de Ciência, Tecnologia e Insumos Estratégicos. Departamento de Assistência Farmacêutica e Insumos Estratégicos.** Formulário terapêutico nacional 2010: Rename 2010. 2. ed.Brasília, 2010. 1135 p., il. (Série B. Textos Básicos de Saúde).

CAMPBELL, S.C. et al. **Calls to a teratogen information service regarding potential exposures in pregnancy and breastfeeding.** BMC Pharmacology and Toxicology, [s. l.], 2016. DOI:10.1186/s40360-016-0076-7. Disponível em: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4958285/>. Acesso em 8 mai 2020.

CARMO, T.A.; NITRINI, S.M.O. **Prescrições de medicamentos para gestantes: um estudo farmacoepidemiológico.** Cad. Saúde Pública, v.20, n.4,p.1004-1013, 2004. Disponível em: <http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0102- 311X2004000400015&lng=en&nrm=iso> . Acesso em: 13 Mai 2020.http://dx.doi.org/10.1590/S0102-311X2004000400015.

CHAVES, R.G.; LAMOUNIER, J.A.; CÉSAR, C.C. **Medicamentos e amamentação: atualização e revisão aplicadas à clínica materno-infantil.** Rev. paul. pediatr., São Paulo, v. 25, n. 3, p. 276-288, Sept. 2007 . Disponível em: <http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0103- 05822007000300014&lng=en&nrm=iso> . Acesso em: 8 mai 2020. https://doi.org/10.1590/S0103-05822007000300014.

COSTA, Cassilda; REIS, Constança; COELHO, Rui. **Uso de psicofármacos nagravidez. Use of psychotropic drugs during pregnancy.** Acta Obstet GinecolPort, 2010C.

DALLA COSTA, E.M. **Perfil de Utilização de Medicamentos por Lactentes do Município de Londrina. Contribuição ao Estudo de Utilização de Medicamentos.** Dissertação de Mestrado. Centro de Ciências da Saúde. Universidade Estadual de Londrina. 1999.

DE WAARD, M et al. **Medication Use During Pregnancy and Lactation in a Dutch Population.** J Hum Lact. 2019 Feb;35(1):154-164. DOI: 10.1177/0890334418775630. Epub 2018 Jul 3, p. 154-164. 3 jul. 2018. Disponível em: <https://journals.sagepub.com/doi/10.1177/0890334418775630> . Acesso em: 10 mai 2020.

DILLON, P. et al. **Prevalence of prescribing in pregnancy using the Irish primary care research network: a pilot study.** BMC Pregnancy and Childbirth,Irlanda, 2015. DOI 10.1186/s12884-015-0489-0. Disponível em: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4389301/>. Acesso em: 10 mai2020.

FDA (FOOD AND DRUG ADMINISTRATION). **Center for Drug Evaluation andResearch (CDER)/ Center for Biologics Evaluation and Research (CBER).** Reviewer Guidance. Evaluation of Human Pregnancy Outcome Data (DraftGuidance),1999

FDA (FOOD AND DRUG ADMINISTRATION). **Center for Drug Evaluation andResearch (CDER). Reproductive Health Drugs, Pregnancy Labeling Subcommittee Meeting.** March 28-29, 2000a.

FUCHS, F.D.; WANNMACHER, L. **Farmacologia Clínica.** Fundamentos da Terapêutica Racional. 4. ed. Porto Alegre: Guanabara Koogan, 2010

HENG Fan et al. **Associations between macrolide antibiotics prescribing during pregnancy and adverse child outcomes in the UK: population basedcohort study.** BMJ 2020; 368 doi: https://doi.org/10.1136/bmj.m331. Disponívelem: <https://www.bmj.com/content/368/bmj.m331>. Acesso em: 11 mai 2020.

HUSSAINY, S. Y., & DERMELE, N. (2011). **Knowledge, attitudes and practices of health professionals and women towards medication use in breastfeeding: A review.** International Breastfeeding Journal, 6, 11. doi:10.1186/1746-4358-6-11. Disponível em: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3180355/>. Acesso em: 11 mai2020.

IRVINE, L et al. **Drugs Dispensed in Primary Care During Pregnancy: A Record-Linkage Analysis in Tayside.** Scotland. Drug Safety, Scotland, 2010. DOI 10.2165/11532330-000000000-00000. Disponível em: <https://link.springer.com/article/10.2165/11532330-000000000-00000>. Acesso em: 10 mai 2020

KASSADA, D.S. et al. **Prevalence and factors associated with drug use in pregnant women assisted in primary care.** Texto & Contexto - Enfermagem, Florianópolis, v. 24, ed. 3, 25 ago. 2015. DOI 10.1590/0104-07072015002770013. Disponível em: https://www.scielo.br/scielo.php?script=sci_arttext&pid=S0104-07072015000300713&lng=en&nrm=iso. Acesso em: 6 maio 2020.

LAMOUNIER, Joel A. et al . **O uso de medicamentos em puérpuras interferenas recomendações quanto ao aleitamento materno?.** J. Pediatr. (Rio J.), Porto Alegre, v. 78, n. 1, p. 57-61, Feb. 2002 . Disponível em: <http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0021- 75572002000100012&lng=en&nrm=iso>. Acesso em: 13 May 2020.http://dx.doi.org/10.1590/S0021-75572002000100012.

MENGUE, Sotero S et al . **Uso de medicamentos por gestantes em seis cidades brasileiras.** Rev. Saúde Pública, São Paulo, v. 35, n. 5, p. 415-420, Oct. 2001 . Disponível em: <http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0034- 89102001000500002&lng=en&nrm=iso>. Acesso em: 10 mai 2020.
http://dx.doi.org/10.1590/S0034-89102001000500002

MINISTÉRIO DA SAÚDE. Secretaria de Políticas de Saúde. **Área Técnica de Saúde da Criança. Amamentação e uso de drogas.** Brasília, DF, 2000.

OLESEN, C.; et al. **Prescribing during pregnancy and lactation with reference to the Swedish classification system. A population-based study among Danish women.** The Euromap Group. Acta Obstet Gynecol Scand, v.78,n.8, p.686-92, 1999. Disponível em: <https://obgyn.onlinelibrary.wiley.com/doi/epdf/10.1034/j.1600-0412.1999.780805.x>. Acesso em: 9 mai 2020.

OSORIO-DE-CASTRO, C.G.S. et al. **Uso indicado e uso referido de medicamentos durante a gravidez.** Cad. Saúde Pública, Rio de Janeiro, v. 20, supl. 1, p. S73-S82, 2004 . Disponível em: <http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0102- 311X2004000700008&lng=en&nrm=iso>. Acesso em: 10 mai 2020.https://doi.org/10.1590/S0102-311X2004000700008.

STULTZ, E.E et al. **Extent of Medication Use in Breastfeeding Women.** Breastfeeding Medicine, Hershey, Pennsylvania, v. 2, ed. 3, set 2007. 145-151. Disponível em: <https://www.liebertpub.com/doi/abs/10.1089/bfm.2007.0010> Acesso em: 9 mai 2020. http://doi.org/10.1089/bfm.2007.0010

VENTURA, M et al. **Drug prescribing during pregnancy in a central region of Italy,** 2008-2012. BMC Public Health 18, 623 (2018). https://doi.org/10.1186/s12889-018-5545-z. Disponível em: <https://bmcpublichealth.biomedcentral.com/articles/10.1186/s12889-018-5545-z#Abs1>. Acesso em 12 mai 2020.

VERSTEGEN, R.H.J; ITO, S. **Drugs in lactation**. The Journal of Obstetrics andGynaecology Research, Toronto, Canadá, 2019. DOI 10.1111/jog.13899. Disponível em: <https://obgyn.onlinelibrary.wiley.com/doi/abs/10.1111/jog.13899>. Acesso em: 7 mai 2020.

WHO (WORLD HEALTH ORGANIZATION). **Department of Child and Adolescent Health and Development. Breastfeeding and Maternal Medication.** Geneva, 2002. Recommendations for Drugs in the Eleventh WHOModel List of Essential Drugs.