

Cosmetics containing endocrine disruptors and pregnancy: health professionals' perception of risk

Cosméticos com presença de disruptores endócrinos e gestação: percepção de risco pelos profissionais de saúde

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ABSTRACT

Objective: to understand the perception of Primary Health Care health professionals regarding the risks associated with the use of cosmetics containing endocrine disruptors during pregnancy. Methods: this was a qualitative study. The participants were 17 health professionals who visited pregnant women in Primary Health Care. Data was collected through semi-structured interviews. The interviews were analyzed using Content Analysis and theoretical references from researchers in the field. Results: the majority of participants had little knowledge of the concept of endocrine disruptors, reported little confidence in recommending or not recommending the use of cosmetics and personal hygiene products, and also showed little knowledge of the risks they may pose to health. Conclusion: health professionals have shown that their knowledge of the risks of endocrine disruptors present in cosmetics is fragile and, consequently, they find it difficult to guide pregnant women to reduce harmful exposure. Contributions to practice: raising awareness among professionals of the need for constant updating to provide safe advice to pregnant women.

Descriptors: Pregnancy; Cosmetics; Endocrine Disruptors; Health Personnel.

RESUMO

Objetivo: conhecer a percepção dos profissionais de saúde da Atenção Primária à Saúde quanto aos riscos associados ao uso de cosméticos que contêm disruptores endócrinos durante a gestação. Métodos: trata-se de um estudo qualitativo. Os participantes foram 17 profissionais de saúde que fazem consultas às gestantes na Atenção Primária à Saúde. A coleta de dados ocorreu por meio de entrevista semiestruturada. Para a análise das entrevistas, contou-se com a Análise de Conteúdo, e com referenciais teóricos de pesquisadores da área. Resultados: observou-se que há pouco conhecimento da maioria dos participantes sobre o conceito de disruptores endócrinos, os quais relataram pouca segurança para recomendarem, ou não, sobre o uso de cosméticos e produtos de higiene pessoal e, ainda, poucos demonstraram conhecer os riscos que possam apresentar à saúde. Conclusão: os profissionais de saúde mostraram que há uma fragilidade quanto ao seu conhecimento sobre os riscos dos disruptores endócrinos presentes nos cosméticos, e, consequentemente, encontram dificuldades para orientar as gestantes a reduzirem as exposições prejudiciais. Contribuições para a prática: sensibilização dos profissionais para a necessidade constante de atualizações para prestarem aconselhamento com segurança às gestantes.

Descritores: Gravidez; Cosméticos; Disruptores Endócrinos; Pessoal de Saúde.

Introduction

Endocrine disruptors are exogenous chemical substances or mixtures of chemical substances that interfere with normal hormonal and reproductive function, alter the direction of the endocrine system, and can negatively affect the health of an intact organism, its offspring, or (sub)populations⁽¹⁾, and have transgenerational effects⁽²⁾.

There are a variety of chemical substances, such as phthalates, bisphenol A, parabens, triclosan, dioxane, organic solvents, pigments, formaldehyde, and heavy metals, which are believed to act as endocrine disruptors⁽³⁾, and which can be found in cosmetic products⁽⁴⁾. These preparations are made up of natural or synthetic substances used externally on various parts of the human body⁽⁵⁾ and are part of women's daily routines. A recent study revealed that 60-80% of pregnant women use these products⁽⁴⁾.

The gestational period is marked by physiological changes at the endocrine, metabolic, immunological, and vascular levels, which are responsible for the manifestation of multiple alterations to the skin and its appendages which, although they pose no risk to the mother/baby binomial, can be aesthetically significant and compromise the biological, psychoemotional and social dimensions of the pregnant woman⁽⁶⁾. These changes lead many pregnant women to use cosmetics. And the endocrine disruptors present can be transferred from pregnant women to the developing fetus via the placenta⁽²⁻³⁾. Exposure can also occur through skin absorption or ingestion and can be detected in urine⁽⁷⁾, breast milk, and amniotic fluid⁽³⁾.

Pregnant women are a particularly vulnerable group to the potential risks of endocrine disruptors contained in cosmetics, as they are in a critical period for fetal development due to their immature metabolism⁽³⁾. Exposure to the known harmful effects of endocrine disruptors in cosmetic products during fetal development may be related to adverse outcomes that cosmetics users are unaware of⁽³⁻⁴⁾. Although exposure is associated with many harmful consequences, they are rarely reported by health professionals in clinical practice, especially concerning pregnant women⁽⁸⁾.

There is little knowledge about which cosmetic products can or cannot be used during pregnancy without risk. Furthermore, health professionals reported difficulty finding this information in the literature⁽⁹⁾. In addition, no studies in the Brazilian literature have assessed the perception of risk from the point of view of health professionals. Most of the studies found in the scientific literature focus on the perception of pregnant women⁽¹⁰⁾ and mothers⁽¹¹⁾. It is understood that the knowledge transmitted by health professionals can modify attitudes and behaviors, constituting a strategy for preventing the exposure of pregnant women to endocrine disruptors⁽⁹⁾.

This led to the following question: How do health professionals advise women about the use of cosmetics containing endocrine disruptors during pregnancy?. Despite knowledge about vulnerabilities during pregnancy, health professionals provide a lot of guidance to pregnant women, but rarely about cosmetics and exposure to endocrine disruptors. This study aimed to understand the perception of Primary Health Care health professionals regarding the risks associated with the use of cosmetics containing endocrine disruptors during pregnancy.

Methods

This was a qualitative study that followed the guidelines of the Consolidated Criteria for Reporting Qualitative Research (COREQ).

The study took place in the Primary Health Care (PHC) services that monitor pregnant women during prenatal care, in a city in the Zona da Mata Mineira. This municipality has approximately 500,000 inhabitants, 75.15% of whom are covered by Primary Care and 60.04% by the Family Health Strategy (FHS)⁽¹²⁾.

The participants were 17 health professionals, including eight nurses, eight doctors, and one dental surgeon, who worked with pregnant women and were selected for convenience. The inclusion criteria for the participants were professionals who provide care to pregnant women linked to the FHS, with at least 12 months of experience in the area, and who expressed a desire to take part in the research voluntarily. Only health professionals from a Basic Health Unit (BHU) contacted did not take part in the study, as they were not allowing research to be carried out in that unit at the moment.

Before data collection, the interviewers were trained to avoid information bias, as well as a pilot study with three obstetric nurses who work in the municipality's health network (who were not included in the study's analysis), to standardize the research procedures. The interviews were conducted by two undergraduate nursing researchers who were able to guarantee scientific rigor.

The individual interview was structured around questions to characterize the participants (age, gender, color, education, profession, and length of professional experience), and open-ended questions related to the object of the study. Nine main questions were addressed to the participants, as a way of finding out the professionals' perception of their approach during clinical practice to the use of cosmetics or personal hygiene products with the presence of disruptors in pregnancy, perception of risk, and the difficulties faced in providing advice in this area.

After approval, the managers of the municipality's BHUs were contacted to inform them about the study, schedule the visit, and ask the professionals to take part. On the day of the interview, the research participants were approached at their place of work in a private room. After being explained the objectives of the research, both orally and in writing, they consented to take part in the study by signing the Informed Consent Form. There was no prior relationship between the participants and the researchers.

Data collection took place on the premises of five BHUs, chosen for convenience, between August and September 2023. To achieve the study's objectives, semi-structured face-to-face interviews were used, which lasted between 15 and 30 minutes (average 20 minutes). After verbal authorization from the participants to record the audio, the interviews were recorded for later transcription, which was carried out by the main researcher immediately after the interviews, and the recordings were permanently deleted after transcription to preserve the confidentiality and anonymity of the participants. There was no validation of the interviews by the participants after transcription.

The decision to stop recruiting new participants and end data collection was based on the criterion of sufficiency, understood as the stage in the development of the research in which the data begins to repeat itself, and this set of data makes it possible to answer the research problem outlined for the study. Saturation was reached in interview 15 when the data obtained showed redundancy or repetition, but two more interviews were carried out to confirm saturation. Data collection ended with 17 interviews. There was no need to repeat any interviews.

The participants were identified by code according to their professional category, with doctors identified by MED, nurses by NUR, and dentists by DEN, accompanied by a number from 1 to 17, listed in ascending order of data collection according to professional category.

The data was analyzed using Content Analysis technique, in the following stages: 1) pre-analysis; 2) exploration of the material; 3) treatment of the results and interpretation⁽¹³⁾. In the first stage, the interview data was read and organized. In the second stage, the data was coded using the recording units. In the last stage, the statements were categorized according to their similarities and by differentiation, with subsequent regrouping according to common characteristics. Five thematic categories emerged, which were discussed according to the theoretical references of researchers in the field.

The study was conducted following the rules for research involving human beings in Resolution 466/2012 of the National Health Council, following approval opinion 6.141.027/2023 and Certificate of Submission for Ethical Appraisal 69872323.0.0000.5147 of the Research Ethics Committee of the Federal University of Juiz de Fora.

Results

The health professionals who took part in the study were aged between 33 and 63; 13 of them were female and 4 were male. The majority were white (n=13), with professional experience ranging from one to over 35 years. All the interviewees had experience of prenatal care, and one of them had experience of prenatal dental care specifically. Concerning academic qualifications, one participant had only completed higher education, 14 had specializations, most of them in family health, one had a master's degree and one had a doctorate.

Data analysis identified five thematic categories related to the use of cosmetics during pregnancy: guidance from health professionals; perception of risk regarding the use of cosmetics and their ingredients for pregnancy and fetal development; trust in professional advice; tools used by health professionals to obtain information, and professional training and knowledge.

Guidance for health professionals

In this category of analysis, the health professionals reported on the moments when they gave advice and guidance to pregnant women on the use of cosmetics and personal hygiene products, as well as which types of products they recommended most. It was observed that, in general, the professionals only advised pregnant women when they asked about the subject during consultations, and that it was not routine for most of the professionals interviewed: *Usually when they ask, it's not routine* (MED01). *No, I just clarify any doubts. When they have questions about a certain type of product and I advise them which products they can't use* (NUR04).

The professionals were asked about the pro-

ducts they recommended most during their visits. Among the most recommended were repellents, sunscreens, oils, and moisturizers. They warned against hair dye, make-up, fluoride-free toothpaste, and unproven aesthetic procedures: I think the most I may have talked about in some situations is hair dye, bleaching the hair, but the rest of the cosmetics themselves, moisturizer, sunscreen, makeup, I never bothered to ask. Moisturizing oil throughout pregnancy, I usually recommend it at the first appointment, and at subsequent ones, to moisturize the skin (NUR03). During pregnancy we don't recommend dye, if you have to use it, if the woman insists too much that it affects her self-esteem, we recommend something more natural. Toothpaste, right? Because many women get sick, right? And then they usually complain a lot about fluoride, and I think, a lot of them vomit, so sometimes we even advise them to try fluoride-free toothpaste, to see if it improves the craving, to avoid the nausea (DEN01).

As a result, many reports stated that, due to the reality of the population they were seeing, often from a lower socioeconomic class in primary care, they didn't attribute brands to the recommended products, advising pregnant women to buy according to their financial situation: *Sunflower oil from the simplest brand you can find* (NUR01). *Look, I don't really look at the brand, ok? Because of the cost, because I work with a poor population, sometimes you can't afford a specific cream for pregnant women, so you don't analyze the brand, you see what's possible within their reality (MED04). In the case of repellents, yes, because repellents are cost-effective, so although some substances aren't very good, parabens and so on, but they're in everything, right? It's in shampoo, it's in a lot of things. I try to leave only the basics up to her because there's no way we can specify (MED05).*

Risk perception regarding the use of cosmetics and their ingredients for pregnancy and fetal development

The interviewees were unaware of the possible complications in pregnancy caused by the endocrine disruptors present in cosmetics. Some mentioned products that could be harmful, although they had not experienced any negative outcomes: *No, I haven't had any experience against the use of any cosmetics* (MED01). *I don't think so,* I've never seen it (NUR01). I've never heard of it, I've heard of it in the general population, right? The issue with nail polish, these hair dves that have a lot of heavy metals, right? This can really alter certain dosages in the blood. But when it comes to pregnant women and the fetus' health, I don't have any guidance or knowledge of what it could cause (NUR02). I imagine that they may even cause some hormonal alteration, some hormonal imbalance, and everything, which could bring some risk to the fetus' development. Sometimes it can even cause some kind of formation, some kind of growth disorder, some kind of growth restriction, or something along those lines (MED07). About the use of dye, in these products, especially during the embryonic period, we avoid any component that isn't indicated, right? Straightening the hair, then those hair sealing products I also advise now that I've remembered, I advise not to use it, because it's a chemical product, right? And dye, these hair straightening products, are strong so as not to be harmful to the baby's development (NUR07).

Trust in professional advice

The majority of those interviewed did not feel able to provide safe advice on this subject and linked this to the fact that they were not prepared during their academic career on the subject and because it is often not a demand that pregnant women bring to professionals during consultations. Other professionals, even though they showed little knowledge of the subject, said they felt comfortable talking about it with the knowledge they already had: No, because I think there's little study, little research, and little training for professionals (NUR04). Not that comfortable, because I've never had any training within the Unified Health System for this, everything I've looked for has been out of personal interest, and curiosity, right? So, I think there really is a lack of specific training, since we do prenatal care, for us to be able to do this safely because not all doctors are going to pursue this, right? (MED04). Yes, because I research, read, and study (MED06).

Tools used by health professionals to obtain information

When asked which tools they used and whether they had difficulty finding information on the use of cosmetics and personal hygiene products and pregnancy, most professionals reported looking for information online, in articles, in books, and consulting other health professionals: *First 1 look for scientific articles, but not everything can be found in databases, so sometimes 1 discuss it with a colleague who has more experience in the area* (MED01). *I have a bit of difficulty. And some 1 like to look up in the Brazilian Society of Dermatology* (MED02). *Generally, we look for sources to find out if there is any research that has already been released or not, we look in the manufacturers' leaflets to see if there is any release or not* (NUR04). *We refer to the specialist, the dermatologist* (MED03). *So, for this information on the components of repellent, that's up to the Health Department. With regard to hair dye, I've already looked it up at the National Health Surveillance Agency* (*ANVISA*). *Scientific articles too, but ANVISA is also a very safe body for us* (NUR07).

The participants also stated that they had difficulty finding information about cosmetics that can be used during pregnancy or that they had never researched the subject: *It's hard to find, that's why we often don't recommend using it when we can't find anything that indicates it or that contraindicates it* (NUR04). *I don't know if there's a website that's a reference for these consultations, you know? But I had a lot of difficulty finding out about the dye, there was something else that I even sent to ANVISA, asking about the component, so I always look into it, right? To check which one is indicated and which one isn't so as not to do any harm* (NUR07).

Training and professional knowledge

All the health professionals interviewed reported that, during their academic career they did not have professional training to advise on the use of cosmetics during pregnancy: *None, only in relation to the repellent that we recommend, because there are studies that prove its safety and benefit, right? So that's it* (MED01). *No. I didn't have any academic training. I did a course in aesthetics on the side, which gave me some knowledge in the area, but not in my traditional training* (MED04). *No, not this very specific thing. Even in the Women's Health and FHS postgraduate courses, it's not covered* (NUR08).

They then reflected on the need for some kind of specific training to provide such advice during their work, which represented divided opinions. The majority of which said it was important to delve deeper into the subject: *I think it's important, because more and more women* are concerned with aesthetics, with using cosmetics, more concerned with aesthetics, above all, and I think we have little information about this in our academic training (MED01). Always, not just for counseling, but always for training and updating, it's extremely important for professionals, isn't it? Sometimes we're limited in the personal field, in terms of seeking this updating individually, but I think that updating courses should be offered frequently and always. The ideal would be continuing education on the subject, wouldn't it? (NUR02).

In terms of knowledge, almost all the professionals reported not knowing about the term endocrine disruptor and having little habit of investigating the composition of cosmetics or personal care products: I don't usually look at the ingredients, I don't have that habit (MED01). No, I don't have time (NUR01). I don't look at the label of what I'm buying and perhaps what I'm going to recommend to others. I can see that there has been a movement towards more natural cosmetics, but I also don't know if it's just marketing or if it's just something to sell more. But I've never bothered myself or my patient to really investigate what kind of substance it is if it's teratogenic and what it's going to cause, I've never bothered (NUR02). Generally, I like to analyze the urea concentration present in moisturizers because it's important for pregnant women, I research some substances that can cause allergies, dyes, some parabens, which are present, possibly carcinogenic substances, which can even be present in sunscreen. Out of curiosity, for my own use and for the benefit of other people too, I have this habit, you know? (MED04).

Discussion

From the analysis of the categories, it was possible to identify that guidance from health professionals on the use of cosmetics during pregnancy is not routine for most of the professionals in this study. Similar data was found in a study of French health professionals, in which 57% of professionals (including obstetricians, general practitioners, and residents) reported that they do not provide information to pregnant women about endocrine disruptors. In this study, although the majority of professionals do not provide advice to pregnant women, 74% of the participants considered it important to raise awareness of the health risks associated with endocrine disruptors and 93% expressed the desire to be well-informed⁽¹⁴⁾.

Health professionals should be better prepared to inform pregnant women about the potential risks and safety of using cosmetics. In addition, according to the literature, this scarce knowledge about the risks of endocrine disruptors shows that public health programs should promote awareness campaigns and adequate training for professionals⁽¹⁵⁾.

Warning mothers about endocrine disruptor use is very important since recent research carried out in France showed that more than half of the women interviewed during pregnancy or after giving birth had never heard of the subject and had used harmful substances during pregnancy^(8,15). This scarce knowledge of the risks has been linked to the limited or even non-existent time that the professionals who accompany mothers during pregnancy devote to instructing them on the prevention of environmental risks⁽¹⁶⁾.

Regarding the risk perception of professionals about the use of cosmetics, there was little knowledge about the possible outcomes and complications that can occur during pregnancy and fetal development. However, although they reported not having experienced any adverse outcomes, some mentioned products which, in their view, could be endocrine disruptors and cause harm. And, despite the fragility of their knowledge about these disruptors, this study showed that some professionals also mentioned substances that in their perception are endocrine disruptors, such as parabens, dyes, heavy metals, and carcinogenic substances.

During pregnancy, exposure to these disruptors is a significant concern, as these substances can cross the placenta and affect the development of the fetus, causing adverse health impacts such as hormonal dysregulation, neurobehavioral effects and even lifelong health problems for the child⁽¹⁷⁻¹⁸⁾. The placenta plays an important role during pregnancy and acts as a protective barrier against external agents. However, it is not completely impermeable and allows the passage of some endocrine disruptors, such as bisphenol A and phthalates, which can reach the developing fetus, which is sensitive to external agents due to its enormous rate of cell differentiation, so small changes in hormone levels have a serious impact⁽¹⁹⁻²⁰⁾.

Consequently, negative pregnancy outcomes can occur, such as fetal growth restriction, low birth weight⁽¹⁴⁾, pre-eclampsia, gestational diabetes mellitus, impaired transport of nutrients to the fetus, prematurity and neonatal death⁽²¹⁾. In recent decades, there has been an increase in the prevalence of these complications, in which exposure to endocrine disruptors has also increased, highlighting a relationship between environmental exposure to these substances and the aforementioned outcomes^(20,22).

Perinatal health professionals considered the use of cosmetics to be a risk to the health of women and their unborn babies. Other health professionals and general practitioners perceived this risk more frequently than obstetricians. Also in this study, 20% of health professionals reported that women often asked about the use of cosmetics, however, the majority did not feel able to answer this question correctly⁽¹⁴⁾.

It is clear that cosmetics are a common source of exposure to these disruptors during pregnancy, and over the last few years, interest has been aroused by studies into the adverse effects and endocrine disruption that may be related to the ingredients found in the composition of personal care products^(4-5,15,23-24). However, regulations vary in different countries, which can affect the presence and quantity of these components in available products^(23,25). In Brazil, ANVISA is the body responsible for publishing the list of substances that cannot be used in personal care products, cosmetics, and perfumes.

Raising awareness about the labels and ingredients contained in personal care products and cosmetics is fundamental to avoiding unwanted exposure, and incorporating clear guidelines on the safety of cosmetics and minimizing exposure to endocrine disruptors into maternal health protocols can be beneficial⁽²⁶⁾. In Brazil, it is mandatory to describe the composition of personal care products, cosmetics, and perfumes in Portuguese, to regulate product labeling and make it easier for consumers to identify the ingredients.

The results of this study also draw attention to the professionals' reports of the difficulty they encounter in finding information in the scientific literature and official documents to guide the team on the use of cosmetics during pregnancy and point to the need to discuss this issue during academic training and with ongoing education in the service.

In this context, more than half of the doctors specializing in Dermatology and Gynaecology/Obstetrics face difficulties finding information in the literature on the use of cosmetic products in pregnancy, with no relevant difference between the two areas. There is also a lack of data proving the safety of these products, which creates challenges for prescribers when deciding what to recommend, with the Internet being the main source of information used by these professionals⁽²⁷⁾. This study also found that consultation with a professional colleague is a strategy often used by professionals.

Within nursing, this is still a little-studied topic. Nurses play a crucial role in informing pregnant women about the possible adverse effects of endocrine disruptors present in cosmetics, and in encouraging them to read product labels, choose safer alternatives, or even reduce their use of cosmetics during this period. In addition, these professionals need to keep up to date with the latest regulations and studies to be more active in the educational process, with care as the core of the profession⁽²⁸⁾.

There is indeed a shortage of information on endocrine disruptors in Brazil. The vast majority of articles and guidelines are in other languages and often don't reflect the reality of the Brazilian population. In an online search on the websites of the Brazilian Societies of Gynecology, Dermatology and Endocrinology and Metabology, only the latter provided some information and a guide: Introduction to endocrine disruptors: a guide for governments and public interest organizations, translated in 2019, but which does not answer the question of guidelines for pregnant women⁽²⁴⁾. In the search on official government websites and Ministry of Health manuals related to pregnancy, it was also not possible to find information on the subject during the gestational period.

Despite some conflicting results about the changes that endocrine disruptors impact on the gestation process and its future consequences, and although more data needs to be collected, reducing exposure to these chemicals is essential to prevent their possible harmful effects, both during pregnancy and for the child in the future⁽²⁹⁻³⁰⁾. In this sense, it is recommended that health professionals encourage pregnant women to restrict their use or not use cosmetics during pregnancy, as the risks they pose to the health of the pregnant woman and the fetus are not yet entirely clear. They need to advise on products that contain fewer ingredients or have a more natural formulation, intending to reduce excessive exposure to endocrine disruptors^(20,25).

In general, it can be said that further research is needed into the presence of endocrine disruptors in personal care products and cosmetics, as well as their safe use in pregnancy, to expand the scientific literature in this area. In addition, it is advisable to develop training programs that allow health professionals to be prepared, attentive, and comfortable to advise and guide pregnant women on the potential risks and safety of using personal care products and cosmetics during pregnancy, alerting them to the cosmetic care they should implement and avoid during this period. In addition, legislation and public health programs run by the government must offer awareness campaigns and adequate training for professionals working in prenatal care.

Study limitations

This study has some limitations that should be considered when interpreting the results. Firstly, the participants are from a specific population, PHC health professionals, which may limit the generalizability of the results to other populations. There was also a low level of participation from dental surgeons, due to the few professionals present in the municipality's PHC units. Furthermore, the difficulty in accessing upto-date scientific literature on the subject restricted the results found and limited the depth of the analysis in some aspects.

Contributions to practice

Given the innovative nature of the topic, this work contributes to the clinical practice of health professionals in a broad way, reaching from specialists in Obstetric and Neonatal Nursing to PHC nurses, dental surgeons, general practitioners, and specialists who daily provide differentiated care to individuals and their families in the context of prenatal care. In this sense, this study takes on the dimension of relevance in professional practice insofar as it raises awareness of the constant need to seek updates for professional practice, as well as scientific evidence on the subject, guaranteeing professionals the knowledge and safety to advise on the risks of exposure to these products.

This strengthens the bond between the professional, the pregnant woman, and the family, with direct repercussions on the qualification of prenatal care, which, by promoting an environment of trust and well-being through safe dialogue during counseling, enhances adherence to monitoring and care throughout the pregnancy-puerperal cycle, and also in early childhood care, thus reaffirming the role of the professionals targeted in this study in maternal and child health care.

Conclusion

Health professionals do not have enough information about the risks of endocrine disruptors in cosmetics for pregnant women. Almost all of the participants reported the difficulty of finding reliable information to support their clinical practice and draw attention to the need for an approach in academic training, and through training courses so that they can educate pregnant women about the adverse risks of

exposure to maternal and child health. This highlights the need for safe and accessible information to be produced and widely disseminated, promoting and facilitating access to these recommendations for health professionals and pregnant women. In particular, the scientific community has an important role in carrying out more studies and producing more evidence on which to base professional practice, to expaned current conclusions.

Authors' contribution

Conception and design or analysis and interpretation of data; Writing of the manuscript or relevant critical revision of the intellectual content: Souza LSR, Oliveira Neta AI, Emídio SCD, Paraiso AF. Final approval of the version to be published and agreement to be responsible for all aspects of the manuscript being adequately investigated and resolved: Souza LSR, Oliveira Neta AI, Gomes JS, Silva EA, Pacheco ZML, Emídio SCD, Paraiso AF.

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