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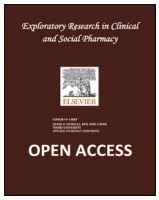

Polypharmacy and high-alert medications in patients with nasally placed feeding tube on admission and at hospital discharge: Multicenter cross-sectional study

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ABSTRACT

Background: Polypharmacy and the use of high-alert medications in patients with nasally placed feeding tube (NPFT) increase the risks of drug related problems.
Objective: Characterize drugs prescribed to patients with NPFT and compare the rates of polypharmacy and high-alert medication use at admission and hospital discharge.
Design and setting: Multicenter cross-sectional study with 327 participants.
Methods: Data of patients with NPFT were obtained from the medical records and recorded in an electronic data collection tool. Mean number of drugs, polypharmacy and number of high-alert medications prescribed on admission and at discharge were compared using Wilcoxon or McNemar's tests. Generalized Estimating Equations analyzed the relationship between polypharmacy and high-alert medications according to age and time point. Primary reason for hospital admission, level of consciousness, severity of comorbid diseases and patient care complexity were also assessed.
Results: Most patients were male, older people, hospitalized for circulatory system diseases and had at least one comorbidity. On admission, a significant number of patients were alert (59.9%), at high risk for death (43.1%) and high dependent on nursing care (35.4%). Additionally, 92% patients were on polypharmacy on admission, versus 84.7% at hospital discharge ($p = 0{,}0011$). The occurrence of polypharmacy was independent of age ($p = 0.2377$). >17% of all drugs prescribed were high-alert medications, with no statistically significant difference between admission and discharge ($p = 0{,}3957$). There was no statistical evidence that the use of high-alert medications increases with age ($n = 0{,}5426$).
Conclusions: These results support the planning of multidisciplinary qualified actions for patients using NPFT.

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1. Background

The use of short-term enteral access devices, such as nasally placed feeding tubes (NPFT), is expanding globally due to the increasing number of older people with Alzheimer's disease or other dementias, patients with poor swallowing reflexes, and nutritional status.[1]

Patients with NPFT often have multiple comorbidities and complex healthcare needs, requiring polypharmacy, defined as the concurrent use of five or more drugs, to manage their conditions.[2,3] Regardless of the benefits of appropriate polypharmacy, it has been associated with adverse drug events (ADEs), hospitalization, nursing home placement, fractures, impaired mobility, pneumonia, malnutrition, and death.[4] Furthermore, polypharmacy in patients with NPFT increases the risks of drug-drug interactions, drug-nutrient interactions, inappropriate dosage form selection, intoxication, tube occlusion, therapeutic failures, and extended hospitalization times and costs[5–7].

One in every 20 patients in a general hospital receives medications through NPFT.[8] The correct administration of drugs via NPFT is primarily a nursing duty and requires special skills, including preparing the medications (solid or liquid), flushing the tube, verifying tube position, and assessing the patient for potential complications and harm.[9,10]

While any drug can potentially cause harm to a patient,[11] high-alert medication bear a heightened risk of causing significant patient harm when used in error[12] and even when given correctly.[11] The risk associated with high-alert medications may be even greater when administered through NPFT. Studies aiming to identify ADEs associated with the administration of high-alert medications have detected one adverse event caused by a high-alert drug for every four patients, with a large proportion being preventable.[13]

Changes in drug regimens during hospitalization have been investigated to some degree[14] but a critical analysis of polypharmacy and high-alert medication rates in patients with NPFT on admission and at discharge has been barely examined. To the best of our knowledge, this is the first study reporting on polypharmacy and high-alert medication use in patients with NPFT on a large scale and at two different time points. This multicenter study aimed to characterize the drugs prescribed to patients with NPFT and to compare the rates of polypharmacy and high-alert medication use from admission to discharge.

2. Methods

2.1. Study design

This is a multicenter study with a cross-sectional design. It is part of a broader research program on feeding tube-related incidents.[15,16]

2.2. Settings

Six centers across Brazil participated in this study, including a mix of community and university hospitals, with and without residency programs, as well as public and private hospitals. The medical wards of these hospitals were chosen because many adult patients in these wards have chronic conditions requiring enteral nutrition and drugs administered through NPFT. The research protocol has been previously published in detail.[15]

2.3. Participants

The inclusion criteria were patients older than 18 years admitted to a medical ward with a nasally placed gastric tube or small bowel feeding tube, or who required the insertion of these tubes during hospitalization and who were hospitalized for at least 24 h. Patients meeting these criteria who were re-admitted during the study period were only counted for their first admission.

The sample size was determined by stratified random sampling with proportional allocation by strata, where each stratum was formed by the units of each hospital. Using parameters of relative error of 20%, a significance level of 5%, and a total population of 4573 patients with a short-term NPFT over six months, a total sample size of 281 patients was calculated. However, 327 patients were included to prevent dropouts from admission to discharge.[15]

The study was approved by the Research Ethics Committee of the University of São Paulo at Ribeirão Preto College of Nursing (Presentation Certificate for Ethical Appreciation number 56166016.1001.5393).

2.4. Source of data

Medical charts constituted our source of data. Three hospitals used electronic medical records (EMR), while the remaining three used paper-based medical charts. At each center, a registered nurse from the medical ward and a research assistant served as liaisons to the study investigators, while a designated nurse coordinator oversaw the thorough and precise collection of data. These personnel attended a total of 16 h of formal training sessions, combining theoretical and practical aspects, under the guidance of the regional study coordinator. These sessions involved a comprehensive overview of the study design and detailed explanations of each electronic data collection form. To ensure consistency in data recording across participating hospitals, a data collection guideline was devised. This guideline encompassed general project information, instructions for accessing electronic data collection forms via mobile devices, definitions of variables, and additional guidance for completing the forms. It was distributed in both printed and electronic formats to support all members of the research team throughout the data collection process. The methodology details have been previously published.[15]

2.5. Data collection procedures

Data were collected prospectively from October 2016 to July 2018 using electronic forms developed by the research team and assessed for face and content validity by a panel of experts. The experts were selected through an analysis of existing curricula in the database of the Brazilian National Council for Scientific and Technological Development (CNPq) and were invited to provide their expertise on the design of the forms. The forms were developed in the Portuguese language using an online platform (Survey Monkey®).

This platform hosts the questionnaires and, in accordance with its privacy policy, the questionnaires/forms/applications and responses collected are private by default. Only the main researcher and the project coordinator had access to the platform, which was password-protected. Links to the electronic forms were made available to experts to obtain consensus and determine the final content of the forms. The modified forms were pilot tested prior to being finalized, involving application to five hospitalized patients from the first day of NPFT use until discharge. [15,16]

All drugs prescribed were recorded within the first 24 h after admission (or 24 h after feeding tube insertion) and within 24 h before discharge (due to death or non-death), regardless of whether drugs were administered or not. When a patient was prescribed a drug in different dosing regimens (e.g. rapid- and moderate-acting insulin), the agent was counted only once.[17] Drugs given topically (such as enemas, eye drops, creams, gels, moisturizers, patches, suspensions) and contrast agents (i.e. contrast for cerebral angiography) were excluded. In this study, polypharmacy was defined as the concurrent use of five or more drugs.[2]

The primary reason for hospital admission was described according to the World Health Organization (WHO) International Classification of Diseases, 10th revision (ICD-10). The level of consciousness was established using the ACDU Scale,[18] which assesses the patients for alertness, confusion, drowsiness, and unresponsiveness. Severity of comorbid diseases was evaluated on admission using the Charlson Comorbidity Index (CCI) score,[19] and patients were divided into three groups: mildly

ill (with CCI scores of 1–2); moderate ill (with CCI scores of 3–4); and severe ill (with CCI scores ≥5).[19] Both the ACDU and CCI were calculated following primary data collection, utilizing the variables gathered through the data collection forms.

Patient care complexity was assessed by an experienced nurse on hospital admission using the Patient Classification System (PCS) proposed by Fugulin.[20] This instrument, recommended by the Federal Nursing Council of Brazil (COFEN),[21] classifies patients according to their degree of dependence on nursing care. The instrument has nine critical indicators: mental status, oxygenation, vital signs, mobility, walking, feeding, body care, elimination, and therapy. Points are divided into five categories that correspond to the complexity of care: minimal care (score 9 to 14), intermediate care (score 15 to 20), high dependence care (score 21 to 26), semi-intensive care (score 27 to 31), and intensive care (score > 31).

High-alert medications prescribed for patients with NPFT were identified according to the Institute for Safe Medication Practices (ISMP) List of High-Alert Medications in Acute Care Settings.[12]

2.6. Data analysis

Patient-related data were downloaded from the Survey Monkey® platform into a computer file by the principal investigator. For data analyses, drugs were classified according to the WHO Anatomical Therapeutic Chemical (ATC) code.

Wilcoxon signed-rank test was used to compare the mean number of drugs the patient was taking on admission or after NPFT insertion and at discharge, and to compare the number of high-alert medications prescribed at both time points. McNemar's chi-squared test was used to analyze the use of polypharmacy (yes/no) on admission or after NPFT insertion and at discharge.

To analyze the relationship between the occurrence of polypharmacy (yes/no) and the occurrence of high-alert medications (yes/no) according to age (adults: 18–60 years and older people: > 60 years) and time point (admission/discharge), the Generalized Estimating Equations (GEE) method was utilized.[22] The GEE method is often used to analyze longitudinal and other correlated data, especially if responses are binary. GEE resulted from an extension of generalized linear models for longitudinal data and produces more efficient and unbiased estimates for the parameters of the regression model when dealing with correlated data, as it considers the correlation structure between the observations.[22] Data were analyzed longitudinally using logistic regression for correlated dichotomous responses estimated by the GEE method. For the regression analysis, the program R version 3.6.1 was used. In all analyses, a significance level of 5% ($\alpha = 0.05$) was adopted.

In Brazil, according to the national statute, adults aged 60 and over are considered older people.[23]

3. Results

A total of 327 patients with a short-term NPFT were included in this study. Most were male (53.8%), older people (63.6%; median age = 66.0 years; Q1 = 54.0; Q3 = 76.3), with a median hospital stay of 11.4 days (Q1 = 6.5; Q3 = 21.6). The main reason for hospitalization was circulatory system diseases (23.2%) and the most common comorbidity was peripheral vascular disease (28.6%) (Table 1).

On admission, a significant number of patients were alert (59.9%), had at least one comorbidity (76.0%), were severely ill (43.1%) with a median CCI score of 4 (Q1 = 2; Q3 = 6), and were highly dependent on nursing care (35.4%), according to the PCS (Table 1). Most patients (n = 189; 57.7%) were using a NPFT on admission, while 42.2% (n = 138) required a NPFT during their hospital stay.

Within the first 24 h after admission, a total of 3045 drugs were prescribed to patients with NPFT, and at hospital discharge, patients were using 3037 drugs. There was no statistically significant difference in the mean number of drugs the patients were taking on admission (mean = 9.3; SD = 3.7) and at discharge (mean = 9.3; SD = 4.1) (p = 0.9837). One hundred and thirty-seven patients (41.9%) were on more drugs when discharged than when admitted, while the number of drugs remained the same for 54 (16.5%) patients. Additionally, 301 (92.0%) patients were on polypharmacy on admission, versus 277 (84.7%) at discharge, a statistically significant result (p = 0.0011) (Table 2).

Table 1
Characteristics of patients with NPFT (n = 327).

Characteristics	n = 327
Gender (male/female)	176 (53.8)/ 151 (46.2)[a]
Age (years)	66.0 (54.0–76.3)[b]
Length of stay (days)	11.4 (6.5–21.6)[b]
CCI[c] score	4 (2–6)[b]
Alert	196 (59.9)[a]
High dependent of nurse care[d]	115 (35.4)[a]
The three main reasons for hospitalization	
Diseases of the circulatory system	76 (23.2)[a]
Neoplasm	53 (16.2)[a]
Diseases of the respiratory system	40 (12.2)[a]
The four most common comorbidities	
Peripheral vascular disease	86 (28.6)[a]
Cerebrovascular disease	56 (18.6)[a]
Diabetes without complication	40 (12.2)[a]
Metastatic solid tumor	35 (10.7)[a]

[a] Number (%).
[b] Median (Q1 - Q3), Q1: first quartile, Q3: third quartile.
[c] Charlson Comorbidity Index.
[d] High dependent of nurse care: score 21 to 26.

On admission, 524 high-alert medications were prescribed to patients with NPFT (out of 3045; 17.2%). At discharge, patients were using 571 high-alert medications (out of 3037; 18.8%) and the difference between the two time points was not statistically significant (p = 0.3957) (Table 2).

It is noteworthy that older people had more than one high-alert medications on admission (n = 177; 63.2%) and at discharge (n = 148; 53.4%), compared to adult patients (n = 103; 31.5% and n = 94; 28.7%, respectively). Furthermore, 74 patients (24.6%) died during hospitalization, and of these, 66 (89.1%) were using high-alert medications.

Table 3 provides the GEE estimates for the occurrence of polypharmacy and high-alert medications in patients with NPFT, according to age and time point (admission vs. discharge). The occurrence of polypharmacy was independent of age (similar for adults and older people; p = 0.2377), but related to the time point. Regarding the occurrence of high-alert medications on admission and at discharge, Table 3 shows no significant difference concerning patients' age (p = 0.5426), from the adjusted model.

Table 2
Description of drugs the patients with NPFT were taking on admission and at discharge.

Variables	Admission (n = 3045)		Discharge (n = 3037)		
	n	%	n	%	p-value
Number of drugs per patient; mean ± SD[a](range)	9.3 ± 3.7 (2–21)	–	9.3 ± 4.1 (2–23)	–	0.9837[b]
Number of patients with ≥5 drugs (polypharmacy)	301	92.0	277	84.7	0.0011[c]
Number of high-alert medications per patient; mean ± SD[a](range)	1.7 ± 1.2 (0–6)	–	1.8 ± 1.2 (0–7)	–	0.3957[b]

[a] SD = standard deviation.
[b] Wilcoxon signed rank test.
[c] McNemar's chi-squared test.

Table 3
Comparison of GEE parameter estimates for the occurrence of polypharmacy and high-alert medications in patients with NPFT.

Variable	Estimate	*SE*	*Z*-statistic	p-value
Polypharmacy				
Intercept	2.2467	0.2738	67.3458	0.0000
Age	0.3329	0.2819	1.3943	0.2377
Time-point	−0.7390	0.2183	11.4641	0.0007
alpha	0.2736	0.0755	13.1326	0.0003
High-alert medication				
Intercept	0.5679	0.0656	74.9082	0.0000
Age	−0.0472	0.0776	0.3707	0.5426
Time point	0.0351	0.0416	0.7116	0.3989
alpha	0.4967	0.0718	47.9145	0.0000

Estimates and *p*-values are shown for the age and time-point.

Most drugs used by patients, both on admission and at discharge, were those acting on the alimentary tract and metabolism ($n = 880$; 28.9% and $n = 941$; 31%, respectively), the nervous system ($n = 759$; 24.9% and $n = 826$; 27.2%, respectively), and drugs acting on blood and blood-forming organs ($n = 509$; 16.7% and $n = 426$; 14%, respectively). Metamizole was the most prescribed drug to patients with NPFT on admission ($n = 296$; 9.7%) and at discharge ($n = 291$; 9.6%). Additional details of the drugs prescribed to patients with NPFT on admission and at discharge are provided in Supplemental Material 1.

The main classes of high-alert medications prescribed to patients with NPFT on admission and at discharge were drugs affecting blood and blood-forming organs and drugs affecting the nervous system (Table 4). Additional data are provided in Supplemental Material 2.

The dataset generated during this study is available in the Figshare Public Dashboard [https://doi.org/10.6084/m9.figshare.7497086; https://doi.org/10.6084/m9.figshare.7497131].

4. Discussion

Using a cross-sectional study design, we found that polypharmacy is common in patients with NPFT, both on admission and at hospital discharge, with high-alert medications making up >17% of prescribed drugs at both time points. To our knowledge, this is the first large-scale study comparing the drugs prescribed to patients with NPFT from hospital admission to discharge, including high-alert drugs and polypharmacy situations.

Patients with NPFT were on a large number of drugs on admission and at discharge (mean of 9.3 per patient at both time points). These results are higher than those found in previous studies conducted with patients from medical wards (4–7 drugs).[24,25] Possible reasons could be the severity of comorbid diseases and patient care complexity. For instance, most patients included in this study were older and had multiple chronic illnesses, including peripheral vascular disease, cerebrovascular disease, diabetes without complication, and metastatic solid tumor. As a result, older people take multiple drugs daily, increasing the potential for drug interactions, adverse drug reactions, non-adherence to drug treatment, duplication of drugs, and higher healthcare costs.[26,27] Another plausible explanation for the high number of drugs prescribed for these patients could be that most hospitals included in our study were university hospitals with residency programs, where resident physicians may be more likely to prescribe more drugs compared to attending physicians.[28–30] However, future studies are needed to explore this hypothesis.

In our study, most patients with NPFT were on polypharmacy (5 or more drugs) on admission (92.0%) and at discharge (84.7%). Polypharmacy is common in patients with NPFT to adequately control chronic medical conditions. According to Prybys and colleagues,[31] the risk of an adverse drug event has been estimated at 13% for two drugs, 58% for five drugs, and 82% for seven or more drugs. Experts emphasize the importance of promoting rational prescribing to reduce adverse drug events and poor patient outcomes, especially in the older population and in administration through NPFT.[32] Polypharmacy in the older age population raises safety concerns due to the decline in cognitive conditions and visual acuity, which can contribute to inadequate drug intake and other health problems. Moreover, clinical ward pharmacy services can help reduce the incidence of polypharmacy in hospital settings by performing activities such as drug reconciliation, pharmacotherapeutic monitoring, and prioritizing the deprescription of therapeutic futility, particularly in patients with NPFT.[33,34]

As previously mentioned, >17% of drugs used by patients with NPFT on admission and at hospital discharge were high-alert medications. One of the international patient safety goals is to improve the safety of high-alert medications because the consequences of an error involving these drugs can be devastating, necessitating the adoption of specific protocols for prevention.[10,12,35] High-alert medications account for 14.6% to 54.6% of all drugs used in hospital settings, especially in older people, and have been linked to >50% of all adverse drug events.[36] Notably, in our study, of the 74 patients who died during hospitalization, 89.1% were using high-alert medications. Although it is difficult to attribute such outcomes directly to the use of high-alert medications, previous studies show that harms caused by these drugs lead to increased morbidity and mortality, prolonged hospital stays, and higher financial costs for patients and healthcare systems.[36]

The ISMP recommends special safeguards to reduce these risks, including improving access to information about the drugs; limiting access to high-alert medications; using auxiliary labels and automated alerts; standardizing the ordering, storage, preparation, and administration of these products; and employing redundancies such as automated or independent double checks when necessary.[12]

In our study, almost 42% of patients were on more drugs at discharge than when admitted. There have been no previous published reports assessing this issue in tube-fed patients. Despite this, our results are similar to findings from a previous study conducted with patients from the general medicine departments at six hospitals in Norway.[14] These results underscore the importance of follow-up plans to reduce the risks for adverse drug events at home. For instance, a study conducted with

Table 4
Main classes of high-alert medications prescribed to patients with NPFT on admission and at discharge.

Drugs Classes[a]	Admission		Discharge	
	n	%	n	%
A Alimentary tract and metabolism	**120**	**22.9**	**138**	**24.2**
Antiarrhythmics, IV	2	0.4	0	0
Insulin, subcutaneous and IV	114	21.7	118	20.7
Specific medication	3	0.6	18	3.1
Sulfonylurea hypoglycemics, oral	1	0.2	2	0.3
B Blood and blood forming organs	**238**	**45.4**	**213**	**37.3**
Antithrombotic agents	185	35.3	168	29.4
Dextrose, hypertonic, 20% or greater	51	9.7	45	7.9
Sodium chloride for injection, hypertonic, >0.9% concentration	2	0.4	0	0
C Cardiovascular system	**10**	**1.9**	**22**	**3.8**
Adrenergic agonists, IV	8	1.5	21	3.7
Antiarrhythmics, IV	1	0.2	1	0.2
Specific medication	1	0.2	0	0
J Antiinfectives for systemic use	**3**	**0.6**	**3**	**0.5**
Liposomal forms of drugs	3	0.6	3	0.5
L Antineoplastic and immunomodulating agents	**1**	**0.2**	**2**	**0.3**
Chemotherapeutic agents, parenteral and oral	1	0.2	1	0.2
Opioid	0	0	1	0.2
N Nervous system	**152**	**29**	**193**	**33.8**
Anesthetic agents, general, inhaled and IV	3	0.6	5	0.9
Moderate sedation agents, IV	0	0	24	4.2
Opioid	149	28.4	164	28.7
Total	**524**	**100**	**571**	**100**

[a] According to WHO Anatomical Therapeutic Chemical (ATC) code and ISMP List of High-Alert Medications.

1000 patients consecutively admitted to 12 wards of UK hospitals showed that one-fifth of patients were re-admitted within one year of discharge due to adverse drug reactions, and up to 50% of these reactions were possibly avoidable.[37] In a systematic review, the authors found that drug-related harms were common in the older population within 30 days after hospital discharge, with ranges varying from 0.4% to 51.2%; additionally, 35% to 59% were considered preventable.[38] According to the authors, better methods of medication review in both hospital and primary care, in conjunction with clinical review and enabling rational prescribing practices, may prevent such events.[37]

As previously mentioned, there is a small increase in the prescription of high-alert medications at discharge while the patient is typically not under healthcare surveillance. This highlights the importance of drug reconciliation, education, and empowerment for safe drug use during the transition from hospital to home. If the patient continues with NPFT at home, especially those using high-alert medications, guidance becomes even more essential, as it significantly increases the complexity of the prescribed pharmacotherapy and the risk of adverse drug events. Empowering patients in the process of hospital discharge can profoundly impact improving drug adherence, avoiding medication errors, and decreasing adverse outcomes in the post-discharge period.[39] However, the literature reveals inconsistency in the knowledge of health professionals about high-alert medications.[40–42]

A study evaluating healthcare professionals' understanding of high-alert medications showed that, prior to interventions, only 42.9% of respondents were confident in their knowledge of these medications and institutional procedures. Following interventions, this confidence level increased to 73.5%.[43] In another study conducted in Brazil, nurses and pharmacists from four hospitals were surveyed about 33 high-alert medications. Surprisingly, none of these medications were unanimously identified as potentially life-threatening by all respondents, despite 17 of them being used by over 95% of respondents.[44]

In addition to healthcare professionals' knowledge of prescription drugs, the literature highlights the importance of strong engagement from family caregivers in care planning and effective communication during the transition of care.[45] These aspects, combined with patient empowerment during hospitalization for the safe use of their drugs at home, are essential when addressing polypharmacy and high-alert medications, particularly in patients whose condition necessitates NPFT and additional care.

4.1. Limitations and strengths

This study has several strengths. First, this is a large-scale study including six hospitals and thousands of drug prescriptions, reducing the risk of selection bias and enhancing external generalizability in Brazil and Latin America. Second, information bias is minimized as we used objective measures of drug prescriptions (medical charts). Third, the self-controlled study design (patients are compared to themselves) enables internal validity of results.

This study also has some limitations. Since there are six different hospitals, there may be variations in practices that can affect both the number and types of drugs used. The fact that drugs were prescribed does not guarantee that patients received the drugs, and we cannot determine how this potential bias would have affected patient outcomes (we only gathered data on deaths in the current study). The generalizability of results is limited to patients with NPFT treated in a universal healthcare system like Brazil's. Prescribing behaviors may vary according to countries' clinical practice guidelines and healthcare access. Finally, drug interactions and adverse drug events were not assessed in this study, which should be considered purely descriptive.

5. Conclusions

Polypharmacy is prevalent among patients with NPFT, particularly older people, who often have multiple comorbidities contributing to the excessive use of medications. The study identified polypharmacy both upon admission and at hospital discharge, with high-alert medications comprising 17% of prescribed drugs at both time points. This underscores the heightened risk of adverse drug events.

The findings of this study prompt considerations for future research and contribute valuable insights to the literature. They can inform healthcare professionals and leaders in developing localized solutions, redefining the roles and responsibilities of professionals, patients, and families, and enhancing the training of multidisciplinary teams to ensure the quality and safety of care for patients using NPFT.

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CRediT authorship contribution statement

Fernanda Raphael Escobar Gimenes: Writing – review & editing, Writing – original draft, Visualization, Supervision, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Juliana Santana de Freitas:** Writing – original draft, Formal analysis, Data curation. **Janine Koepp:** Writing – original draft, Supervision, Formal analysis, Data curation. **Patrícia Rezende do Prado:** Writing – original draft, Supervision, Formal analysis, Data curation. **Rochele Mosmann Menezes:** Writing – review & editing, Formal analysis. **Jacinthe Leclerc:** Writing – review & editing, Validation, Formal analysis. **Adriane Pinto de Medeiros:** Writing – review & editing, Writing – original draft, Methodology, Data curation. **Thalyta Cardoso Alux Teixeira:** Writing – original draft, Supervision, Formal analysis, Data curation. **Rhanna Emanuela Fontenele Lima de Carvalho:** Writing – original draft, Supervision, Formal analysis, Data curation. **Maria Olívia Barboza Zanetti:** Writing – review & editing, Validation, Formal analysis. **Adriana Inocenti Miasso:** Writing – review & editing, Formal analysis. **Jennifer Midiani Gonella:** Writing – review & editing, Writing – original draft, Methodology, Investigation, Data curation.

Declaration of competing interest

The authors declare no conflicts of interest that are directly relevant to the content of this study.

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None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.rcsop.2024.100474.

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