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Invasive mechanical ventilation in postterm neonates with meconium aspiration syndrome: an integrative review

Ventilação mecânica invasiva em neonatos pós-termo com síndrome de aspiração de mecônio: uma revisão integrativa

Danielly Gomes Lobato [1*], Enathanael Ribeiro Soares [2], Flávio Vinícius Fagundes Xavier [2], Juvêncio César Lima de Assis [3], Rayane Sales de Oliveira [2], Glêbia Alexa Cardoso [3], Rafaela Macêdo Feitosa [1], Joel Freires de Alencar Arrais [3]

[1]Dr. Leão Sampaio University Center – UNILEÃO, Juazeiro do Norte, CE, Brazil.

[2]São Camilo University Center, Juazeiro do Norte, CE, Brazil.

[3]Rio Grande do Norte State University – UERN, Mossoró, RN, Brazil.

*danielly.lobato@outlook.com.br

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ABSTRACT

Meconium Aspiration Syndrome (MAS) is a clinical condition that affects neonates exposed to amniotic fluid containing meconium. This situation can result in serious respiratory complications, leading to respiratory failure. The use of oxygen and/or Invasive Mechanical Ventilation (IMV) are crucial treatments for newborns with respiratory problems. The aim of the study is to identify the impacts of IMV on full-term neonates with SAM. This is an integrative review, carried out in five electronic databases: SciELO, ScienceDirect, LILACS, MEDLINE and PubMed. Studies published between 2013 and 2023 in English and Portuguese were considered, with intervention methods in full-term neonates, of both sexes, of any ethnicity, who have been subjected to mechanical ventilation. Four studies were chosen, totaling 204 participants with an average gestational age between 37.4 and 40.16 weeks. The professionals employed basic and advanced ventilation methods in the treatment of respiratory dysfunction, along with the use of Helium gas. An improvement in oxygenation and a reduction in mechanical ventilation time were noted. The positive effectiveness of IMV in improving oxygenation is evident, especially when combined with other strategies, such as the use of helium gas, which can result in shorter ventilation time. This highlights the importance of ventilatory strategies in lung protection for these newborns.

Keywords: Artificial respiration. Meconium aspiration syndrome. Positive pressure breathing.

RESUMO

A Síndrome de Aspiração de Mecônio (SAM) é uma condição clínica que afeta neonatos expostos ao líquido amniótico contendo mecônio. Essa situação pode resultar em complicações respiratórias sérias, levando à insuficiência respiratória. Usar oxigênio e/ou Ventilação Mecânica Invasiva (VMI) são tratamentos cruciais para neonatos com problemas respiratórios. O objetivo deste estudo é identificar os impactos da VMI em neonatos nascidos a termo com SAM. Trata-se de uma revisão integrativa, realizada em cinco bases de dados eletrônicas: SciELO, ScienceDirect, LILACS, MEDLINE e PubMed. Foram considerados estudos publicados entre 2013 e 2023 em inglês e em português, com métodos de intervenção em neonatos nascidos a termo, de ambos os sexos, de qualquer etnia, que tenham sido submetidos à ventilação mecânica. Quatro estudos foram escolhidos, totalizando 204 participantes com idade gestacional média entre 37,4 e 40,16 semanas. Os profissionais empregaram métodos ventilatórios básicos e avançados no tratamento da disfunção respiratória, juntamente com a utilização de gás Hélio. Foi notada melhora na oxigenação e uma redução no tempo de ventilação mecânica. É evidente a eficácia positiva da VMI na melhoria da oxigenação, especialmente quando combinada com outras estratégias, como o uso de gás Hélio, o que pode resultar em menor tempo de ventilação. Isso destaca a importância das estratégias ventilatórias na proteção pulmonar desses neonatos.

Palavras-chave: Respiração artificial. Respiração com pressão positiva. Síndrome de aspiração de mecônio.

INTRODUCTION

Meconium Aspiration Syndrome (MAS) is a clinical condition in neonates exposed to meconium-stained amniotic fluid. It is characterized by the presence of unexplained respiratory distress and typical radiological features. Symptoms can range from mild to severe, posing a life-threatening risk (Encina, 2022).

MAS is one of the leading causes of respiratory difficulties in term and postterm neonates. It is related to atelectasis, hypoxia, hypercapnia, persistent pulmonary hypertension, pulmonary inflammation, and deficiency in pulmonary surfactant production (Vijayalakshmi, Venugopal, Chandrashekar & Veeresh, 2015; Santhaligam, Ali & Greenough, 2017). As gestational age increases, so does the likelihood of MAS occurrence (Ward & Caughey, 2022).

This occurs due to meconium, a viscous and greenish fluid in the fetus's intestines during gestation, released after the maturation of the digestive system, either after birth or still in the uterus. Meconium can activate inflammatory mediators, such as cytokines, prostaglandins, and reactive oxygen species (Lindenskov, Castellheim, Saugstad & Mollnes, 2015).

When meconium is aspirated into the lungs, it can cause severe complications, such as chemical pneumonitis, pulmonary hypertension, pneumothorax, and often systemic complications, including hypotension. The diagnosis is confirmed by diffuse and irregular pulmonary infiltrates on chest radiographs (Strand & Perlman, 2022). About 40% of neonates who acquire meconium aspiration syndrome require mechanical ventilation. Due to the highly heterogeneous nature of the lungs, with atelectatic and hyperinflated areas, the parameters used vary according to each patient's individuality (Swarnam, Soraisham & Sivanandan, 2012; Keszler, 2017).

In the Neonatal Intensive Care Unit (NICU), the Invasive Mechanical Ventilation (IMV) plays an essential role in treating neonates with increased respiratory needs. This intervention aims to stabilize lung function, improve gas exchange, and promote more uniform alveolar ventilation (Keszler, 2017). The physiotherapist, a member of the NICU multidisciplinary team, stands out in the care of these patients, contributing to the reduction of complications during hospitalization and to the decrease in mortality through the management of IMV, an essential technique in the treatment of MAS. In this context, a relevant question emerges: "What is the evidence on the effects of IMV in premature neonates admitted to NICU with MAS?". From the above, the study aims to identify the repercussions of mechanical ventilation in postterm neonates with MAS.

MATERIALS AND METHODS

This study is an integrative literature review. We used the PICo strategy to formulate the guiding question: "What are the repercussions of IMV in postterm neonates admitted to the Intensive Care Unit with MAS?".

The research occurred from January to June 2023 across five electronic databases: Latin American and Caribbean Health Sciences Literature (LILACS), Scientific Electronic Library Online (SciELO), Science, Health and Medical Journals (ScienceDirect), Medical Literature Analysis and Retrieval System Online (MEDLINE), and the National Library of Medicine (PubMed).

Eligibility criteria included studies published from January 2013 to January 2023 in English and Portuguese, with intervention methodological designs, whose subjects were postterm neonates admitted to neonatal ICUs, of both sexes, of any ethnicity, who were undergoing IMV, and that the study design presents the ventilatory strategies used. Gray literature, review studies, duplicate studies with search strategies, and studies involving other populations were excluded.

The primary outcomes considered were the ventilatory strategies used in IMV. Secondary outcomes were the clinical repercussions of ventilation on pulmonary function and the clinical status of neonates with MAS.

For formulating the search strategy, we used the following descriptors: "Meconium Aspiration Syndrome", "Physical Therapy Specialty", "Respiration, Artificial", and "Positive-Pressure Respiration", adopting "AND" and "OR" as Boolean operators. All descriptors are indexed in the Health Sciences Descriptors (DeCS) and Medical Subject Headings (MeSH) platforms (Table 1).

Table 1
Strategies for searching and selecting studies.

Databases	Boolean operators	Search strategies
LILACS SciELO ScienceDirect MEDLINE	*AND*	*"Physical Therapy Specialty" AND "Meconium Aspiration Syndrome"* *"Respiration, Artificial" AND "Meconium Aspiration Syndrome"* *"Positive-Pressure Respiration" AND "Meconium Aspiration Syndrome"*
PubMed	*AND/OR*	*"Respiration, Artificial/therapeutic use" OR "Respiration, Artificial/therapy" AND "Meconium Aspiration Syndrome/complications" OR "Meconium Aspiration Syndrome/physiopathology" OR "Meconium Aspiration Syndrome/therapy"* *"Positive-Pressure Respiration/therapeutic use" OR "Positive-Pressure Respiration/therapy" AND "Meconium Aspiration Syndrome"*

Source: The authors.

The selection of studies was carried out according to the following norms: from the reading of the titles and abstracts of the studies found, followed by reading the full text of these studies to consider their relevance to the research and their methodological quality. The data obtained were represented by means of a table built in Microsoft Office Excel software, version 2016. Table 2 includes the following information: author(s) name, year of publication, type of study, sample size, gestational age in weeks, mean number of IMV hours, ventilatory interventions and strategies, and study outcomes.

RESULTS AND DISCUSSION

After using the search strategies, we found seven articles in the LILACS database, none in SciELO, there were 286 in MEDLINE, five in ScienceDirect, and 568 in PubMed, totaling 869 publications, of which, after applying language and publication year filters, 220 studies remained for eligibility criteria evaluation, culminating in four papers for this review (Figure 1).

Four studies were selected, with a total sample of 204 neonates. Methodologically, these included two randomized controlled trials (Wu et al., 2016; Ma et al., 2021) and two observational studies, one of which was retrospective (Sharma, Clark, Abubakar & Keszler, 2015; Yang et al., 2021) (Table 2).

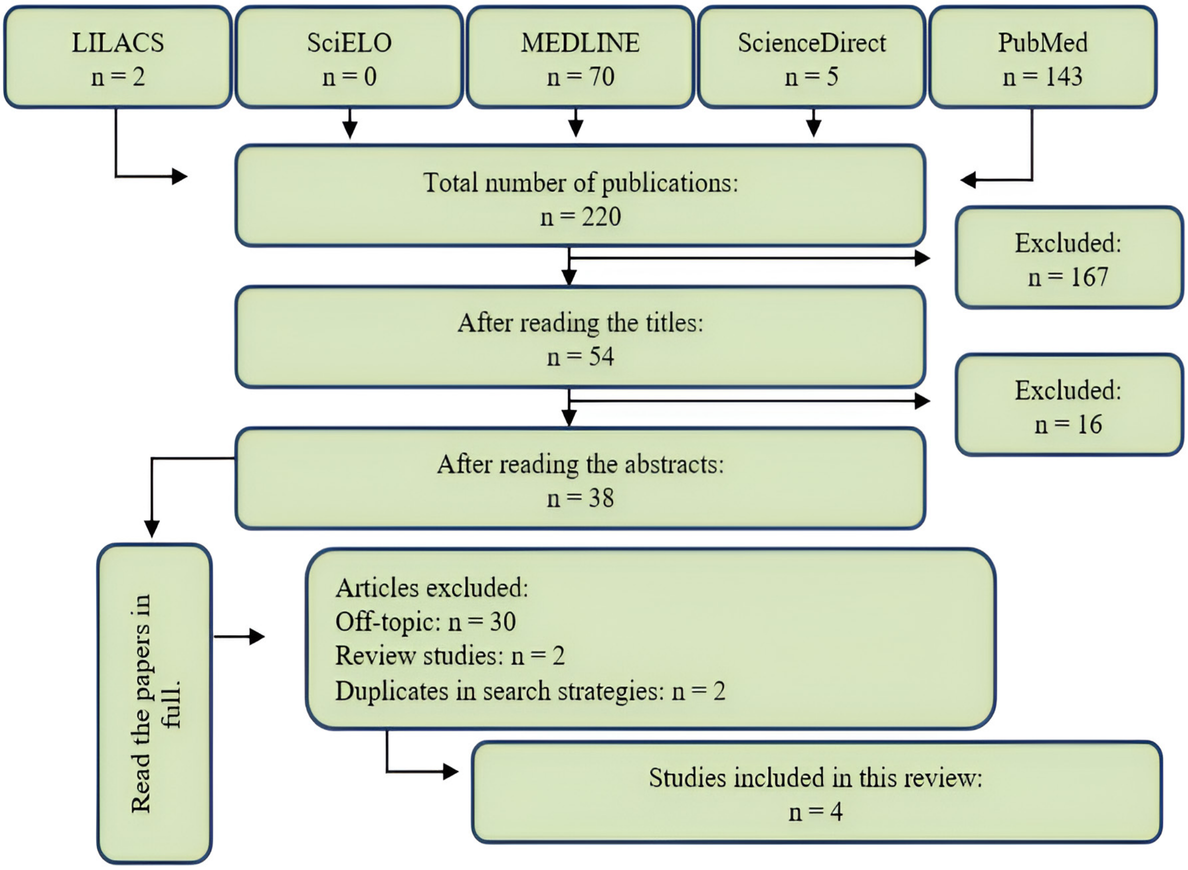
According to Sharma et al. (2015) and Yang et al. (2021), MAS results in pulmonary obstruction and alveolar inflammation that causes significant changes in the ventilation of smaller airways. When MAS causes partial obstruction, areas of pulmonary hyperinflation with a consequent increase in functional residual capacity (FRC) appear. When the alveolar obstruction is complete, areas of atelectasis are present. When these areas are associated with hyperinflation, it leads to a ventilation/perfusion (V/Q) mismatch, increasing areas of pulmonary shunt. As a result, the neonate may develop hypoxemia and/or hypercapnia.

Currently, ventilation strategies focus on lung preservation, aiming to reduce damage such as volutrauma, barotrauma, and atelectrauma. Common approaches to preventing such injuries include spontaneous breathing or assisted ventilation modes with low volumes and pressures (Wu et al., 2016).

The analyzed studies presented divergent strategies, in which Wu et al. (2016) and Ma et al. (2021) discuss Synchronized Intermittent Mandatory Ventilation (SIMV) with helium gas, compared to a control group, compared to Proportional Assisted Ventilation (PAV). Yang et al. (2021) contrasted High-Frequency Oral Ventilation (HFOV) with Conventional Mechanical Ventilation (CMV), and Sharma et al. (2015) compared Volume Guarantee Ventilation (VGV) with Pressure Support Ventilation with volume guarantee (PSV).

Considering the need to guarantee gas exchange, the study by Yang et al. (2021) indicated that HFOV compared to CMV leads to an improvement in the Arterial Oxygen Pressure/Inspired Oxygen Fraction (PaO_2/FiO_2) ratio with ($p = 0.045$) and a reduction in IMV time ($p<0.001$). Ma et al. (2021) also analyzed the PaO_2/FiO_2 ratio and IMV time, in which the group that used helium gas associated with SIMV mode had a better PaO_2/FiO_2 ratio, as well as shorter IMV time ($p<0.001$). This is not the case when comparing SIMV mode with PAV, as the latter excels in reducing Mechanical Ventilation (MV) time and in the greatest reduction in FiO_2 supplementation ($p<0.05$), which may presuppose an improvement in the PaO_2/FiO_2 ratio (Wu et al., 2016).

Figure 1
Flowchart of study selection in the databases.



Source: The authors.

The studies by Wu et al. (2016) and Ma et al. (2021) address the hospitalization time of neonates with MAS, showing that hospital stay may be associated with an increase in oxygen (O_2) dependence and longer duration of ventilatory support, as well as complications caused by IMV, such as pneumothorax and bronchopulmonary dysplasia.

Yang et al. (2021) compared PaO_2 and arterial carbon dioxide pressure ($PaCO_2$) values, demonstrating that PaO_2 was higher in the HFOV group (6 hours = 60.61±3.30; 12 hours = 68.32±5.12; 24 hours = 74.35±3.06; 48 hours = 78.37±5.22; 72 hours = 78.37±5.22) until the first 48 hours ($p<0.05$), compared to the control group (6 hours = 57.26±4.83; 12 hours = 65±7.06; 24 hours = 70.56±6.81; 48 hours = 74.41±4.57; 72 hours = 82.44±6.82). After 72 hours of ventilatory support, however, there were no statistical differences ($p = 0.349$).

The HFOV group had lower $PaCO_2$ values up to the first 48 hours ($p<0.005$) (6 hours = 54.03±3.77; 12 hours = 50.42±5.20; 24 hours = 46.97±5.60; 48 hours = 42.74±3.68; 72 hours = 39.97±3.38), compared to the control group (6 hours = 57.09±5.46; 12 hours = 54.44±3.70; 24 hours = 51.41±5.03; 48 hours = 46.91±5.41; 72 hours = 41.24±4.06). In contrast, the study by Ma et al. (2021) found differences using SIMV mode together with helium gas in PaO_2 and $PaCO_2$ parameters ($p<0.005$). While Sharma et al. (2015), using the VGV mode compared to the PSV mode, found no statistical difference when evaluating $PaCO_2$ = 41±3.9 versus 41.5±3.12, respectively ($p = 0.55$).

Patients who received heliox in IMV had higher P/F ratio values when compared to the control group (301±22 vs. 260.64±24.83, $p<0.001$). The researchers also analyzed that after six hours of ventilatory support, inflammatory factors, including IL-6, IL-8, CRP and TNF-α, were decreased in the heliox group (15.00±2.53 vs. 20.24±3.22 [IL-6]; 30.65±3.68 vs. 35.84±4.23 [IL-8]; 37.72±3.58 vs. 43.71±3.66 [TNF-α]; 5.45±0.51 vs. 5.81±0.65 [CRP]) with a value of ($p<0.001$ [IL-6/IL-8/TNF-α]; $p = 0.012$ [CRP]). After 24 hours of respiratory support, myocardial injury markers in the heliox group decreased significantly (129.2±15.41 vs. 157.16±15.83, $p<0.001$ [CK]; 20.0±3.98 vs. 24.43±8.65, $p = 0.041$ [CK-MB] (Ma et al., 2021).

Yang et al. (2021) observed the progress of patients on HFOV and CMV during 6, 12, 24, and 48 hours after the implementation of ventilatory parameters, resulting in higher PaO_2 and lower $PaCO_2$ in the first 48 hours of therapy for patients on HFOV, but with no significant differences after 72 hours. The result was a higher PaO_2/FiO_2 ratio in patients ventilated with HFOV than those on CMV. At the same time, the study carried out by Ma et al. (2021) shows that it was the use of SIMV mode associated with heliox that led to higher values in the PaO_2/FiO_2 ratio compared to the control group.

Neonates with MAS require 26% higher Tidal Volume (TV) (MAS Group: 6.11±1.05 vs. Control: 4.86±0.77) ($p<0.0001$), and 46% higher Minute Volume (MV) (MAS Group: 371±110 vs. Control: 262±53) ($p<0.0001$) to reach alveolar minute volume. Wu et al. (2016) found that MV was significantly lower in the APV group (5.1±0.4) compared to the SIMV group (5.7±0.7) ($p<0.05$) (Sharma et al., 2015).

Wu et al. (2016) observed that, after artificial ventilation, there were changes in Heart Rate, as well as in Respiratory Rate, generating a consequent reduction in respiratory muscle work in both groups. There was no major difference in Mean Arterial Pressure.

Table 2
Description of the main information from the selected studies.

Authors Year	Study type	N	GA (weeks)	IMV time (hours)	Interventions	Outcomes
Sharma et al. (2015)	Retrospective observational study	28	Control group 37.4±1.5 SAM group 39.7±0.08	*	Ventilatory parameters: TD: 4.5-5 ml/kg PEEP: 5-6 cmH_2O RR: 40 ipm Mode: assist/control (A/C) with volume guarantee (VG) Mode: PSV with volume guarantee (VG)	Tidal volume: (p<0.0001) SAM group: 6.11±1.05 Control group: 4.86±0.77 Respiratory Rate: (p<0.01) SAM group: 60±14.23 Control group: 54±6.6 Minute Ventilation: (p<0.0001) SAM group: 371±110 Control group: 262±53 $PaCO_2$: (p = 0.55) SAM group: 41±3.9 Control group: 41.5±3.12 PIP: (p = 0.25) SAM group: 18.5±5.9 Control group: 20±4.9
Wu et al. (2016)	Randomized controlled trial	40	PAV group 39.6±2.0 SIMV group 39.5±1.7	PAV group 82.6±17.9 SIMV group 88.4±22.1	PAV group FiO_2: 0.4-0.8 PEEP: 4-6 cmH_2O TD: 4-8 ml/kg Mode SIMV FiO_2: 0.4-0.8; RR: 20-40 ipm; PEEP: 4-6 cmH_2O TD: 4-8 ml/kg Adjusting peak inspiratory pressure (PIP), respiratory rate (RR), and PEEP.	IMV time: (p<0.05) PAV group: 82.6±17.9 SIMV group: 88.4±22.1 Hospitalization: (p<0.05) PAV group: 8.5±1.5 SIMV group: 9.1±2.2 FiO_2 (After 48 hours): (p<0.05) PAV group: 0.46±0.03 SIMV group: 0.48±0.03 TD (After 48 hours): (p<0.05) PAV group: 5.1±0.4 SIMV group: 5.7±0.7
Ma et al. (2021)	Randomized controlled trial	71	Heliox group 39.5±1.3 Control group 39.7±1.1	Heliox group 78±30 Control group 114±28.07	Mode: SIMV PIP de 15-18 cmH_2O PEEP: 4-10 cmH_2O RR:15-45 ipm FiO_2: 21%-100% Heliox group: SIMV with heliox adjusted according to the infant's needs for six hours. Control group: SIMV with air-oxygen mixture.	P/F ratio: (p<0.001) Heliox group: 301±22 Control group: 260.64±24.83 IMV time: (p<0.001) Heliox group: 78±30 Control group: 114±28.07 Length of stay: (p<0.001) Heliox group: 15.3±4.2 Control group: 19.11±4.01 There was a difference in blood gas indices (PaO_2, pH, and $PaCO_2$) between the groups at 2, 6, 12, 24, and 48 hours after IMV (p<0.005).
Yang et al. (2021)	Observational study	65	HFOV group 39.43±1.37 CMV group 40.13±1.44	HFOV group 85.57±5.30 CMV group 95.62±4.39	HFOV group Volume: 8-10ml/kg Oscillation Amplitude: 20-30 cmH_20 FiO_2: 40%-100% RR: 9-15Hz Mean Airway Pressure: 10-15 cmH_2O CMV group PIP: 18-25 cmH_2O PEEP: 4-6 cmH_2O FiO_2: 40%-100% Volume: 8-10ml/kg Mode A/C or SIMV	IMV time: (p<0.001) HFOV group: 85.57±5.30 CMV group: 95.62±4.39 P/F ratio: (p = 0.045) HFOV group: 347.74±20.79 CMV group: 338.03±17.44 Oxygen time: (p<0.01) HFOV group: 102.03±10.64 CMV group: 109.62±8.59 Air leak: (p = 0.032) HFOV group: 2 (6.5) CMV group: 9 (26.5) There was a difference in blood gas indices (PaO_2 and $PaCO_2$) between the groups at 2, 6, 12, 24, 48, and 72 hours after IMV (p<0.005).

Source: The authors.
Note. Legend: * - Not informed; GA – Gestational age; IMV – Invasive mechanical ventilation; SIMV – Synchronized intermittent mandatory ventilation; PIP – Peak inspiratory pressure; PEEP - Positive end-expiratory pressure; cmH_2O – Centimeters of water column; RR – Respiratory Rate; bpm – Breaths per minute; FiO_2 – Fraction of inspired oxygen; P/F – Arterial oxygen pressure/Fraction of inspired oxygen; PaO_2 – partial pressure arterial oxygen; pH – Potential of hydrogen; $PaCO_2$ – Partial pressure of carbon dioxide; HFOV – High-frequency oscillatory ventilation; CMV – Conventional mechanical ventilation; TD - Tidal volume; ml/Kg – Milliliters per kilogram; A/C – Assist/Control; PAV – Proportional assist ventilation; PSV – Pressure support ventilation; VG – Volume guarantee ventilation; MAS – Meconium aspiration syndrome.

CONCLUSION

The studies in this review indicate positive results regarding the use of IMV in patients, such as the improvement in the PaO_2/FiO_2 ratio and the reduction in MV time, with effective ventilatory strategies. Thus, emphasizing the importance of lung protection measures in neonates. It can also be seen that the application of HFOV, PAV and helium gas strategies may represent viable alternatives, associated with shorter ventilation times and, consequently, a reduction in the length of hospital stay. Additionally, VGV, which offers a greater tidal volume, could be considered for neonates with a hypercapnic pattern, although this possibility requires further investigation.

Given the aspects observed, there is a clear lack of interventional studies on the use of IMV in neonates with MAS, with a special focus on strategies and protocols for protective mechanical ventilation. This highlights the need to conduct new research that explores and offers greater methodological quality to those interested.

CONFLICTS OF INTEREST

The authors declare that there are no conflicts of interest.

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AUTHOR CONTRIBUTIONS

Conceptualization: D. G. L. *Data curation*: E. R. S., F. V. F. X. *Formal analysis*: D. G. L., E. R. S., F. V. F. X., R. S. O. *Investigation*: D. G. L., E. R. S., F. V. F. X., R. S. O. *Methodology*: R. M. F., J. F. A. A., G. A. C. *Project administration*: J. F. A. A. *Resources*: D. G. L., E. R. S., F. V. F. X., G. A. C., R. M. F., R. S. O., J. F. A. A., J. C. L. A. *Supervision*: G. A. C., R. M. F., J. F. A. A. *Visualization*: D. G. L., J. C. L. A. *Writing the initial draft*: D. G. L., E. R. S., F. V. F. X., J. C. L. A. *Revision and editing of writing*: G. A. C., R. M. F., J. F. A. A.

PEER REVIEW

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