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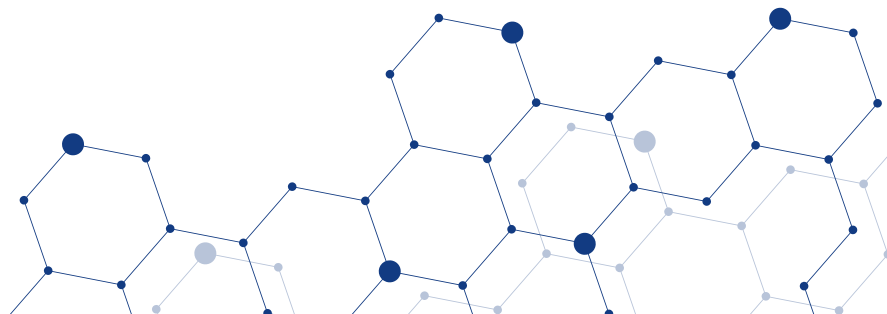
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## BALANCED GENERAL ANESTHESIA IN A PATIENT WITH CARDIAC PACEMAKER EXTRUSION: A CASE REPORT

MATHEUS SILVA DE OLIVEIRA<sup>1</sup>, ESTEVAM BORGES LOPES<sup>1</sup>, GABRIEL PEIXOTO DO NASCIMENTO<sup>1</sup>, STANLEY DE OLIVEIRA LOYOLA<sup>1</sup>, GUSTAVO SIQUEIRA ELMIRO<sup>1</sup>, GIULLIANO GARDENGHI<sup>1,2</sup>

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### ABSTRACT

Pacemaker (PM) generator extrusion is a rare complication, and may be associated with local infections, skin fragility, and local trauma. Treatment may involve simple surgical repair of the device site or, in more severe cases, removal of the entire system, requiring anesthetic support. This article reports the anesthetic management of a 79-year-old patient with complete PM extrusion after a fall from a standing position, followed by PM site infection, requiring surgical removal of the device. The patient underwent balanced general anesthesia with intraoperative transesophageal echocardiography monitoring, which revealed significant findings that changed the case's outcome.

**Keywords:** General anesthesia, Artificial pacemaker, Lead extraction, Echocardiography, Transesophageal, Surgical wound infection.

### INTRODUCTION

Pacemaker (PM) extrusion is a rare complication, with an approximate prevalence of 1%, usually associated with skin fragility, local infections (surgical site infections), local trauma (including scratching), or a small subcutaneous surgical pocket.<sup>1,2,3</sup>

Between 32% and 42% of local infections involving PM generators are associated with device extrusion; however, it is important to note that most of these cases are also linked to some degree of patient immunodeficiency (for example, corticosteroid users or poorly controlled diabetics), poor local hygiene, or cognitive impairment.<sup>1,2</sup>

Treatment generally consists of antibiotic therapy and removal of the device, followed by reimplantation on the contralateral side. In more subtle cases (such as erosions without signs of infection), surgical exploration with preservation of the generator in its original site may be attempted. Preventive measures include adequate management of concomitant diseases (such as diabetes mellitus), strict perioperative asepsis, and appropriate postoperative local hygiene.<sup>1,2</sup>

### CASE REPORT

The patient was a 79-year-old male with a significant medical history, including systemic arterial

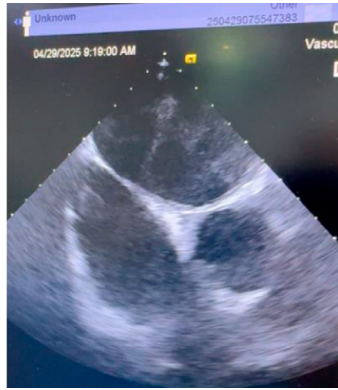
hypertension and prostate cancer. He also had a history of previous surgical procedures, such as laparoscopic cholecystectomy, hernia repair, and two valve replacement surgeries: the first in 1990 with implantation of a mechanical valve, and the second in 2021, when the mechanical valve was replaced with a biological prosthesis. Additionally, in 2021, he underwent pacemaker implantation. He was admitted to a hospital service with a complaint of a condition that had begun approximately five months earlier. After a fall from standing height, he started physiotherapy. Since then, he developed ulceration and purulent discharge at the site of the cardiac pacemaker, progressing to extrusion of the device in the left hemithorax (Figure 1).



**Figure 1.** Pacemaker generator extrusion in the left hemithorax region, associated with local inflammatory signs.

After evaluation by the multidisciplinary team, it was decided to proceed with the removal of the pacemaker system under general anesthesia. During the procedure, the patient was subjected to multiparameter monitoring, including pulse oximetry, electrocardiogram, and invasive blood pressure, the latter obtained by right radial artery puncture with a 20G catheter guided by ultrasonography. Pre-oxygenation was performed with 100% oxygen. The anesthetic induction consisted of 20 mg of ketamine, 100 mcg of fentanyl, 100 mg of 2% lidocaine, 150 mg of propofol, and 50 mg of rocuronium. Direct laryngoscopy was performed, classified as Cormack 2a, followed by orotracheal intubation (OTI) with an 8.0 cuffed tube, properly secured. Anesthetic maintenance was achieved with 2% sevoflurane and remifentanyl in a target-controlled infusion (TCI) pump. At the end of the procedure, 200 mg of sugammadex was administered, and extubation occurred without complications. The patient was then transferred to the Intensive Care Unit (ICU).

During the procedure, the transesophageal echocardiogram (TEE) revealed significant findings: a left atrium (LA) with a sessile thrombus and a right atrium (RA) with two serpentine, mobile images, suggestive of a thrombus or endocarditis (Figure 2). Given these findings, subcutaneous enoxaparin 80 mg every 12 hours was initiated for the probable thrombus, and an empirical antibiotic regimen with ampicillin, oxacillin, and gentamicin was started for the suspected endocarditis.



**Figure 2:** Transesophageal echocardiogram (TEE) image in the mid-esophageal plane showing a sessile thrombus in the left atrium (LA) and serpentine images in the right atrium (RA).

In the days following pacemaker (PM) removal, the patient developed a subcutaneous collection in the left breast region, associated with soft tissue swelling and pleural effusion. A chest computed tomography (CT) scan performed three days after PM removal confirmed the presence of a hematoma at the surgical site, leading to suspension of enoxaparin. Two days after the diagnosis, the hematoma was drained and enoxaparin was reintroduced. Despite the intervention, the patient remained prostrate and anorexic. Culture of the intracardiac pacemaker lead tip grew *Pseudomonas aeruginosa*, although blood cultures were negative. In view of the culture result and the unsatisfactory clinical course, the infectious disease team evaluated the case and decided to discontinue the empirical endocarditis regimen and initiate cefepime 2 g every 8 hours, with a planned treatment duration of 21 days.

One day after the infectious disease evaluation, the patient experienced significant clinical deterioration, developing acute kidney injury and hypotension, requiring return to the ICU. A sepsis protocol was initiated, with escalation of antimicrobial therapy to meropenem and vancomycin. An abdominal CT scan revealed partial intestinal obstruction due to an adhesion/internal hernia. Over the following two days, the patient's condition progressively worsened, requiring placement of a central venous catheter (CVC), invasive arterial blood pressure monitoring, initiation of total parenteral nutrition (TPN), and orotracheal intubation (OTI). During intubation, the patient suffered a cardiac arrest, with return of spontaneous circulation after three cycles of resuscitation. Approximately eight hours after the first cardiac arrest, the patient experienced a second arrest, this time refractory to resuscitative efforts, and died 18 days after the pacemaker removal procedure.

## DISCUSSION

Cardiac pacemakers are widely used devices for the treatment of symptomatic bradyarrhythmias and sinoatrial node (SAN) dysfunction, resulting in improvement of patient hemodynamics compromised by low heart rate. Pacemakers are traditionally composed of a generator and one or more leads, which stimulate the myocardium (Figure 3). More recently, so-called leadless pacemakers have been developed, in which both subunits (generator and electrodes) are integrated into a single device.<sup>1</sup>



Figure 3: Pacemaker composed of a generator and leads.

The generators are the component of the pacemaker that contain the device battery and where the electrical impulses transmitted through the leads are generated. They are most commonly placed in the infraclavicular region of the anterior chest wall. The leads originate from the generator and are advanced via the transvenous route to the myocardium.<sup>1</sup> Alternative configurations include epicardial generator placement; lead positioning in the His bundle or left bundle branch; and, in the case of leadless pacemakers, the entire unit being housed within the right ventricle (RV).<sup>1</sup>

One of the complications that may occur after pacemaker implantation is generator extrusion associated with erosion of the thoracic wall. This is a rare complication, with a prevalence of approximately 0.8%, and is mainly associated with local infections (most commonly caused by *Staphylococcus* species), fragile skin (particularly in elderly patients), impaired immunity, cognitive deficits, trauma caused by scratching, and thin subcutaneous tissue with an inadequately sized pocket for the device.<sup>2,3</sup> The first two factors were present in the patient described in our case, as evidenced by inflammatory signs at admission and advanced age.

Local infection may manifest as involvement of the generator pocket or as an exclusively intravascular process. Isolated pocket infection accounts for approximately 60% of device-related infections and usually results from contamination during surgery or subsequent manipulation. This infectious process may progress to skin erosion, contributing to device extrusion.<sup>4</sup>

Definitive diagnosis of pacemaker-related infection is primarily based on the presence of three findings: purulent collection or externalization of the device, microorganism growth in blood cultures, and the presence of vegetations on the tricuspid valve or on leads and electrodes as demonstrated by transesophageal echocardiography (TEE). In the present case, all three major criteria were met. When these criteria are insufficient to establish the diagnosis, additional imaging studies, such as PET-CT, may be required.<sup>4</sup>

Additionally, a case report published in Malaysia in 2011 described pacemaker extrusion following minor trauma to the chest wall (the patient's grandchild had jumped onto his chest), with the onset of pain, edema, and skin erosion occurring within two days after the incident.<sup>5</sup> It is therefore reasonable to hypothesize that, in our case, symptom onset may have followed the fall from standing height experienced by the patient. Could local trauma have occurred at that time, even if not reported by the patient?

In general, treatment of pacemaker extrusion may follow two approaches: surgical revision of the device pocket without system removal, or, in more severe cases—such as the present one, with complete generator extrusion and signs of infection—extraction of the entire system, as it is

considered contaminated.<sup>6</sup>

Regarding intraoperative management, the use of sevoflurane for maintenance of anesthetic depth was controversial when compared with a Danish cohort study published in 2007, in which propofol demonstrated superiority over inhalational agents in patients with cardiovascular instability or undergoing emergency surgery/acute events.<sup>7</sup> Thus, total intravenous anesthesia with propofol could have been considered instead of sevoflurane in this case.

Furthermore, a 2023 editorial published in the Journal of the American College of Cardiology emphasized that cases of endocarditis related to cardiac implantable electronic device infection require device removal as the gold-standard treatment, as mortality risk may reach up to 66%. Device extraction is associated with low complication rates, whereas delayed removal is linked to increased mortality and higher rates of adverse events.<sup>8</sup>

Finally, regarding the use of TEE in the intraoperative setting, its application has been shown to reduce 30-day mortality, shorten hospital length of stay, and significantly contribute to intraoperative decision-making in cardiopulmonary bypass, valvular, and aortic surgeries.<sup>9</sup> Although its routine use for pacemaker implantation or removal is not yet formally recommended, in this specific case it proved to be critically important for identifying and documenting images suggestive of thrombus/endocarditis, which completely altered the clinical management and ultimate outcome of the patient.

## CONCLUSION

Pacemaker extrusion is a rare event, usually associated with local infections and physiological and/or biopsychosocial aspects of the individual. Once diagnosed, its treatment is based on device removal in addition to antibiotic therapy, since its complications may even lead to death. In this context, this case report brings to light the discussion of a dramatic clinical scenario in which, from an anesthesiology perspective, propofol could have been better employed than sevoflurane for anesthetic maintenance. Furthermore, the use of transesophageal echocardiography (TEE) provided a broad spectrum of findings and guidance for subsequent management throughout the course of the case, despite the fact that its use in this type of surgical approach still lacks sufficient evidence for formal recommendation.

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## APPLICATIONS OF ARTIFICIAL INTELLIGENCE IN OBSTETRICS: REVIEW ARTICLE

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### ABSTRACT

**Introduction:** Artificial intelligence (AI) has emerged as a transformative technology in medicine, particularly in obstetrics and maternal–fetal medicine. By enabling automated analysis of large volumes of clinical and imaging data, AI offers new opportunities to improve screening, prediction, diagnosis, and clinical decision support. Despite the rapid growth of AI applications, concerns remain regarding methodological standardization, external validation, and real-world clinical applicability. **Objective:** To describe and critically analyze the main applications of artificial intelligence in obstetrics and maternal–fetal medicine, focusing on diagnostic and predictive performance, methodological limitations, and potential impact on clinical practice. **Methods:** A literature review was conducted using the PubMed database, including studies published between 2021 and 2025. Original research articles, systematic reviews, and meta-analyses addressing practical applications of AI in obstetrics and reporting algorithm performance metrics were included. The selected studies were categorized into four main domains: gestational age and fetal weight estimation, fetal and neonatal neurological assessment, prediction of hypertensive disorders of pregnancy, and prenatal screening for structural and genetic anomalies. **Results:** Twelve studies met the inclusion criteria. AI-based systems demonstrated performance comparable to that of experienced clinicians in gestational age estimation, particularly in low-resource settings. In fetal and neonatal neurological assessment, deep learning models showed high accuracy in detecting cerebral lesions and enabled dynamic evaluation of fetal brain activity through automated facial expression recognition. For the prediction of hypertensive disorders of pregnancy, AI models—especially those based on placental texture analysis—showed promising results, although with considerable methodological heterogeneity. AI-assisted screening for structural and genetic anomalies also achieved robust diagnostic performance, reducing operator dependency. **Conclusion:** Current evidence suggests that artificial intelligence has the potential to enhance diagnostic accuracy, reduce interobserver variability, and improve efficiency in obstetric care. However, challenges related to model interpretability, external validation, generalizability, and safe clinical integration remain. AI should be regarded as a complementary tool to clinical judgment rather than a replacement, and its successful implementation requires evidence-based guidelines and adequate training of healthcare professionals.

**Keywords:** Artificial intelligence, Obstetrics, Ultrasonography, Maternal–fetal medicine, Machine learning.

## INTRODUCTION

Artificial intelligence (AI) refers to the ability of computational systems to perform tasks traditionally associated with human intelligence, such as reasoning, learning, adaptation, and sensory interpretation. Its conceptual foundations date back to the pioneering work of Alan Turing in 1950, when he proposed the test to evaluate whether a machine's behavior could be indistinguishable from that of a human, followed by the formalization of the term "artificial intelligence" by John McCarthy. Although the field began to be academically structured in the 1970s, it was only with advances in computational power and the availability of large volumes of data that the development of modern algorithms became possible. Unlike traditional rule-based algorithms, AI systems learn patterns directly from data, a concept famously demonstrated by historical milestones such as Deep Blue's victory in chess in 1997 and AlphaGo's success in the game of Go in 2016.<sup>1</sup>

This technological evolution has driven widespread applications in everyday life and, more recently, has generated significant interest in clinical medicine due to AI's potential to extract meaningful information from large healthcare datasets. In the medical field, particularly in obstetrics and gynecology, AI has been successfully applied to screening, prediction, triage, diagnosis, monitoring, and image interpretation, contributing to greater accuracy and supporting clinical decision-making.<sup>1,2</sup>

However, the available evidence remains limited, and further studies are needed to confirm the clinical applicability of artificial intelligence. In addition, it is essential to ensure improved physician training in the use of these systems and to develop evidence-based guidelines on the subject in order to maximize the benefits of AI technologies while minimizing their limitations.<sup>3</sup>

Therefore, the aim of this review is to describe the main modalities of artificial intelligence, their utility in daily clinical practice, and their contribution to the clinical decision-making process in obstetrics, providing a critical synthesis of recent evidence regarding the effectiveness, limitations, and transformative potential of this technology.

## METHODOLOGY

This study presents a review of the scientific literature on applications of artificial intelligence in maternal-fetal medicine and obstetrics.

A search was conducted in the PubMed database for articles published between 2021 and 2025. The search terms used were "artificial intelligence in obstetrics" and "maternal-fetal medicine," combined using Boolean operators (AND, OR) to optimize the retrieval of relevant studies. The search strategy was designed to capture publications describing practical applications of AI in obstetrics, including original studies, systematic reviews, and meta-analyses.

Inclusion criteria included original research articles describing AI applications in obstetrics or maternal-fetal medicine; systematic reviews and meta-analyses on AI in obstetrics; studies published in journals indexed in PubMed; studies written in English or Portuguese; and studies reporting performance metrics of AI algorithms. Exclusion criteria included opinion articles, editorials, or commentaries; studies lacking evaluation of AI algorithm performance; studies focused exclusively on other medical specialties; and duplicate articles or studies with redundant data.

Data were extracted from each included article using a standardized form containing information on study identification (first author, year of publication, journal), study characteristics (design, setting, sample size), AI application (type of algorithm, input data), outcomes (performance measures), comparison with reference standards or human professionals, and methodological

limitations. The identified studies were categorized into four main areas of application: estimation of gestational age and fetal weight; fetal and neonatal neurological assessment; prediction of hypertensive disorders of pregnancy; and prenatal screening for structural and genetic anomalies.

## RESULTS

The PubMed search identified a total of 93 records using the specified search terms. After application of the inclusion and exclusion criteria, 12 publications were included in the final analysis.

**Table 1. Applications of Artificial Intelligence in Obstetric and Neonatal Ultrasound**

| Author / Year                | Study design                          | AI application  | Population / Sample                              | Key findings   |
|------------------------------|---------------------------------------|---|--|--|
| <b>Stringer et al., 2024</b> | Prospective diagnostic accuracy study | AI-based estimation of gestational age from blinded ultrasound sweeps | 400 pregnant women (Zambia and USA)              | The AI tool demonstrated accuracy comparable to standard biometry performed by experienced sonographers, with a similar mean absolute error ( $\pm 2$ days). |
| <b>Naz et al., 2025</b>      | Systematic review and meta-analysis   | AI models for gestational age estimation                              | 17 studies (10 included in the meta-analysis)    | AI demonstrated good accuracy, particularly in the second trimester, with promising performance in low-resource settings.                                    |
| <b>Horky et al., 2025</b>    | Prospective cohort study              | AI-assisted estimation of term fetal weight                           | 300 term fetuses                                 | AI showed greater variability and lower accuracy than experienced specialists, indicating the need for further optimization before routine clinical use.     |
| <b>Lin et al., 2025</b>      | Multicenter observational study       | Deep learning-based screening of neonatal brain lesions               | Neonates evaluated by cranial ultrasound (China) | The model identified brain lesions with high sensitivity and specificity, outperforming conventional assessments in some scenarios.                          |

|                            |                                  |  |  |   |
|----------------------------|----------------------------------|--|--|---|
| <b>Miyagi et al., 2021</b> | Observational study              | Fetal facial expression recognition using 4D ultrasound                    | Fetuses between 27 and 37 weeks of gestation     | AI was able to identify fetal facial patterns, suggesting an association with neurological activity.  |
| <b>Miyagi et al., 2023</b> | Analytical observational study   | Dynamic analysis of fetal brain activity using AI-based facial recognition | Fetuses evaluated by 4D ultrasound               | Integration of spectral and chaotic analysis with AI-based scoring revealed regular cycles and distinct states of fetal brain activity, extending beyond purely morphological classification. |
| <b>Arora et al., 2025</b>  | Observational study              | AI-based placental texture analysis  | Pregnant women evaluated by placental ultrasound | AI showed potential to predict hypertensive disorders of pregnancy.   |
| <b>Khalil et al., 2024</b> | Predictive study                 | Neural networks for preeclampsia prediction                                | Pregnant women with clinical data and biomarkers | The combination of biomarkers and clinical data improved the predictive performance of the AI model.  |
| <b>Malik et al., 2024</b>  | Systematic review                | Machine learning for preeclampsia prediction                               | Observational and predictive studies             | ML models showed promising performance, although with substantial methodological heterogeneity.   |
| <b>Tang et al., 2023</b>   | Development and validation study | Deep learning-based detection of genetic disorders                         | Fetuses evaluated by ultrasound                  | AI was able to identify both common and rare genetic disorders from fetal imaging.  |
| <b>Miyagi et al., 2024</b> | Observational study              | AI applied to coagulation management in massive obstetric hemorrhage       | Parturients with severe hemorrhage               | The model defined objective fibrinogen and fibrin degradation product (FDP) thresholds, supporting clinical decision-making in time-critical settings.  |
| <b>Aoyama et al., 2024</b> | Methodological study             | Automated assessment of the fetal pulmonary artery-to-aorta ratio          | Fetuses evaluated by fetal cardiac ultrasound    | AI demonstrated high accuracy in screening for congenital heart disease.  |

## DISCUSSION

### Estimation of Gestational Age and Fetal Weight

Accurate estimation of gestational age is fundamental to prenatal care, influencing critical clinical decisions such as fetal growth surveillance, identification of prematurity, and delivery planning. The observational study conducted by Stringer et al. (2024) provides evidence that an integrated AI-based tool is capable of estimating gestational age with accuracy equivalent to fetal biometry performed by experienced sonographers, even when operated by novice users without prior training.<sup>4</sup> A mean absolute error of less than four days, within the prespecified equivalence margin, demonstrates not only the algorithm's accuracy but also its consistency across different socioeconomic contexts, including low-resource settings such as Zambia. These findings reinforce the potential of AI as a supportive technology to expand access to reliable gestational dating, aligning with World Health Organization recommendations for the universalization of obstetric ultrasound.

Corroborating these results, the systematic review and meta-analysis by Naz et al. (2025) demonstrated good accuracy of AI models for gestational age estimation, particularly when applied to blind sweep videos, which showed lower mean error compared with static two-dimensional images.<sup>5</sup> Subgroup analysis revealed better performance during the second trimester, a period characterized by lower fetal biological variability, which may explain the observed reduction in error. Despite the high heterogeneity among included studies, the review indicates that most studies had low or unclear risk of bias, suggesting that the findings are consistent and clinically relevant.

In contrast, when AI is applied to term fetal weight estimation, the results are more heterogeneous and warrant greater caution. The comparative study by Horky et al. (2025) demonstrated that AI-assisted algorithms performed worse than experienced sonographers, with greater variability and lower diagnostic accuracy, even after adjustment for daily fetal weight gain.<sup>6</sup> Although manual estimation also failed to achieve optimal accuracy, remaining below 80%, AI models exhibited significant limitations, suggesting that, unlike gestational age dating, fetal weight estimation involves greater biological and technical complexity that is not yet fully captured by current models.

### Fetal and Neonatal Neurological Assessment

The incorporation of artificial intelligence into ultrasonography has emerged as a promising strategy to enhance diagnostic capability, standardize interpretations, and optimize clinical workflows, as early and accurate assessment of fetal and neonatal neurological development and integrity remains one of the greatest challenges in medicine.

The observational study conducted by Lin et al. (2025) demonstrates the potential of AI in screening for severe neonatal brain lesions using cranial ultrasonography.<sup>7</sup> The deep learning-based system showed exceptional performance, with areas under the curve (AUCs) exceeding 0.94 in both internal and external datasets, as well as high sensitivity, outperforming junior radiologists and achieving performance comparable to that of intermediate-level professionals. These findings are particularly relevant given that neonatal cranial ultrasound is highly operator-dependent and often performed in high-demand clinical settings. Automation of standard view acquisition and identification of severe lesions not only increases diagnostic efficiency - markedly reducing examination time - but may also contribute to earlier detection of conditions associated with adverse neurological outcomes, enabling timely interventions.

Complementarily, studies conducted by Miyagi et al. (2021; 2023) further expand this perspective by demonstrating that AI can explore functional aspects of the fetal nervous system through automated recognition of fetal facial expressions using four-dimensional ultrasonography.<sup>8</sup> In the pilot study, the authors achieved high overall accuracy (0.985) in classifying facial expressions considered related to brain development, such as blinking, mouth movements, and yawning. These results suggest that AI may provide an objective and reproducible assessment of fetal behavioral patterns, which have traditionally been evaluated subjectively.

The methodological evolution observed in the subsequent study by Miyagi et al. (2023) reinforces this perspective by integrating spectral and chaotic analyses with the confidence scores generated by the AI classifier.<sup>9</sup> The identification of regular cycles of facial activity, as well as distinct states (dense and sparse), provides quantitative evidence of fluctuations in fetal brain activity over time. These findings are particularly innovative, as they suggest that AI can transcend simple morphological classification and contribute to a dynamic understanding of fetal brain function, opening new avenues for the assessment of intrauterine neurodevelopment.

### **Prediction of Hypertensive Disorders of Pregnancy**

Hypertensive disorders of pregnancy, particularly preeclampsia, remain among the leading causes of maternal and perinatal morbidity and mortality worldwide. The possibility of early prediction of these conditions represents a strategic opportunity for preventive interventions, such as timely initiation of low-dose aspirin, intensification of prenatal surveillance, and appropriate organization of care across different levels of the healthcare system.

The observational study by Arora et al. (2025) innovatively demonstrates the potential of deep learning-based placental texture analysis from ultrasonographic images for the prediction of hypertensive disorders of pregnancy.<sup>10</sup> The use of different architectures—including convolutional neural networks (CNNs), transfer learning approaches, and Vision Transformers (ViT) combined with a TabNet classifier—resulted in high accuracy as early as the first trimester, with values exceeding 90% and areas under the curve (AUC) above 0.90 across the evaluated gestational periods. These findings support the hypothesis that microscopic and structural placental alterations precede clinical disease manifestation and may be detected early through texture patterns imperceptible to conventional human assessment.

These results are consistent with the pathophysiological concept of preeclampsia as a placental disorder, in which impaired spiral artery remodeling and abnormal placentation occur early in gestation. The ability of AI to capture subtle information from placental imaging therefore represents a significant advance over traditional approaches based solely on clinical risk factors or uterine artery Doppler assessment, particularly in settings where specialized examinations are not widely available.

Conversely, the multicenter study by Khalil et al. (2024) explored a different strategy, integrating routine clinical features and cell-free DNA biomarkers using artificial neural network models.<sup>11</sup> The results demonstrated similar performance between logistic regression and neural network models, with moderate AUCs for the prediction of preterm and early-onset preeclampsia. Although total cell-free DNA and fetal fraction showed statistically significant associations with preeclampsia, their incremental contribution to overall model performance was limited, especially for term disease.

The study by Malik et al. (2024) consisted of a systematic review evaluating the performance of machine learning models for preeclampsia prediction.<sup>12</sup> The authors analyzed various algorithms, including artificial neural networks, random forests, support vector machines, and logistic

regression, applied to clinical, laboratory, and demographic data. Overall, machine learning-based models demonstrated superior predictive performance compared with traditional statistical methods, particularly when combined datasets were used. The review concludes that artificial intelligence holds substantial potential to support early identification of preeclampsia, while emphasizing the need for methodological standardization, external validation, and prospective studies prior to widespread clinical implementation.

The importance of model interpretability and clinical validation becomes even more evident when considering applications in obstetric emergency settings. The study by Miyagi et al. (2024) illustrates a pragmatic application of AI in defining objective threshold criteria for coagulation dysfunction in cases of massive obstetric hemorrhage.<sup>13</sup> By employing different machine learning algorithms to establish cutoff values for fibrinogen and fibrin degradation products, the authors demonstrate how AI can support the development of more robust diagnostic criteria that are less dependent on empirical judgment. Although not directly related to preeclampsia prediction, this study reinforces the broader potential of AI in obstetrics to support critical decision-making in high-risk situations, where speed and precision are essential for maternal outcomes.

### **Prenatal Screening for Structural and Genetic Anomalies**

The studies by Tang et al. (2023)<sup>14</sup> and Aoyama et al. (2024)<sup>15</sup> demonstrate complementary approaches to the automated detection of fetal structural and genetic abnormalities, reinforcing the role of artificial intelligence as a clinical decision-support tool.

The study by Tang et al. proposes Pgds-ResNet, a fully automated deep learning algorithm capable of identifying both common and rare genetic disorders from fetal ultrasound images.<sup>14</sup> Considering that approximately 8% of the global population is affected by genetic syndromes and that most diagnoses are made only after birth, this approach has significant clinical impact. The high sensitivity and specificity achieved for common trisomies (21, 18, and 13), as well as for rare genetic diseases, indicate that automated analysis of fetal facial features may represent an effective complementary method to traditional screening examinations. Furthermore, the algorithm's performance comparable to that of experienced sonographers suggests that AI may help reduce exclusive reliance on operator expertise, which remains one of the main limitations of conventional ultrasonography.

In contrast, the study by Aoyama et al. focuses on screening for congenital heart disease through automated assessment of the pulmonary artery-to-ascending aorta ratio in the three-vessel view (3V).<sup>15</sup> Manual measurement of these structures is associated with substantial intra- and interobserver variability, particularly among less experienced examiners. The AI-based approach, combining YOLOv7 and UNet3+ algorithms, demonstrated performance superior to that of residents and fellows, achieving a high area under the ROC curve. These findings further support the potential of AI to standardize quantitative assessments, reduce human bias, and improve diagnostic accuracy in fetal cardiac screening examinations.

### **CONCLUSION**

Artificial intelligence represents a transformative opportunity for obstetrics, with the potential to improve diagnostic accuracy, reduce interobserver variability, and expand access to high-quality care in resource-limited settings. However, its integration into clinical practice must be approached cautiously, with emphasis on rigorous validation, interpretability, safety, and equity.

AI should not be viewed as a replacement for clinical judgment, but rather as a complementary tool

capable of enhancing evidence-based decision-making. Only through continuous collaboration among researchers, clinicians, engineers, and policymakers will it be possible to fully realize the potential of AI in obstetrics, ultimately contributing to improved maternal and fetal outcomes on a global scale.

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## ACCIDENTAL ASPIRATION OF A FOREIGN BODY INTO THE AIRWAY DURING ANESTHETIC MANAGEMENT: A CASE REPORT

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### ABSTRACT

**Introduction:** Accidental aspiration of a foreign body into the airway during anesthetic management is a rare but potentially serious complication. This event can occur during airway manipulation, especially when using devices for topical anesthesia, intubation, or ventilation, resulting in airway obstruction and significant risk to the patient. Immediate identification and appropriate management are essential to avoid complications. **Case report:** A 38-year-old female patient, ASA II, underwent bodytite liposuction and miniabdominoplasty. During periglottic anesthesia with lidocaine using an atomizer (Mucosal Atomization Device), the tip of the device came loose and was aspirated into the trachea. An initial attempt to remove it with an orotracheal tube was unsuccessful. Flexible bronchoscopy was performed, which allowed the location and safe removal of the foreign body on the first attempt. After the procedure, the patient was reintubated, the surgical procedure was uneventful, and the patient had an uneventful postoperative period. **Discussion:** Iatrogenic foreign body aspiration during anesthetic management is a high-risk situation. This case reinforces the importance of rigorous inspection of devices before use, in addition to the need to prepare the team for emergency airway situations. The prompt use of bronchoscopy was essential for the effective resolution of the event, preventing major complications. Safety protocols and review of medical devices are fundamental strategies for prevention.

**Keywords:** Foreign body aspiration, Anesthesia, Airway management, Intraoperative complications, Bronchoscopy.

### INTRODUCTION

Loose materials that enter the airways during intubation, ventilation, or advanced airway management - a phenomenon known as foreign body aspiration - may result in partial or complete airway obstruction. Early identification and management of these situations reduce patient morbidity and mortality; however, promptly recognizing accidental aspiration of a foreign body can be challenging, as the patient may be sedated and/or anesthetized, and may therefore be misdiagnosed postoperatively with asthma, chronic obstructive pulmonary disease, or stridor.<sup>1</sup>

Iatrogenic foreign bodies in the aerodigestive tract are rare events, as evidenced by the limited

number of cases reported in the literature.<sup>2</sup> Accidental and iatrogenic aspiration during procedures is most commonly encountered during dental interventions.<sup>3</sup> Other authors describe aspiration of components from commonly used respiratory equipment, including materials routinely handled by anesthesiologists. These iatrogenic incidents may be related to equipment malfunction or accidental events during medical treatment and airway management.<sup>3</sup> A foreign body lodged in the esophagus typically presents with dysphagia, whereas aspiration into the respiratory tract may lead to coughing, dyspnea, and stridor, and can progress to complications such as infection and pulmonary atelectasis.<sup>4,5</sup>

Appropriate management for removal of a foreign body from the airway may involve rigid or flexible bronchoscopy under general or local anesthesia, depending on the material and location of the obstruction.<sup>5</sup>

This case report aims to describe the management of foreign body removal from the airway during an anesthetic procedure, highlighting the need for preventive strategies, precautions, and essential safety measures to avoid such incidents and ensure safe anesthetic care.

## CASE REPORT

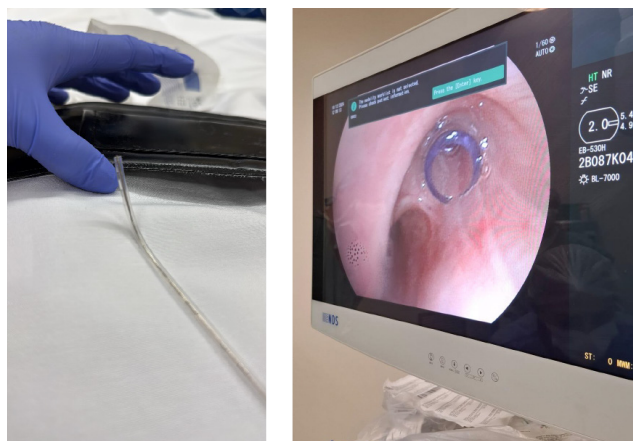
A 38-year-old female patient, 72 kg, 1.62 m, was admitted for bodytite liposuction and mini-abdominoplasty. The pre-anesthetic evaluation classified her as ASA II, with a history of fibromyalgia treated with pregabalin (75 mg) and zolpidem (5 mg). Safety protocols, including equipment checks and rescue drug verification, were rigorously followed.

In the operating room, standard monitoring was established: electrocardiography, pulse oximetry, non-invasive blood pressure, temperature, capnography, and bispectral index (BIS). A Foley catheter was inserted for urine output monitoring. After peripheral venous access (20G) was obtained in the right upper limb, supplemental oxygen (2 L/min) was administered. Initial sedation was performed with fentanyl (50 mcg) and midazolam (5 mg).

For epidural anesthesia, the patient was positioned in the seated position. A single puncture at T9-T10 was performed using an 18G Tuohy needle, without complications. The test dose was negative, and ropivacaine 0.5% (40 mL) plus morphine (0.3 mg) were administered slowly and fractionally. The epidural catheter was successfully inserted. After the block, the patient was repositioned in the supine position and preoxygenated with 100% oxygen (5 L/min via face mask).

Gradual intravenous induction was carried out with fentanyl (150 mcg), lidocaine without vasoconstrictor (50 mg), rocuronium (50 mg), and a target-controlled propofol infusion (target 3.5 µg/mL). Orotracheal intubation was performed under videolaryngoscopic guidance (McGrath, blade 3) after periglottic lidocaine atomization.

During atomization, the tip of the atomizer (Mucosal Atomization Device – GCMEDICA®) accidentally detached and was aspirated into the trachea. An attempt to retrieve it was made using a 4.5 mm orotracheal cannula, inflating the cuff and applying gentle traction, but it was unsuccessful. The orotracheal tube was left in place, and mechanical ventilation was started with low parameters, without PEEP and without inspiratory plateau.



**Figure 1.** Atomizer without the tip / atomizer tip inside the airway

In coordination with the medical team, bronchoscopy was performed to remove the foreign body. The scope was introduced parallel to the orotracheal tube, and the fragment was located and successfully removed on the first attempt using extraction forceps. After removal, the cuff of the tube was deflated to facilitate withdrawal of the tube and passage of the scope, minimizing the risk of airway injury.



**Figure 2.** Bronchofibroscopy showing grasping of the atomizer tip / atomizer tip after removal from the airway.

Immediately after removal of the foreign body, a new videolaryngoscopy was performed, followed by orotracheal intubation with a 7.0 mm cuffed tube using a bougie. Intubation was confirmed by capnography and bilateral lung auscultation. Ventilatory parameters were adjusted to a tidal volume of 450 mL, respiratory rate of 11 breaths per minute, maximum airway pressure of 30 cmH<sub>2</sub>O, and PEEP of 5 cmH<sub>2</sub>O. Three alveolar recruitment maneuvers were performed.

The surgical procedure lasted 8 hours. Anesthetic maintenance was achieved with intravenous propofol infusion (target 3.5 µg/mL), combined with intermittent doses of fentanyl, midazolam, and

rocuronium. Additional doses of ropivacaine were administered through the epidural catheter. The patient's positioning was carefully maintained, with thermal protection, extremity padding, and continuous hemodynamic monitoring.

At the end of the procedure, the patient was reversed with sugammadex (200 mg) and awoke calmly. Extubation occurred without complications or pain. The epidural catheter was removed without difficulty. The patient was transferred to the post-anesthesia care unit, where she remained for 80 minutes. After achieving a score of 10 on the Aldrete and Kroulik scale, she was discharged to the ward.

## DISCUSSION

Foreign body aspiration during intubation, although rare, requires rapid and effective management to prevent complications, as noted by Sands et al.<sup>2</sup> The team's readiness to identify the event and the availability of bronchoscopy were crucial for the successful removal of the fragment. This case illustrates the importance of continuous vigilance and preparedness for unexpected situations in anesthesia. Appropriate airway management and adequate mechanical ventilation following foreign body removal were fundamental for the patient's pulmonary recovery.

Although more common in children, aspiration can also occur in adults - particularly in the context of general anesthesia, deep sedation, or airway manipulation - as described by Farkas et al.<sup>3</sup> This report highlights the aspiration of the tip of an atomizer (Mucosal Atomization Device) during periglottic anesthesia, requiring bronchoscopic intervention for foreign body removal and subsequent orotracheal reintubation.

Several reports in the literature corroborate the possibility of similar iatrogenic events. In a review of 38 cases of foreign body aspiration in adults, Wang et al. found that most incidents occurred in patients with altered levels of consciousness or during anesthesia. The authors emphasize the effectiveness of bronchoscopy under general anesthesia, with a 97.4% success rate, as a safe and efficient approach for the removal of these foreign bodies.<sup>5</sup>

Similar situations have been described in other publications. Cho et al. reported the aspiration of a connector from an improvised nebulizer during general anesthesia in an asthmatic patient, highlighting the importance of attention when using modified or nonstandard equipment. Rapid bronchoscopic intervention allowed safe removal of the foreign body, preventing severe respiratory complications.<sup>6</sup> Mohnssen and Greggs described iatrogenic aspiration of components from respiratory devices, such as a washer from a closed suction system and the metallic tip of an intubation stylet, reinforcing the need for rigorous inspection of airway equipment.<sup>7</sup>

An alert issued by the United Kingdom's National Patient Safety Agency emphasizes that small loose or unidentified objects may inadvertently be introduced into the airway during intubation, ventilation, or anesthetic maneuvers. The agency recommends preventive measures such as prior inspection of all devices, replacement of equipment with unsecured moving parts, and keeping materials covered until use to prevent contamination and aspiration.<sup>1</sup>

This case reinforces the importance of standardizing devices used in anesthetic practice. Structural failure of a seemingly simple item—such as a lidocaine atomizer—can lead to a serious event. The actions taken by the team, including immediate communication, bronchoscopy, and guided reintubation, were decisive for the favorable outcome, with no airway injury and no compromise to the continuation of the surgical procedure.

Furthermore, this case highlights the relevance of preparing the anesthesia team for emergencies

of this nature, ensuring the availability of equipment and training in advanced airway management techniques. Active vigilance and the implementation of safety protocols, such as preoperative equipment checklists, should be reinforced to prevent such incidents.

## CONCLUSION

This report highlights a successful case of foreign body removal from the airway by bronchoscopy during anesthetic induction, followed by an uncomplicated respiratory recovery. Team coordination and the availability of resources were decisive for the favorable outcome. This case contributes to the literature by describing a rare event, emphasizing the importance of thorough inspection of medical devices and the prompt response of the multidisciplinary team when faced with adverse situations.

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## BURNOUT AMONG HEALTHCARE PROFESSIONALS: A LITERATURE REVIEW ON CAUSES AND COPING STRATEGIES

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### ABSTRACT

Healthcare professionals face various stressors, such as long working hours, limited resources, traumatic situations, and insufficient institutional support, factors that contribute to the development of burnout syndrome. This condition is characterized by physical, emotional, and mental exhaustion, depersonalization, and reduced personal and professional accomplishment. It is associated with a higher incidence of depression, suicidal ideation, absenteeism, occupational accidents, and a decline in the quality of care provided. This study conducted an integrative review aiming to identify the causes of burnout among healthcare professionals and analyze the coping strategies adopted. The research was carried out in the PubMed database between 2020 and 2025, using the descriptors "Burnout" and "Healthcare Professionals" in both Portuguese and English, from which eight articles were selected. The studies showed that ineffective coping strategies increase vulnerability to burnout, whereas individual interventions, such as cognitive-behavioral therapy, mindfulness, and relaxation techniques proved effective in reducing stress, strengthening interpersonal relationships, and improving well-being. However, there is a highlighted need for institutional measures that reorganize work routines, enhance organizational support, and promote practices that foster mental health, engagement, and resilience among healthcare professionals. Thus, integrating individual and organizational strategies is essential for the prevention and management of burnout.

**Keywords:** Burnout, Occupational stress, Mindfulness, Health personnel, Mental health.

### INTRODUCTION

Healthcare professionals face numerous challenges and stressors in their daily practice, such as time constraints, inadequate support, and frequent exposure to trauma, morbidity, and mortality. In addition, they often work with limited resources and insufficient infrastructure, which compromises their ability to provide the quality of care they strive to offer their patients.<sup>1</sup> These conditions can lead to burnout, depersonalization, and exhaustion.

Burnout syndrome is defined as a chronic response to workplace stress, characterized by

physical, mental, and emotional exhaustion that diminishes the sense of personal and professional accomplishment. Risk factors may include workplace conflicts and financial pressures, task overload, and communication or organizational problems. Some professions are more susceptible than others, and healthcare professionals—who are the focus of this work—face daily contact with severely ill individuals and stressful, urgent situations.<sup>2</sup>

Thus, healthcare professionals may be more susceptible to burnout due to exhausting workloads and situations that demand significant mental and emotional effort.

This syndrome is considered a complex and multidimensional problem because of its wide range of symptoms, such as depersonalization, anxiety, lack of motivation, mental fatigue, and diminished personal and professional fulfillment.<sup>2</sup>

Several studies demonstrate the relationship between burnout, depression, and suicidal behaviors, highlighting the interconnectedness of these conditions. Burnout syndrome has been consistently associated with a higher risk of suicidal ideation among healthcare professionals.<sup>3</sup>

Furthermore, among healthcare workers, burnout not only results in negative consequences for the individual's health but also leads to reduced patient safety, poorer quality of care, decreased professionalism, a higher incidence of workplace accidents, and increased absenteeism.<sup>4</sup>

Therefore, coping mechanisms are essential to manage stress and its associated factors.<sup>2</sup>

## OBJECTIVES

To identify and analyze the causes of burnout episodes among healthcare professionals.

To investigate coping strategies used to manage this syndrome.

## METHODOLOGY

Foreign Data collection was carried out in 2024 using the PubMed database, including studies indexed within a 5-year time frame (2020 to 2025). For this study, the following descriptors were used: "Burnout" and "Healthcare Professionals", along with their corresponding English terms. These descriptors were extracted from the Health Sciences Descriptors (DeCS) and combined to identify high-quality articles relevant to the study.

The inclusion criteria were: articles written in English, Spanish, or Portuguese; articles published between 2020 and 2025; and studies containing the descriptors listed above. Exclusion criteria included: undergraduate theses, simple abstracts, reviews, manuals, letters, news articles, editorials, case studies, and narrative literature reviews. A total of 6,976 studies were retrieved, of which 8 articles were selected for analysis.

## RESULTS AND DISCUSSION

Healthcare professionals are exposed to a wide range of stressors in the medical environment, encompassing both traditional stressors inherent to clinical practice (long working hours, night shifts, contact with patients' pain and suffering, caring for individuals with potentially fatal illnesses, among others) and those that have emerged more recently (shortage of human resources, an increasing number of patients with complex clinical conditions, diversification of healthcare financing models, rapid technological and regulatory changes, etc.). Continuous exposure to these stressors may lead to the development of burnout syndrome, professional withdrawal, depressive symptoms, and manifestations of aggressive behavior. The occurrence of burnout and the

consequent reduction in quality of life among physicians and nurses negatively affect individual well-being, professional performance, and the quality of patient care.<sup>5</sup>

Coping is defined as the set of cognitive and behavioral efforts directed at managing specific internal and/or external demands perceived as taxing or exceeding the individual's available resources. Psychological vulnerability to a given situation arises when a person lacks sufficient coping resources to manage it adequately, while simultaneously assigning high relevance to the perceived threat implicit in the potential consequences of ineffective management.<sup>2</sup>

A variety of strategies may be adopted to deal with stress, including cognitive or behavioral coping, cognitive or behavioral avoidance, emotion-focused coping, or the use of substances. From this perspective, burnout syndrome can be understood as a progressive condition resulting from the adoption of ineffective coping strategies, through which professionals attempt to shield themselves from stressors inherent to the work environment.<sup>2</sup>

Mindfulness can be defined as the process of intentionally directing one's attention to the present moment with curiosity, openness, and acceptance of each experience, without judgment. This state is achieved through an attitude characterized by acceptance, clarity, non-evaluative awareness, patience, authenticity, openness to the unexpected, kindness, care, and compassion toward one's lived experience. Such practice facilitates the transition from habitual patterns of automatic reactions to more conscious and deliberate responses, enabling a greater understanding of oneself and the surrounding environment.<sup>5</sup>

The use of mindfulness techniques helps reduce the so-called "autopilot mode," which is often associated with rumination—that is, the recurrence of negative thoughts about oneself related to the past or the future. Evidence shows that attributes related to mindfulness are associated with lower levels of stress, depression, and anxiety, while training in this approach enhances emotional awareness, increases the use of stress-coping strategies, improves judgment in diverse situations, and results in more effective responses to stimuli. Together, these elements can positively impact professional performance in healthcare settings and within medical education.<sup>5</sup>

Additionally, individual-level interventions using cognitive-behavioral therapy or other psychotherapeutic approaches, as well as relaxation techniques, may be considered effective in reducing stress and can be easily applied in the workplace.<sup>6</sup> A study conducted by Micali and Chiarella<sup>7</sup> in 2023 confirmed this by showing that healthcare professionals felt more attentive toward patients and reported better interpersonal relationships, improved problem-solving, and fewer workplace conflicts after using the described techniques.

## CONCLUSION

Despite the fact that burnout syndrome and its treatment are often approached at the individual level, it is essential that the issue be addressed as a broad organizational problem within healthcare institutions. While the acute management of burnout is indeed linked to the individual needs of the affected professional, this integrative review makes it clear that reducing the occurrence of the syndrome requires interventions that reshape how work is conducted on a systemic level. Burnout stems from causes that affect all - or at least the vast majority - of healthcare workers, meaning the solutions must also be collective and institutional.

In the short term, burnout can be effectively managed through simple strategies such as psychological support, art therapy, and moments of relaxation in the workplace. Similarly, scheduled retreat periods

- short vacations or time off - have shown significant benefit in both treating and preventing burnout. However, despite their effectiveness, such measures often clash with market-driven dynamics that aim for maximum productivity at minimal cost. Therefore, it is crucial that management bodies and institutional leaders engage in proactive planning to prevent burnout rather than merely respond to it.

This review highlights the urgent need to promote activities that mitigate burnout in healthcare work environments. Exhausting routines, high-pressure situations, and lack of self-care are key contributing factors. Consequently, initiatives that foster well-being, resilience, and group engagement have been shown to reduce burnout and improve overall workplace climate.

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## LATE DIAGNOSIS OF AORTIC DISSECTION (14 DAYS): ANESTHETIC CHALLENGES – CASE REPORT

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### ABSTRACT

**Introduction:** Acute type A aortic dissection (ATAAD) is a highly lethal cardiovascular emergency, with mortality exceeding 50% within the first 24 hours if untreated. Early diagnosis is critical for prognosis, yet atypical clinical presentations frequently delay both suspicion and confirmation. **Case report:** An 80-year-old male with a history of systemic arterial hypertension, hypothyroidism, dyslipidemia, chronic hepatitis C, and epilepsy was initially admitted to a regional hospital with nonspecific symptoms of nausea, vomiting, and abdominal pain. During hospitalization, he developed seizures and aspiration, receiving empirical antibiotic therapy. Fourteen days after symptom onset, chest CT angiography revealed an intimal flap in the ascending aorta, consistent with type A dissection, and he was transferred to a referral center. He underwent surgical repair under target-controlled total intravenous anesthesia (TIVA-TCI), with multimodal monitoring and massive transfusion due to associated coagulopathy. Initially, he remained stable, with early extubation and progressive weaning from vasopressors. On postoperative day six, however, he developed septic shock caused by *Pseudomonas aeruginosa*, followed by progressive multiorgan failure and death. **Discussion:** The atypical presentation of ATAAD, with gastrointestinal and neurological manifestations, delayed diagnosis. Survival beyond seven days without surgical intervention is uncommon and was likely related to clot formation sealing the false lumen. Anesthetic management required slow, titrated induction, stable maintenance with TIVA-TCI, judicious use of vasopressors, and aggressive correction of coagulopathy, underscoring the complexity of such cases. Despite technically successful surgical repair, the outcome was unfavorable due to late infectious complications, consistent with the high morbidity and mortality reported in elderly patients undergoing prolonged cardiopulmonary bypass. **Conclusion:** This case highlights the importance of early clinical suspicion in atypical presentations, the pivotal role of the anesthesiologist in hemodynamic and hemostatic management, and the need for individualized strategies to optimize survival in cases of type A aortic dissection with delayed diagnosis.

**Keywords:** Aortic dissection, Anesthesia, Cardiac tamponade, Blood coagulation, Shock septic.

### INTRODUCTION

Acute type A aortic dissection (ATAAD) is a rapidly progressive cardiovascular emergency associated with high lethality. It is characterized by a tear in the intimal layer of the aorta, usually in the ascending portion, allowing blood to enter the tunica media and form a false lumen.<sup>1</sup> Its incidence ranges from 5

to 30 cases per million inhabitants per year, with an estimated mortality of 1–2% per hour during the first 48 hours if untreated, reaching up to 50% within the first 24 hours.<sup>2,3</sup> The Stanford classification is the most widely used method for anatomical stratification, with type A defined as any dissection involving the ascending aorta, regardless of distal extension.<sup>4</sup>

Clinically, ATAAD typically presents with sudden, severe chest pain, often described as tearing or stabbing, which may radiate to the back, abdomen, or limbs, depending on the extent of the dissection. Many patients have a history of systemic arterial hypertension, a risk factor present in up to 80% of cases. Clinical presentation may be variable and nonspecific, ranging from acute neurological deficits, lower limb ischemia, and syncope to signs of cardiac tamponade or shock. Due to symptom overlap with other cardiovascular emergencies, the main differential diagnoses include acute coronary syndrome (ACS), pulmonary embolism, stroke, and ruptured aortic aneurysm. Diagnostic accuracy depends on a high index of clinical suspicion and the early use of imaging studies, particularly contrast-enhanced computed tomography, which is considered the gold standard for confirming the diagnosis and defining the extent of aortic involvement.<sup>5</sup> Early diagnosis is essential and may be supported by laboratory markers such as D-dimer, troponin, and NT-proBNP, in addition to imaging modalities such as contrast-enhanced computed tomography or transesophageal echocardiography.<sup>6</sup>

Cases of delayed diagnosis, such as the one reported herein, are rare and are usually associated with atypical clinical evolution or failures in the initial diagnostic workup. Survival beyond seven days without intervention is uncommon, and partial chronicity may lead to complications such as aortic rupture, aortic valve insufficiency, cardiac tamponade, and visceral or cerebral malperfusion syndromes.<sup>7,8</sup> Anesthetic management in ATAAD is complex, requiring strict blood pressure control, neurological protection, and specific strategies during cardiopulmonary bypass and circulatory arrest, including hypothermia and cerebral perfusion monitoring.<sup>9</sup> The presence of consumptive coagulopathy, inherent to the dissection process itself, is further exacerbated by cardiopulmonary bypass, necessitating careful replacement of coagulation factors and fibrinogen.<sup>5</sup> In addition, patients with ongoing dissection may develop progressive organ dysfunction (renal, respiratory, neurological), which makes anesthetic planning even more challenging, particularly in the setting of delayed diagnosis.<sup>2,6</sup> In this context, we report the case of a patient with ATAAD diagnosed 14 days after symptom onset, with atypical clinical evolution and complex anesthetic management, highlighting the strategies employed and the challenges encountered.

## CASE REPORT

The patient was an 80-year-old male, 1.63 m tall and weighing 63 kg, with a medical history of systemic arterial hypertension, hypothyroidism, dyslipidemia, chronic hepatitis C, and epilepsy. His regular medications included olmesartan/hydrochlorothiazide 40/12.5 mg, amlodipine 5 mg, metoprolol 25 mg, levothyroxine 50 mcg, rosuvastatin 10 mg, and levetiracetam XR 500 mg. He had no known drug allergies.

The clinical course began 15 days prior to definitive hospitalization, when the patient sought medical care at a hospital in the southwestern region of Goiânia with nonspecific symptoms, including nausea, vomiting, and diffuse abdominal pain. Initial diagnostic hypotheses included urinary tract or gastrointestinal infection, and conservative clinical management was initiated. During hospitalization, the patient developed a generalized tonic-clonic seizure and was transferred to the intensive care unit (ICU), where he remained under neurological surveillance and supportive care.

Approximately seven days after admission, the patient experienced global clinical deterioration,

with a new seizure episode and an event of bronchoaspiration. In the context of an associated respiratory infectious condition, empirical antibiotic therapy with ceftriaxone and clindamycin was initiated. Due to persistent chest pain and progression to dyspnea, further investigation with chest computed tomography angiography was performed, which demonstrated a flap in the ascending aorta, highly suggestive of acute type A aortic dissection. The diagnosis was confirmed by an official radiology report, and the patient was immediately transferred to the Hospital do Coração de Goiás, a referral center for high-complexity cardiac surgery.

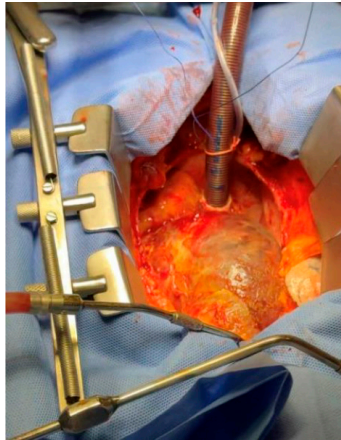
Upon admission to the ICU of the receiving institution, the patient was in poor general condition but conscious and oriented, breathing spontaneously with nasal cannula oxygen supplementation. Vital signs were abnormal, with a blood pressure of 182 × 110 mmHg and a heart rate of 110 beats per minute. Initial stabilization was undertaken, and surgery was scheduled for the following morning under a controlled urgent setting.

In the operating room, the patient was transferred on a stretcher with active thermal blanket support and underwent standard monitoring, including continuous electrocardiography, pulse oximetry, and noninvasive blood pressure measurement. A large-bore peripheral venous access (16G) was obtained in the left upper limb under ultrasound guidance. Right radial arterial cannulation was performed with an 18G catheter for continuous invasive blood pressure monitoring. Airway assessment was not performed prior to anesthetic induction. Definitive central venous access was established by the surgical team. Additional monitoring included anesthetic depth sensors, capnography, and a nasal temperature probe, all placed after tracheal intubation.

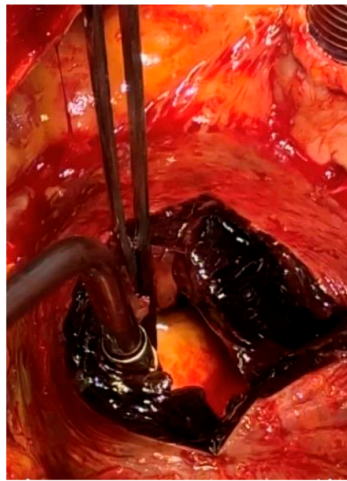
Antibiotic prophylaxis was administered with cefuroxime 1.5 g, with an intraoperative reinforcement dose of 750 mg. Anesthetic induction was performed gradually with strict hemodynamic control, using sufentanil 30 mcg, midazolam 15 mg, and rocuronium 50 mg. Orotracheal intubation was achieved using videolaryngoscopy (Cormack–Lehane grade 2A), with placement of an 8.0-mm endotracheal tube on the first attempt, without complications. Anesthetic maintenance was provided with propofol using a target-controlled infusion system (TIVA-TCI), oxygen at 2 L/min, and intermittent boluses of rocuronium, midazolam, and sufentanil as clinically indicated.

As intraoperative adjuvants, hydrocortisone 500 mg, dexamethasone 10 mg, calcium gluconate (one ampoule), epsilon-aminocaproic acid 4 g, vitamin C (four ampoules), and metaraminol as needed for blood pressure support were administered.

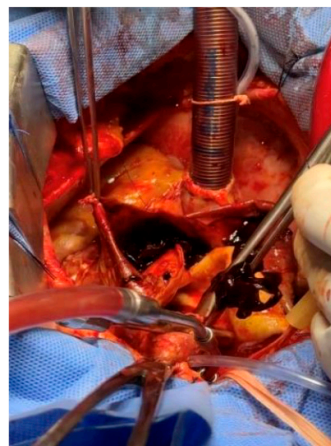
During the surgical procedure, cardiac tamponade was identified (Figure 1), along with a large clot at the site of the dissection (Figures 2 and 3), which, according to the surgical team, was a determining factor in containing bleeding and preserving the patient's life until transfer and definitive repair of the aortic dissection (Figure 4). Reconstruction of the ascending aorta was performed using cardiopulmonary bypass (CPB), with CPB and aortic cross-clamp times of 240 and 149 minutes, respectively. The total surgical time was 8.5 hours.



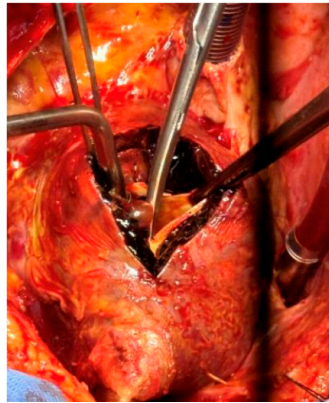
**Figure 1.** Tamponed pericardium.



**Figure 2.** Formation of clots near aortic dissection.



**Figure 3.** Removal of clots near an aortic dissection.



**Figure 4.** Access to the dissected aorta.

Total intraoperative urine output was 400 mL, with a positive fluid balance of 1,662 mL. The estimated blood balance was negative by 800 mL, and volume replacement was performed with 4 L of Plasma-Lyte®, seven units of leukoreduced filtered packed red blood cells, four units of fresh frozen plasma, nine units of cryoprecipitate, and one pool of leukoreduced random donor platelets (five units).

At the end of the procedure, the patient was transferred intubated to the intensive care unit (ICU), under assisted mechanical ventilation and continuous infusion of vasoactive agents: dobutamine (2.64 mcg/kg/min) and norepinephrine (0.17 mcg/kg/min), with hemodynamic stability and light sedation (RASS –1).

The patient remained intubated for 8.5 hours in the immediate postoperative period and was successfully extubated in a gradual manner, with maintenance of vasoactive amines and subsequent weaning according to clinical response. He progressed satisfactorily until postoperative day six, when he developed hemodynamic instability, decreased level of consciousness, and signs suggestive of septic shock. He was reintubated, and intensive supportive care was reinstated. Subsequent cultures isolated *Pseudomonas aeruginosa*, and targeted antimicrobial therapy was initiated. Despite the measures adopted, the patient progressed to progressive organ failure and died nine days after surgery.

## DISCUSSION

ATAAD represents a cardiovascular emergency with high lethality, in which survival is intrinsically linked to the rapidity of diagnosis and surgical intervention. The delayed clinical presentation observed in the present case, occurring 14 days after symptom onset, is a rare and atypical finding. The literature reports an early mortality rate for untreated patients that may reach 50% within the first 24 hours and exceed 80% within two weeks, underscoring the exceptional nature of this patient's survival over such a prolonged period.<sup>9</sup>

The patient's initial presentation, which included gastrointestinal and neurological symptoms (seizure episodes), diverted diagnostic attention away from cardiovascular causes. This observation is consistent with extensive literature describing the atypical clinical presentation of ATAAD, particularly in elderly patients and those with comorbidities, which may include mesenteric ischemia, focal neurological deficits, or absence of classic chest pain.<sup>1,9</sup> In such scenarios, computed

tomography angiography of the chest and abdomen emerges as an indispensable diagnostic tool. The incorporation of biomarkers such as D-dimer and troponins, although useful for initial screening, does not replace imaging confirmation.<sup>2</sup>

The patient's hemodynamic stability, maintained for a prolonged period prior to surgical intervention, suggests the formation of a clot within the false lumen, acting as a natural "plug" that temporarily limited progression of the dissection. However, such stability is inherently precarious and does not eliminate the need for immediate surgical correction, given the imminent risk of rupture.<sup>7</sup>

From an anesthetic standpoint, the management of patients with ATAAD poses significant challenges. Perioperative care requires extreme caution to avoid abrupt changes in blood pressure that could exacerbate aortic injury. A slow, titrated anesthetic induction using hypnotic agents, potent opioids, and neuromuscular blockers proved effective in preserving hemodynamic stability in the present case. Anesthetic maintenance with TIVA-TCI combined with vasopressor support was appropriate for hemodynamic control and protection of target organs.<sup>4</sup>

Invasive and multimodal monitoring, including cerebral oximetry, capnography, and anesthetic depth monitoring, was crucial to guide hemodynamic management and ensure adequate tissue perfusion, particularly during the pre-cardiopulmonary bypass (CPB) phase. Judicious use of vasopressors, such as metaraminol, was essential to maintain arterial pressure at levels sufficient to ensure perfusion of vital organs, including the brain and kidneys.<sup>8</sup>

Consumptive coagulopathy, a common pathophysiological phenomenon in ATAAD, is exacerbated by CPB, requiring rigorous hemostatic management. Exposure of the aortic subendothelium and platelet activation induce coagulation disturbances that necessitate volume resuscitation and replacement of blood components guided by laboratory and clinical parameters.<sup>5</sup> In the present case, the need for massive transfusion of packed red blood cells, plasma, cryoprecipitate, and platelets, in addition to the administration of aminocaproic acid, underscores the severity of the associated hemostatic disorder.

Despite an initially favorable recovery and early extubation, the patient developed septic shock due to *Pseudomonas aeruginosa* on postoperative day six, resulting in multiple organ failure and death. This outcome is consistent with the literature, which identifies late septic shock as one of the leading causes of in-hospital mortality following surgical repair of ATAAD.<sup>2</sup> Factors such as advanced age and prolonged cardiopulmonary bypass time may have contributed to postoperative morbidity and mortality.

## CONCLUSION

The present case highlights the importance of maintaining a high index of clinical suspicion for the diagnosis of acute type A aortic dissection in atypical and delayed presentations. This report reinforces the strategic role of the anesthesiologist throughout all phases of perioperative care, emphasizing the need for individualized planning, rigorous monitoring, and a dynamic approach to mitigate risks and optimize patient survival in such a challenging condition.

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## RETROSPECTIVE STUDY OF THE INCIDENCE OF SYPHILIS AND ITS EPIDEMIOLOGICAL PROFILE ASSOCIATED WITH THE INCIDENCE OF FETAL DEATH 2013–2023

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### ABSTRACT

**Introduction:** Maternal syphilis remains a major public health concern worldwide and is strongly associated with adverse pregnancy outcomes. Untreated *Treponema pallidum* infection may lead to spontaneous abortion, preterm birth, stillbirth, neonatal death, and congenital syphilis. **Objective:** To analyze the incidence of syphilis in pregnant women and its association with fetal death, as well as to characterize the epidemiological profile of this population in Brazil, the state of Goiás, and the municipality of Anápolis from 2013 to 2023. **Methodology:** A retrospective, observational, descriptive, and analytical epidemiological study was conducted using secondary data from official health information systems. Reported cases of syphilis in pregnant women and fetal deaths were analyzed through rate calculations and temporal trend assessment. **Results:** An increasing trend in syphilis incidence among pregnant women was identified during the study period, accompanied by a rise in congenital syphilis cases and associated fetal deaths. Previous studies demonstrate that untreated maternal syphilis is strongly associated with adverse pregnancy outcomes, particularly stillbirth and perinatal mortality. **Conclusion:** Maternal syphilis remains a preventable condition, and its persistence reflects gaps in prenatal screening, timely treatment, and follow-up care. Strengthening early diagnosis, adequate treatment, and surveillance strategies is crucial to reduce fetal deaths and prevent vertical transmission.

**Keywords:** Maternal syphilis, Congenital syphilis, Fetal death, Epidemiology, Maternal and child health.

### INTRODUCTION

Syphilis is a sexually transmitted bacterial infection that is preventable and curable. In 2022, cases increased by more than 1 million, reaching a total of 8 million worldwide. The Americas currently face the highest global incidence, with 3.37 million cases (or 6.5 cases per 1,000 people), accounting for 42% of all new cases<sup>1</sup>.

Syphilis is a curable, exclusively human sexually transmitted infection (STI) caused by the bacterium *Treponema pallidum*. Although infection by *Treponema pallidum* through blood transfusion or

contaminated piercing materials is possible, the main and most significant routes of transmission are sexual (genital, oral, and anal) and vertical transmission, which may result in fetal death or congenital syphilis. The disease may present with multiple clinical manifestations and different stages (primary, secondary, latent, and tertiary syphilis).<sup>2-3</sup>

Syphilis during pregnancy is associated with preterm birth, spontaneous abortion, stillbirth, non-immune fetal hydrops, perinatal death, and two characteristic clinical syndromes: early and late congenital syphilis. In addition, the placenta of infants with congenital syphilis is often enlarged, thickened, and pale. In Brazil, syphilis in pregnant women is a notifiable disease, and epidemiological data indicate a growing trend in cases in recent years.<sup>4</sup>

The diagnosis of congenital syphilis may be challenging due to the presence of maternal antibodies in newborns; therefore, diagnosis generally focuses on maternal syphilis. Serological testing for syphilis is recommended at the first prenatal visit, at 28 weeks of gestation, and at the time of delivery. Screening of pregnant women and early treatment of syphilis can significantly reduce infant morbidity and mortality.<sup>5</sup>

Therefore, the aim of this study is to analyze the incidence of syphilis in pregnant women and its association with fetal death, as well as to characterize the epidemiological profile of this population during the period from 2013 to 2023 in Brazil, Goiás, and Anápolis.

## METHODOLOGY

A cross-sectional study was conducted using public data from TabNet/DATASUS, an online tool developed by the Brazilian Ministry of Health that allows rapid and interactive access to epidemiological data on syphilis cases (acquired syphilis, syphilis in pregnant women, and congenital syphilis) recorded in the Notifiable Diseases Information System (SINAN) throughout Brazil. The platform generates tables, graphs, and maps to support situation analysis, planning, and management of public health actions, and is essential for understanding the magnitude of the disease and monitoring syphilis control policies.

Data were filtered for the following indicators: cases and detection rates (per 1,000 live births) of syphilis in pregnant women by year of diagnosis; cases of syphilis in pregnant women according to gestational age by year of diagnosis; cases of syphilis in pregnant women according to clinical classification by year of diagnosis; cases of congenital syphilis in children under one year of age and their incidence rates; and deaths due to congenital syphilis in children under one year of age according to year of death. Data were analyzed for Brazil, the state of Goiás, and the municipality of Anápolis.

The analysis period ranged from January 2013 to December 2023. Some data related to 2024 had not yet been consolidated in the system at the time of analysis.

Regarding ethical considerations, publicly available data (open-access sources such as DATASUS) do not require approval from a Research Ethics Committee (CEP/CONEP) when they do not allow identification of individuals, in accordance with guidelines that complement Resolution No. 466/12, such as Resolutions No. 510/2016 and No. 674/2022, as there is no direct involvement of or risk to participants.

## RESULTS

The findings of this retrospective study reveal a concerning trend of a significant increase in the incidence of syphilis among pregnant women across all three geographic levels studied during the period from 2013 to 2023.

**Table 1.** Cases and detection rate (per 1,000 live births) of syphilis among pregnant women by year of diagnosis in Brazil

| Syphilis in Pregnant Women | Total   | 2013   | 2014   | 2015   | 2016   | 2017   | 2018   | 2019   | 2020   | 2021   | 2022   | 2023   |
|----------------------------|---------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| Cases                      | 608,435 | 20,923 | 26,637 | 32,795 | 38,319 | 49,864 | 63,448 | 64,619 | 66,151 | 75,373 | 84,195 | 86,111 |
| Detection rate             | -       | 7.2    | 8.9    | 10.9   | 13.4   | 17.1   | 21.5   | 22.7   | 24.2   | 28.2   | 32.9   | 34     |

**Table 2.** Cases of syphilis among pregnant women according to gestational age by year of diagnosis in Brazil

| Gestational age           | Total   | 2013      | 2014      | 2015   | 2016   | 2017       | 2018   | 2019   | 2020   | 2021       | 2022   | 2023   |
|---------------------------|---------|-----------|-----------|--------|--------|------------|--------|--------|--------|------------|--------|--------|
| 1 <sup>st</sup> trimester | 247,037 | 5,36<br>1 | 7,69<br>8 | 10,567 | 14,222 | 19,82<br>5 | 24,724 | 25,051 | 27,532 | 31,83<br>1 | 38,805 | 41,421 |
| 2 <sup>nd</sup> trimester | 145,749 | 6,64<br>8 | 8,16<br>5 | 9,763  | 11,014 | 13,90<br>5 | 15,929 | 15,549 | 14,339 | 15,57<br>9 | 17,237 | 17,621 |
| 3 <sup>rd</sup> trimester | 179,650 | 7,37<br>2 | 8,87<br>3 | 10,481 | 10,770 | 13,41<br>3 | 18,830 | 19,474 | 19,695 | 22,63<br>0 | 24,337 | 23,775 |
| Gestational age unknown   | 34,913  | 1,54<br>2 | 1,90<br>1 | 1,980  | 2,238  | 2,556      | 3,676  | 4,371  | 4,468  | 5,202      | 3,733  | 3,246  |
| Unknown                   | 787     | -         | -         | 3      | 54     | 87         | 90     | 174    | 117    | 131        | 83     | 48     |

**Table 3.** Cases of syphilis among pregnant women according to clinical classification by year of diagnosis in Brazil

| Clinical classification | Total   | 2013      | 2014      | 2015       | 2016       | 2017       | 2018       | 2019       | 2020       | 2021       | 2022       | 2023       |
|-------------------------|---------|-----------|-----------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| Primary syphilis        | 160,907 | 6,79<br>8 | 8,51<br>3 | 10,10<br>6 | 11,15<br>9 | 14,10<br>7 | 16,78<br>4 | 15,87<br>5 | 15,98<br>8 | 19,73<br>3 | 21,12<br>0 | 20,72<br>4 |
| Secondary syphilis      | 28,042  | 1,30<br>7 | 1,66<br>3 | 1,901      | 2,160      | 2,620      | 3,206      | 3,061      | 2,661      | 3,162      | 3,171      | 3,130      |
| Tertiary syphilis       | 54,865  | 2,20<br>0 | 3,00<br>3 | 3,501      | 4,114      | 5,389      | 6,127      | 5,305      | 5,476      | 6,113      | 7,029      | 6,608      |
| Latent syphilis         | 224,552 | 4,42<br>3 | 6,00<br>9 | 8,103      | 10,64<br>0 | 15,21<br>0 | 21,77<br>5 | 25,05<br>5 | 27,76<br>0 | 29,71<br>5 | 35,87<br>1 | 39,99<br>1 |
| Unknown                 | 140,069 | 6,19<br>5 | 7,44<br>9 | 9,184      | 10,24<br>6 | 12,53<br>8 | 15,55<br>6 | 15,32<br>3 | 14,26<br>6 | 16,65<br>0 | 17,00<br>4 | 15,65<br>8 |

**Table 4.** Cases of congenital syphilis in children under one year of age and incidence rate (per 1,000 live births) by year of diagnosis in Brazil

|                            | Total   | 2013  | 2014  | 2015  | 2016  | 2017  | 2018  | 2019  | 2020  | 2021  | 2022  | 2023  |
|----------------------------|---------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| <b>Congenital syphilis</b> | 251,791 | 14,11 | 16,49 | 19,92 | 21,55 | 25,36 | 26,85 | 25,40 | 23,44 | 27,10 | 26,51 | 25,01 |
|                            |         | 7     | 3     | 2     | 3     | 9     | 2     | 6     | 3     | 8     | 7     | 1     |
| <b>Congenital syphilis</b> | -       | 4.9   | 5.5   | 6.6   | 7.5   | 8.7   | 9.1   | 8.9   | 8.6   | 10.1  | 10.4  | 9.9   |

**Table 5.** Deaths due to congenital syphilis in children under one year of age by year of death in Brazil

| Deaths due to congenital syphilis in children under one year of age | Total | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 | 2021 | 2022 | 2023 |
|---|-------|------|------|------|------|------|------|------|------|------|------|------|
| <b>Cases</b>  | 2,212 | 160  | 174  | 235  | 195  | 222  | 261  | 178  | 192  | 192  | 207  | 196  |

**Table 6.** Cases and detection rate (per 1,000 live births) of syphilis among pregnant women by year of diagnosis in Goiás

| Syphilis in Pregnant Women | Total  | 2013 | 2014 | 2015  | 2016  | 2017  | 2018  | 2019  | 2020  | 2021  | 2022  | 2023  |
|----------------------------|--------|------|------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| <b>Cases</b>               | 19,835 | 815  | 917  | 1,034 | 1,097 | 1,518 | 2,011 | 2,119 | 2,059 | 2,363 | 2,818 | 3,084 |
| <b>Detection rate</b>      | -      | 8.6  | 9.2  | 10.3  | 11.5  | 15.6  | 20.3  | 22    | 22.2  | 26    | 31.4  | 33.6  |

**Table 7.** Cases of syphilis among pregnant women according to gestational age by year of diagnosis in Goiás

| Gestational age                 | Total | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 | 2021 | 2022  | 2023  |
|---------------------------------|-------|------|------|------|------|------|------|------|------|------|-------|-------|
| <b>1<sup>st</sup> trimester</b> | 6,265 | 125  | 168  | 203  | 258  | 411  | 630  | 673  | 695  | 791  | 1,014 | 1,297 |
| <b>2<sup>nd</sup> trimester</b> | 7,501 | 332  | 382  | 392  | 407  | 643  | 690  | 732  | 655  | 757  | 830   | 835   |
| <b>3<sup>rd</sup> trimester</b> | 7,011 | 301  | 326  | 407  | 391  | 425  | 646  | 655  | 652  | 750  | 905   | 878   |
| <b>Gestational age unknown</b>  | 713   | 57   | 41   | 32   | 41   | 39   | 45   | 59   | 57   | 65   | 69    | 74    |
| <b>Unknown</b>                  | -     | -    | -    | -    | -    | -    | -    | -    | -    | -    | -     | -     |

**Table 8.** Cases of syphilis among pregnant women according to clinical classification by year of diagnosis in Goiás

| Clinical classification | Total | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 | 2021 | 2022  | 2023  |
|-------------------------|-------|------|------|------|------|------|------|------|------|------|-------|-------|
| Primary syphilis        | 5,638 | 288  | 254  | 298  | 252  | 324  | 548  | 557  | 568  | 671  | 843   | 1,035 |
| Secondary syphilis      | 3,125 | 126  | 157  | 183  | 221  | 288  | 359  | 358  | 332  | 442  | 397   | 262   |
| Tertiary syphilis       | 1,244 | 49   | 94   | 83   | 79   | 198  | 118  | 117  | 108  | 132  | 153   | 113   |
| Latent syphilis         | 6,604 | 129  | 236  | 291  | 373  | 464  | 665  | 721  | 712  | 773  | 1,073 | 1,167 |
| Unknown                 | 3,224 | 223  | 176  | 179  | 172  | 244  | 321  | 366  | 339  | 345  | 352   | 507   |

**Table 9.** Cases of congenital syphilis in children under one year of age and incidence rate (per 1,000 live births) by year of diagnosis in Goiás

| Congenital syphilis in children under one year of age | Total | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 | 2021 | 2022 | 2023 |
|---|-------|------|------|------|------|------|------|------|------|------|------|------|
| Cases   | 5,762 | 239  | 343  | 393  | 425  | 446  | 550  | 608  | 563  | 608  | 785  | 802  |
| Detection rate  | -     | 2.5  | 3.4  | 3.9  | 4.4  | 4.6  | 5.6  | 6.3  | 6.1  | 6.7  | 8.7  | 8.7  |

**Table 10.** Deaths due to congenital syphilis in children under one year of age by year of death in Goiás

| Deaths due to congenital syphilis in children under one year of age | Total | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 | 2021 | 2022 | 2023 |
|---|-------|------|------|------|------|------|------|------|------|------|------|------|
| Cases   | 67    | 4    | 5    | 2    | 3    | 7    | 6    | 4    | 8    | 8    | 11   | 9    |

**Table 11.** Cases and detection rate (per 1,000 live births) of syphilis among pregnant women by year of diagnosis in Anápolis

| Syphilis in Pregnant Women | Total | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 | 2021 | 2022 | 2023 |
|----------------------------|-------|------|------|------|------|------|------|------|------|------|------|------|
| Cases                      | 1,340 | 65   | 52   | 59   | 76   | 84   | 128  | 153  | 113  | 175  | 184  | 251  |
| Detection rate             | -     | 11.1 | 8.5  | 9.3  | 12.4 | 13.5 | 21   | 25.2 | 20.1 | 30.9 | 32.2 | 43.1 |

**Table 12.** Cases of syphilis among pregnant women according to gestational age by year of diagnosis in Anápolis

| Gestational age           | Total | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 | 2021 | 2022 | 2023 |
|---------------------------|-------|------|------|------|------|------|------|------|------|------|------|------|
| 1 <sup>st</sup> trimester | 447   | 16   | 7    | 18   | 26   | 30   | 50   | 48   | 42   | 34   | 68   | 108  |
| 2 <sup>nd</sup> trimester | 405   | 21   | 19   | 18   | 24   | 28   | 36   | 46   | 41   | 57   | 50   | 65   |
| 3 <sup>rd</sup> trimester | 431   | 24   | 24   | 22   | 24   | 26   | 41   | 41   | 22   | 66   | 63   | 78   |
| Gestational age unknown   | 57    | 4    | 2    | 1    | 2    | -    | 1    | 18   | 8    | 18   | 3    | -    |
| Unknown                   | -     | -    | -    | -    | -    | -    | -    | -    | -    | -    | -    | -    |

**Table 13.** Cases of syphilis among pregnant women according to clinical classification by year of diagnosis in Anápolis

| Clinical classification | Total | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 | 2021 | 2022 | 2023 |
|-------------------------|-------|------|------|------|------|------|------|------|------|------|------|------|
| Primary syphilis        | 585   | 32   | 20   | 6    | 16   | 29   | 46   | 39   | 49   | 95   | 94   | 159  |
| Secondary syphilis      | 47    | -    | 2    | 3    | 1    | 8    | 5    | 6    | 4    | 1    | 12   | 5    |
| Tertiary syphilis       | 28    | 1    | -    | -    | 2    | 1    | 6    | 3    | -    | 3    | 8    | 4    |
| Latent syphilis         | 584   | 25   | 25   | 46   | 55   | 43   | 69   | 61   | 44   | 75   | 63   | 78   |
| Unknown                 | 96    | 7    | 5    | 4    | 2    | 3    | 2    | 44   | 16   | 1    | 7    | 5    |

**Table 14.** Cases of congenital syphilis in children under one year of age and incidence rate (per 1,000 live births) by year of diagnosis in Anápolis

| Congenital syphilis in children under one year of age | Total | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 | 2021 | 2022 | 2023 |
|---|-------|------|------|------|------|------|------|------|------|------|------|------|
| Cases   | 354   | 18   | 24   | 10   | 28   | 23   | 46   | 42   | 16   | 32   | 48   | 67   |
| Detection rate  | -     | 3.1  | 3.9  | 1.6  | 4.6  | 3.7  | 7.6  | 6.9  | 2.8  | 5.6  | 8.4  | 11.5 |

**Table 15.** Deaths due to congenital syphilis in children under one year of age by year of death in Anápolis

| Deaths due to congenital syphilis in children under one year of age | Total | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 | 2021 | 2022 | 2023 |
|---|-------|------|------|------|------|------|------|------|------|------|------|------|
| Cases   | 5     | -    | -    | -    | -    | -    | 2    | 1    | -    | -    | 2    | -    |

## DISCUSSION

The 286% increase in the number of syphilis cases among pregnant women in Anápolis between 2013 and 2023, with a rise in the detection rate from 11.1 to 43.1 per 1,000 live births, reflects an epidemic of significant proportions. This growth is particularly concerning when considered in the context that the detection rate in Anápolis in 2023 is 28% higher than that of the state of Goiás and 27% higher than the national rate, positioning the municipality as a hotspot for syphilis among pregnant women. Gómez et al., in a meta-analysis of studies on maternal syphilis, demonstrated that similar increases in the incidence of syphilis in pregnant women are associated with significant adverse outcomes, including a two- to threefold increase in fetal and neonatal mortality rates.<sup>6</sup> The accelerated growth pattern observed in Anápolis, particularly between 2020 and 2023 (36.6% per year), suggests that specific local factors may be contributing to this epidemic, differentiating it from the national pattern.

The volatility observed in congenital syphilis data, with significant reductions in 2015 (–58.3%) and 2020 (–61.9%), followed by substantial increases, reflects variations in screening and diagnostic practices. Nevertheless, the overall increase of 272% in congenital syphilis cases between 2013 and 2023 (rising from 18 to 67 cases) demonstrates that, despite annual fluctuations, the general trend is one of consistent growth. The detection rate of congenital syphilis in Anápolis in 2023 (11.5 per 1,000 live births) is 32% higher than the state rate and 16% higher than the national rate. Qin et al., in a meta-analysis study on estimates of adverse outcomes in pregnant women with syphilis, reported that each 1% increase in the prevalence of syphilis among pregnant women is associated with an approximately 0.3% increase in the incidence of congenital syphilis, suggesting that the increases observed in Anápolis are likely to result in sustained pressure on local health systems.<sup>7</sup>

A particularly notable finding of this study is the distinct epidemiological pattern observed in Anápolis, characterized by a predominance of primary syphilis (41.3% of cases in 2023, increasing to 63.3% when considering only cases with known clinical classification). This proportion is significantly higher than that observed at the state (28.4%) and national (26.4%) levels, suggesting a different pattern of clinical presentation. The exponential growth of primary syphilis in Anápolis, with an increase of 397% between 2013 and 2023 (from 32 to 159 cases), represents the largest increase among all clinical classifications, indicating important changes in local epidemiological characteristics.

This pattern contrasts with the predominance of latent syphilis observed in Goiás (33.2%) and Brazil (36.9%). Primary syphilis, characterized by the presence of a genital ulcer, is more easily diagnosed clinically and may indicate better access to healthcare services or greater awareness of symptoms. Alternatively, it may reflect differences in screening practices or in the population served. Schlueter et al., in a review on the clinical management of syphilis in pregnant women, emphasized that early identification of primary syphilis offers critical opportunities for the prevention of vertical transmission, as appropriate penicillin treatment at any stage of pregnancy is highly effective<sup>8</sup>. The pattern observed in Anápolis may therefore represent an opportunity for early intervention, provided that healthcare systems are adequately prepared for diagnosis and treatment.

The distribution of cases by gestational age in Anápolis is more balanced across trimesters (first trimester 33.4%, second trimester 30.2%, third trimester 32.2%) compared with Goiás and Brazil. This more uniform pattern may reflect more consistent access to prenatal care throughout pregnancy. Particularly noteworthy is the 575% increase in the number of cases diagnosed in the first trimester between 2013 and 2023, the largest increase among all trimesters, suggesting a significant improvement in early prenatal screening. This finding is positive, as early diagnosis

allows timely treatment and reduces vertical transmission.

De Santis et al., in a study on syphilis during pregnancy, demonstrated that diagnosis and treatment in the first trimester reduce the rate of vertical transmission from approximately 90% to less than 10%, whereas diagnosis in the third trimester still offers protection, albeit with reduced effectiveness<sup>9</sup>. The pattern observed in Anápolis, with accelerated growth in first-trimester diagnoses, suggests that prenatal screening strategies are functioning adequately in identifying cases early. The excellent quality of documentation in Anápolis (only 4.3% with unknown gestational age) further facilitates epidemiological analyses and intervention planning.

Despite the high incidence of syphilis among pregnant women and congenital syphilis in Anápolis, the absolute number of deaths due to congenital syphilis is notably low. During the period from 2013 to 2023, only five deaths due to congenital syphilis were recorded in Anápolis, with an average of 0.45 deaths per year. The ratio of deaths to congenital syphilis cases was 1.4%, slightly higher than the state (1.2%) and national (0.8%) ratios, but still representing a relatively low proportion. Importantly, no deaths due to congenital syphilis were reported in 2023, indicating that access to treatment for newborns with congenital syphilis in Anápolis is adequate.

This finding is encouraging and suggests that, despite the high incidence of maternal and congenital syphilis, healthcare systems in Anápolis are successfully identifying and appropriately treating affected newborns. Nascimento et al., in a study on pregnancies complicated by maternal syphilis, reported that mortality from congenital syphilis is preventable through adequate diagnosis and treatment, and that most deaths occur in contexts of limited access to care<sup>10</sup>. The pattern observed in Anápolis therefore likely reflects adequate access to neonatal diagnosis and treatment, despite persistent challenges in preventing vertical transmission.

A concerning finding is that while the number of syphilis cases among pregnant women increased by 286%, the number of congenital syphilis cases increased by 272%, a much closer proportion than that observed in Goiás or Brazil. This suggests that in Anápolis, improvements in the screening of pregnant women did not result in a proportional reduction in vertical transmission. This pattern may indicate that, despite improved diagnosis of pregnant women, adequate and timely treatment is not being guaranteed in all cases, or that barriers to treatment adherence persist. Strategies to ensure complete and timely treatment of all pregnant women diagnosed with syphilis, as well as screening and treatment of sexual partners, are essential to reduce vertical transmission.

## CONCLUSION

The 286% increase in the number of syphilis cases among pregnant women in Anápolis between 2013 and 2023 is alarming. Primary syphilis is the predominant clinical form (63.3%), differing from Goiás and Brazil, where latent syphilis predominates, suggesting a distinct epidemiological pattern. Despite the increase in congenital syphilis cases (272%), mortality due to congenital syphilis in Anápolis remains very low (five deaths over 11 years), indicating that access to treatment for affected newborns is adequate. The implementation of robust strategies for universal screening, education on STI prevention, appropriate treatment with penicillin, treatment of sexual partners, and investigation of local factors facilitating transmission are essential to control the syphilis epidemic in Anápolis and to reduce the incidence of congenital syphilis and its adverse outcomes.

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## IMPACT OF EARLY INTERVENTIONS ON THE DEVELOPMENT OF CHILDREN WITH AUTISM SPECTRUM DISORDER

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### ABSTRACT

**Introduction:** Autism spectrum disorder (ASD) can be defined as a complex developmental disorder with multiple etiologies and varying degrees of severity. The main characteristics of ASD are persistent impairments in social interaction and reciprocal communication, along with restricted and repetitive patterns of behavior, activities, and interests. Furthermore, symptoms appear from early childhood and may impair or limit the individual's daily functioning. **Objective:** To establish the importance of early interventions in children with ASD, which contribute to a better prognosis. **Method:** An integrative literature review conducted through database searches, including studies published between 2017 and 2023. **Results:** A positive relationship was observed between early interventions in children with ASD and better clinical outcomes. Some studies suggest that the earlier the intervention is carried out, the better the results. An association was also identified between the children's pre-existing characteristics and the magnitude of the benefits obtained. Additionally, there was a positive correlation between the active involvement of parents and caregivers and the effectiveness of the intervention. **Conclusions:** Early interventions, combined with the active participation of parents and caregivers, are associated with a better prognosis in children with ASD, especially when initiated as early as possible and tailored to the child's individual characteristics.

**Keywords:** Autism spectrum disorder, Child, Early medical intervention, Clinical evaluation, Multidisciplinary treatment.

### INTRODUCTION

Loose Autism Spectrum Disorder (ASD) is a complex neurodevelopmental disorder characterized by multiple etiologies and wide variability in clinical presentation and symptom severity. It represents a condition that affects different domains of human functioning, ranging from communication to adaptive behavior, and requires a careful clinical approach. Currently, the term ASD encompasses a range of diagnoses that were previously classified as distinct entities, such as childhood autism,

Kanner's autism, atypical autism, high-functioning autism, childhood disintegrative disorder, pervasive developmental disorder not otherwise specified (PDD-NOS), and Asperger's syndrome. This unification of diagnoses was proposed to better reflect the continuous spectrum of manifestations and to facilitate the standardization of diagnostic criteria, thereby broadening clinical understanding of the condition.<sup>1,2</sup>

The core features of ASD include persistent deficits in social interaction and reciprocal communication, as well as restricted and repetitive patterns of behavior, interests, and activities. These signs may range from subtle difficulties in social communication to severe impairments in interpersonal contact, often accompanied by cognitive rigidity and increased sensory sensitivity. Such manifestations typically emerge in the first years of life, often before the age of three, and tend to persist throughout the lifespan, significantly impacting an individual's daily functioning. The definition and recognition of these characteristics are essential for diagnosis, which is based on the clinical criteria established by the Diagnostic and Statistical Manual of Mental Disorders (DSM).<sup>2</sup>

Regarding epidemiology, ASD shows a higher prevalence among boys, with an estimated ratio of 3.5 to 4 boys for every girl diagnosed. The World Health Organization (WHO) estimates that, on average, one in every 160 children worldwide presents some degree of the disorder, although more recent population-based studies suggest even higher rates, possibly due to advances in diagnostic methods and greater public awareness. Furthermore, research conducted over the past five decades has shown a significant increase in the global prevalence of ASD, which may reflect both a true rise in cases and the broadening of diagnostic criteria alongside improvements in detection.<sup>3</sup>

Although there is no cure for Autism Spectrum Disorder (ASD), there is a growing range of therapeutic interventions that have demonstrated effectiveness in improving social, communicative, and motor skills, as well as in reducing maladaptive behaviors. Scientific literature highlights that early intervention, especially when initiated in the first years of life, is strongly associated with better outcomes, due to greater neuronal plasticity and the potential to positively influence the course of neurodevelopment. Multidisciplinary strategies involving physicians, psychologists, speech therapists, occupational therapists, and educators have shown particularly promising results when combined with the active participation of the family in the therapeutic process.<sup>1</sup> Given the functional impact of ASD, its clinical and social relevance, and the progressive increase in its prevalence, the choice of this topic as the object of study is well justified. A comprehensive understanding of the disorder's characteristics, combined with knowledge of the most effective interventions, is essential to improve care and prognosis for these individuals. Therefore, this study aims to discuss the importance of early identification of ASD and to present the main multidisciplinary intervention strategies, highlighting their contribution to more functional development and to the improvement of the quality of life of individuals diagnosed with the disorder.

## METHOD

The method chosen to achieve the objective of this study was an integrative literature review. This method aims to identify, analyze, and synthesize the results of independent studies regarding the existing evidence in health practice, thus enabling the development of protocols, policies, procedures, and critical thinking.<sup>4</sup>

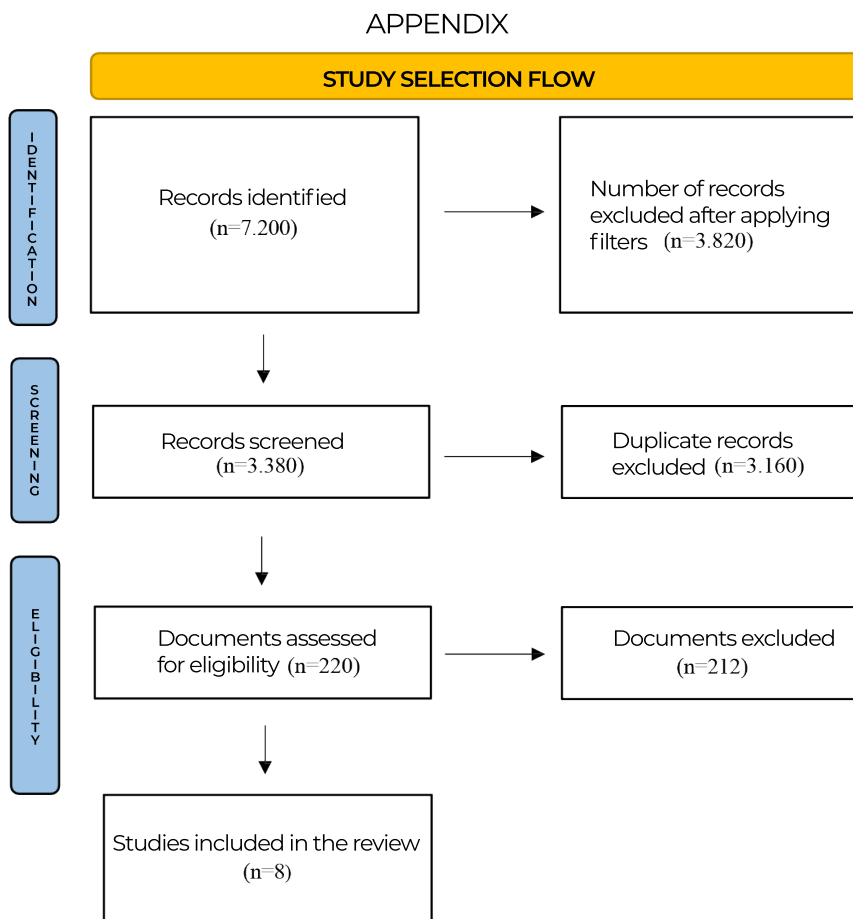
The integrative review consists of six phases. The first phase involves formulating a guiding research question; the second proposes a comprehensive search or sampling in the literature; the third focuses on data collection from the selected articles; the fourth emphasizes critical data analysis according to

the levels of evidence; the fifth aims at discussion of the results; and the sixth involves the clear and complete presentation of the integrative review.<sup>4</sup>

To select the articles, a search was conducted in the following databases: Scientific Electronic Library Online (SciELO), Virtual Health Library (BVS), PubMed, and Google Scholar. The following descriptors and their combinations in Portuguese were used for the search: “autismo” (autism), “transtorno do espectro autista” (autism spectrum disorder), “intervenção precoce” (early intervention), and “criança” (child).

The inclusion criteria were defined as follows: time frame from 2017 to 2023, articles published in Portuguese and English, full-text availability, and indexing in the aforementioned databases. The exclusion criteria included duplicate records, articles not available in full text, and those that, after reading the title and abstract, did not meet the eligibility criteria for this study. The search results are presented in Figure 1, which details the number of studies included and excluded at each stage of the selection process.

**Figure 1.** Flowchart of the study selection process for the articles included in the review



**Source:** Prepared by the authors. Adapted from PRISMA (2020).

## RESULTS AND DISCUSSION

The study conducted by Vivanti et al.<sup>5</sup> investigated the application of the Group Early Start Denver Model (G-ESDM) in 58 preschool-aged children diagnosed with Autism Spectrum Disorder (ASD). The children were divided into two types of classrooms: one in an inclusive setting, predominantly composed of typically developing children, and another in a specialized setting, consisting exclusively of children with ASD.

According to the authors, no significant differences were found between the groups at baseline regarding age, autism symptom severity, and verbal and nonverbal developmental quotients. Moreover, all caregivers had high levels of professional training. The inclusive classrooms had an average of 12 typically developing children and 1 to 3 children with ASD, while the specialized classrooms accommodated up to 10 children with ASD per day. Professionals in both settings were trained in the implementation of the G-ESDM, which defines specific developmental goals for each child based on their individual profile, covering verbal and nonverbal communication, socialization, cognition, and adaptive skills. These goals were addressed through routine classroom activities and cooperative play, employing naturalistic developmental techniques.<sup>5</sup>

The study found that children with greater social initiative demonstrated more significant benefits in inclusive environments. Those with higher initial social interest showed greater progress after one year of G-ESDM in inclusive classrooms compared to those with lower initial social interest. However, among children in the specialized group, the initial level of social interest did not significantly influence the outcomes.<sup>5</sup>

These findings suggest that both the child's social interest level and developmental stage should be considered by families and professionals when selecting the most appropriate intervention environment. While children with high social interest tend to perform well in both settings, those with low social interest achieved better outcomes in specialized environments. In any case, there were significant improvements in communication and social behavior in both groups, underscoring the benefits of early intervention, regardless of the context in which it is implemented.

In parallel, a meta-analysis conducted by Yu et al.<sup>6</sup> evaluated the effectiveness of interventions based on Applied Behavior Analysis (ABA) in treating various symptoms in children with ASD. A total of 14 clinical trials were included, comprising 555 participants aged 6 to 102 months (up to 8 years and 6 months). Of these, 278 were in the experimental group and 277 in the control group. The analyzed methods included the Early Start Denver Model (ESDM), the Picture Exchange Communication System (PECS), Discrete Trial Training (DTT), and Pivotal Response Treatment (PRT).

The Early Start Denver Model (ESDM) focuses on building affective bonds between the child and the therapist, promoting responsiveness and communication. The Picture Exchange Communication System (PECS) teaches nonverbal children to communicate using pictures. Discrete Trial Training (DTT) is based on direct and repetitive instruction, while Pivotal Response Treatment (PRT) structures the environment to stimulate responses according to the child's interests, functioning as a naturalistic intervention.<sup>6</sup>

The meta-analysis revealed significant effectiveness of ABA-based interventions in socialization, communication, and expressive language. However, no significant differences were found between ABA and ESDM regarding socialization and daily living skills. Effectiveness was considered low for receptive language, adaptive behavior, and cognition. Additionally, it was observed that longer and more comprehensive interventions produced medium-to-large effects on children's functional development,

especially when parents acted as mediators, enhancing reciprocity and social interaction. Nevertheless, the authors highlighted that the limited number of studies makes it difficult to establish conclusive comparisons between methods.<sup>6</sup>

In addition, Towle et al.<sup>7</sup> conducted a review including 14 studies grounded in the theory of neuroplasticity, which considers “critical periods” of development as ideal windows for effective interventions. Early ASD symptoms usually manifest between 12 and 18 months of age, and interventions implemented during this period have the potential to positively alter the developmental trajectory.

Of the 14 reviewed studies, 12 reported positive effects of early intervention, with improvements observed in motor skills, receptive language, self-care, and social behavior. The age at which intervention began proved to be a significant predictive factor in approximately half of the studies, reinforcing the importance of early action. To assess the outcomes, instruments such as ADOS, MSEL, and VABS were used.<sup>7</sup>

Torres et al.<sup>8</sup> reviewed 51 studies that evaluated the role of parents in 15 early intervention programs, categorized into four groups according to methodology and focus. The most notable were P-ESDM (Parent-Mediated ESDM), JASPER, and ImPACT (targeting the core symptoms of autism), and PCIT and FTP (focused on parenting and play). The authors emphasized that parent training is essential for the effectiveness of interventions, contributing to better developmental outcomes in children. Among these programs, the Parent Training Program derived from ABA and P-ESDM showed stronger evidence, while PCIT and FTP presented lower levels of empirical support. Overall, active parental involvement and promotion of parent-child interaction were identified as promising strategies to enhance the effectiveness of interventions.

Kitzerow et al.<sup>9</sup> proposed Naturalistic Developmental Behavioral Interventions (NDBI) through the Frankfurt Early Intervention Program for Autism (A-FFIP), a low-intensity, therapist-led approach. The method promotes parent-child interaction, joint engagement, play, imitation, and language development. With a focus on individualization, the intervention covers six key developmental domains, adjusted according to each child's stage. Proper training across these domains aims to enhance child-initiated social learning, generating a positive impact on overall development.

Maye et al.<sup>10</sup> emphasized the importance of positive affect in naturalistic ABA-based interventions (NDBI). The use of facial expressions, gestures, and play seeks to increase child engagement and strengthen emotional bonds. However, few studies have directly analyzed the impact of playfulness on children's responsiveness to interventions. A clinical case illustrated that when adopting a more playful and engaging approach, a previously nonverbal child began to express herself verbally, highlighting the potential of this strategy. The authors noted, however, that responsiveness to playfulness may vary among children, underscoring the need for further research to fully understand its effects.

The study by Viswanathan and Russel<sup>11</sup> investigated predictive factors in parent-mediated early intervention for children with ASD in India. Data from 77 children, with an average age of 3 years, diagnosed according to the DSM-5 and submitted to a 12-week evidence-based intervention, were analyzed. Assessments were conducted before and after the program using the Psychoeducational Profile - Revised (PEP-R), which measures general developmental age, imitation, perception, fine and gross motor skills, eye-hand coordination, and cognitive and verbal subscales. The sessions, structured as closed-group formats, were conducted by two therapists, five times a week, lasting 2 to 4 hours, and included weekly meetings to set individualized goals. Parents received training and were encouraged to continue adapted activities at home.

The results showed that children in residential programs exhibited greater improvement in fine

motor skills compared to those treated on an outpatient basis. Reduced home activity led to declines in gross motor performance, while longer intervention hours in the hospital setting favored eye-hand coordination and cognitive-verbal skills. The study concluded that intensive interventions, approximately 40 hours per week, preferably with active parental participation, maximize motor, cognitive, and language gains, reinforcing the positive role of the family in ASD treatment.<sup>11</sup>

Gomes et al.<sup>12</sup>, similar to Viswanathan and Russel<sup>11</sup>, advocate for the training of parents and caregivers to carry out early behavioral interventions in children with Autism Spectrum Disorder (ASD). The study included nine children, aged 1 year and 3 months to 2 years and 11 months, all with a diagnosis or suspected diagnosis of autism. The intervention, lasting 8 to 13 months, used the Psychoeducational Profile – Revised (PEP-R) and the Operationalized Portage Inventory (OPI) for evaluation. Activities were conducted at home by trained caregivers, five times per week, three hours per day (totaling 15 hours per week), under weekly supervision by two professionals.

The results showed developmental gains in all children, although four did not show progress in cognitive-verbal performance. Younger children with better initial cognitive and language skills demonstrated the greatest improvements, reinforcing the importance of age and baseline abilities for the effectiveness of early intervention.<sup>12</sup>

## CONCLUSION

This article presented an integrative review on early interventions in children diagnosed with Autism Spectrum Disorder (ASD). Although the studies analyzed employed different approaches, they all consistently indicated that early intervention has a positive impact on treatment outcomes, regardless of the method used. The evidence reinforces that initiating treatment as early as possible enhances results, supported by the principle of brain neuroplasticity.

Preexisting child characteristics, such as verbal skills and greater social engagement, were also found to be associated with better outcomes. Another recurring finding was the central role of parents as active agents in the implementation of interventions, which increases their effectiveness. Despite the limited number of studies, which constrains the definition of an ideal age to begin treatment, the evidence suggests that the earlier the intervention starts, the better the outcomes tend to be. Further research is needed to clarify the relationship between the age of onset, type of intervention approach, and the magnitude of improvements in the management of ASD symptoms.

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## TRIGEMINAL NEURALGIA SECONDARY TO INFECTIOUS AND INFLAMMATORY PROCESSES OF THE SKULL BASE: CLINICAL, ANATOMICAL, AND DIAGNOSTIC CORRELATIONS

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### ABSTRACT

Trigeminal neuralgia is a neuropathic condition characterized by acute and recurrent facial pain, usually unilateral, with a significant impact on quality of life. While the classical form of the disease is related to neurovascular compression, trigeminal neuralgia secondary to infectious and inflammatory processes of the skull base is a rare but important etiology, often underdiagnosed. This study conducted an integrative literature review to analyze the clinical, anatomical, and diagnostic correlations of this condition. Six articles published between 2021 and 2024 were selected, involving 41 patients, with infections such as sphenoidal sinusitis, mastoiditis, necrotizing otitis media, and parapharyngeal abscesses associated with trigeminal neuralgia. The most common symptoms include intense unilateral pain accompanied by local infectious signs. Computed tomography revealed bone changes suggestive of infection, while magnetic resonance imaging showed signs of neuritis and perineural involvement. Treatment based on antibiotic therapy, drainage, and debridement resulted in significant pain improvement in 92% of cases. The anatomical proximity of the trigeminal nerve to infected structures favors nerve irritation or compression. Early recognition of this etiology and the appropriate use of imaging are crucial for differential diagnosis and proper therapeutic choice, preventing complications and the chronification of pain. This study highlights the importance of a multidisciplinary approach and points to the need for future research with larger samples and longer follow-up.

**Keywords:** Acute pain, Paranasal sinuses, Skull base, Trigeminal nerve, Trigeminal Neuralgia.

### INTRODUCTION AND RATIONALE

Trigeminal neuralgia is a neuropathic disorder characterized by recurrent episodes of acute facial pain, usually unilateral, described as electric shock-like, stabbing, or lancinating, lasting from seconds to minutes. This pain is typically triggered by innocuous sensory stimuli, such as chewing, speaking, or touching the skin of the face. Involvement of the trigeminal nerve, the fifth cranial nerve responsible for facial sensation and part of masticatory motor function, gives this condition a debilitating clinical

expression with a direct impact on patients' quality of life.<sup>1</sup>

According to the International Classification of Headache Disorders (ICHD-3), trigeminal neuralgia is divided into three main categories—classical, secondary, and idiopathic—based on clinical criteria and imaging findings. The classical form corresponds to most cases and is generally related to neurovascular compression of the nerve at its emergence from the brainstem, particularly by an arterial loop such as the superior cerebellar artery. The idiopathic form, in turn, is characterized by the absence of detectable structural lesions, even with high-resolution imaging techniques.

The secondary form, however, results from identifiable underlying causes, such as intracranial tumors, multiple sclerosis, vascular malformations, trauma, and, less commonly but clinically relevant, infectious and inflammatory processes involving the skull base. Although rare, this etiology has gained prominence in recent studies for its ability to produce facial pain with neuropathic characteristics similar to the classical forms, yet with different prognosis and management implications. Infectious or inflammatory processes affecting deep structures of the skull base—such as sphenoid sinusitis, acute otitis media, mastoiditis, parapharyngeal abscesses, and petrous osteomyelitis—may cause facial pain through direct involvement of the trigeminal nerve branches.<sup>2,3</sup>

Clinical reports in the literature demonstrate that such conditions can irritate or compress trigeminal branches, generating symptoms often indistinguishable from the more common forms of the disease.<sup>4,5</sup> In certain cases, anatomical variations, such as the proximity between the sphenoid sinus and the foramen rotundum, facilitate this involvement. Failure to recognize an infectious origin may delay accurate diagnosis and compromise treatment effectiveness, thereby prolonging patient suffering.

In this context, the role of imaging examinations is fundamental.<sup>6</sup> Computed tomography (CT) is particularly useful for detecting bone alterations consistent with infection, whereas magnetic resonance imaging (MRI)—especially with contrast—allows for the identification of inflammatory changes, abscesses, and even signs of nerve involvement. The accuracy of these imaging modalities enables a more targeted therapeutic approach, whether through antibiotic therapy, surgical drainage, or other interventions, thereby increasing the likelihood of pain control and prevention of neurological sequelae.

Given these considerations, it becomes justified to deepen the analysis of the correlations between secondary trigeminal neuralgia and infectious or inflammatory processes of the skull base. Although rare, this association carries significant clinical implications and deserves greater recognition among both healthcare professionals and researchers. Infectious facial pain remains underdiagnosed and is often misclassified as idiopathic or vascular in origin, which delays appropriate interventions and prolongs patient suffering.

Thus, a better understanding of the clinical and anatomical mechanisms underlying this specific type of neuralgia, as well as the diagnostic tools available, may significantly improve early and effective management of such cases. Moreover, by integrating clinical and imaging evidence, this study aims to broaden the perspective on a condition that, although not among the most common causes of neuralgia, can lead to severe consequences when overlooked.

## OBJECTIVE

The objective of this study is to analyze the clinical, anatomical, and diagnostic correlations of trigeminal neuralgia secondary to infectious and inflammatory processes of the skull base, aiming to broaden the understanding of this condition and its implications for clinical practice. The study intends to critically review the existing scientific literature, identifying the anatomical and pathophysiological

mechanisms that explain the relationship between infectious or inflammatory alterations of the skull base and the occurrence of trigeminal neuralgia.

Furthermore, the study aims to systematize the main clinical manifestations described in the literature, discuss the diagnostic methods employed—particularly imaging studies and neurological assessment—and to emphasize the importance of early recognition of these correlations for differential diagnosis, appropriate therapeutic management, and prevention of neurological complications. In this way, the study seeks to provide an updated and evidence-based synthesis capable of supporting clinical decision-making and encouraging future research on the topic.

## METHODOLOGY

The methodology used to achieve the objective of this study, entitled “Trigeminal Neuralgia Secondary to Infectious and Inflammatory Processes of the Skull Base: Clinical, Anatomical, and Diagnostic Correlations”, was an integrative literature review. This method sought to integrate and analyze scientific evidence on the clinical, anatomical, and diagnostic aspects of trigeminal neuralgia associated with infectious and inflammatory processes of the skull base.

To conduct this review, the methodological framework described by Broome<sup>7</sup> was followed, comprising four main stages: (a) identification of the problem and definition of the guiding question; (b) systematic search of studies in scientific databases; (c) application of inclusion and exclusion criteria; and (d) analysis and synthesis of the data obtained. The guiding question established was: “What are the clinical, anatomical, and diagnostic correlations between trigeminal neuralgia and infectious or inflammatory processes of the skull base?”

The search was performed in the PubMed database using the following advanced strategy with Boolean operators: (“Trigeminal Neuralgia” OR “Trigeminal Neuropathy”) AND (“Sinusitis” OR “Paranasal Sinusitis” OR “Sphenoid Sinusitis” OR “Rhinosinusitis”). Initially, 288 articles were identified. After applying the “free full text” filter, the number was reduced to 44 articles, and with the additional filter limiting the results to the last five years, 14 full-text publications remained.

After reviewing the titles and abstracts, twelve studies were selected because they directly addressed the proposed theme. The inclusion criteria were articles published in English, full-text availability, and studies discussing trigeminal neuralgia secondary to infectious or inflammatory processes of the skull base, with emphasis on their clinical, anatomical, and diagnostic correlations. Studies focusing exclusively on idiopathic trigeminal neuralgia, on traumatic causes, or on noninfectious/noninflammatory etiologies were excluded.

## RESULTS AND DISCUSSION

The Six scientific articles published between 2021 and 2024 were analyzed. The sample consisted of three clinical case reports<sup>8-10</sup>, two retrospective series<sup>11,12</sup>, and one systematic review<sup>13</sup>, totaling 41 patients. The studies were conducted mainly in tertiary centers in Asia and North America, involving predominantly adult populations with a recent history of otorhinolaryngological infections.

Among the reported cases, the conditions most frequently associated with secondary trigeminal neuralgia included sphenoid sinusitis, petrous extension of mastoiditis, necrotizing otitis media, and parapharyngeal or peritonsillar abscesses. Skull base osteomyelitis was also described as a predisposing factor, particularly in immunocompromised patients. The most common pain pattern involved unilateral, severe, burning or lancinating pain radiating to the maxillary (V2) or mandibular (V3) divisions of the

trigeminal nerve. Pain typically presented with an acute onset and a close temporal association with infectious symptoms, such as otalgia, nasal obstruction, or odynophagia.

Computed tomography (CT) enabled the detection of bony abnormalities such as cortical rarefaction, mastoid sclerosis, erosion of the medial wall of the sphenoid sinus, and osseous destruction of the middle fossa floor. Magnetic resonance imaging (MRI) revealed findings suggestive of neuritis, including perineural enhancement, asymmetric thickening, and T2 hyperintensity in the intraforaminal segments of the trigeminal branches. In some cases, contrast enhancement was observed along the dura mater adjacent to the Gasserian ganglion, suggesting reactive meningeal involvement. Importantly, no evidence of vascular compression or tumoral lesions compatible with classical trigeminal neuralgia was reported.

Therapeutic management included broad-spectrum antibiotic therapy, surgical drainage of purulent collections, and, in selected cases, osseous debridement of regions with confirmed osteomyelitis. Pain improvement was observed in 92% of patients following infection control, allowing for discontinuation or significant dose reduction of neuromodulators such as carbamazepine and gabapentin. Only two patients developed chronic refractory pain, both presenting with extensive bilateral osteomyelitis.

Trigeminal neuralgia secondary to otorhinolaryngological infectious processes is an uncommon yet potentially underdiagnosed condition in clinical practice. The results of this analysis highlight the importance of early recognition of atypical pain patterns in patients presenting with head and neck infections, considering the possibility of trigeminal nerve involvement either through anatomical contiguity or indirect inflammatory mechanisms.

The trigeminal nerve, the fifth cranial nerve, has three major branches: the ophthalmic (V1), maxillary (V2), and mandibular (V3) divisions, which emerge from the Gasserian ganglion located in the middle cranial fossa. The V2 passes through the foramen rotundum and enters the pterygopalatine fossa, a region in close proximity to the maxillary and sphenoid sinuses. The V3, in turn, exits via the foramen ovale and extends into the infratemporal fossa, where it maintains intimate anatomical relationships with the lateral pharyngeal wall, mastoid base, and parapharyngeal space. This proximity to structures frequently affected by infections makes the trigeminal nerve particularly vulnerable to irritation or compression resulting from local inflammatory processes.<sup>14</sup>

Among the infectious processes described, sphenoid sinusitis deserves particular attention due to its insidious progression and high risk of intracranial complications. The lateral wall of the sphenoid sinus borders the V2 canal, and extensive inflammation may lead to perineural edema or localized osteitis. Necrotizing otitis media, when extending to the skull base, can compromise the V3 branch through osseous infiltration or inflammation involving the foramen ovale. Peritonsillar and parapharyngeal abscesses may cause referred facial pain by stimulating the mandibular nerve along its deep course, even without direct invasion.<sup>9</sup>

The pathophysiological mechanisms underlying trigeminal neuralgia in these settings include: (1) Direct inflammation of the nerve caused by locally released proinflammatory cytokines; (2) Indirect compression from edematous adjacent tissues, fascia, or purulent collections; (3) Segmental ischemia induced by regional infectious vasculitis; and (4) Immune-mediated demyelinating injury, particularly in immunologically predisposed patients. These mechanisms result in alterations of the firing threshold of trigeminal sensory neurons, leading to neuropathic pain that may manifest as continuous or paroxysmal episodes.<sup>10</sup>

The role of imaging studies is central in this context. Computed tomography (CT) allows for the assessment of bony integrity, being particularly useful in the early detection of osteomyelitis and erosive changes. Magnetic resonance imaging (MRI)—especially with contrast-enhanced and fat-suppressed sequences—is highly sensitive for detecting perineural inflammation and trigeminal ganglion abnormalities. The presence of asymmetric enhancement, neural thickening, or T2 hyperintensity, even in the absence of overt collections, may indicate secondary neuritis and guide the early initiation of antimicrobial therapy<sup>13</sup>.

A critical review of the available studies reveals significant methodological limitations: few employed standardized imaging protocols; case reports lacked uniformity in describing pain patterns and disease duration; and no long-term follow-up studies evaluated symptom chronicity or neuralgia recurrence. Nonetheless, the collective evidence underscores the importance of considering infectious etiologies in patients presenting with atypical or treatment-refractory trigeminal neuralgia. The complete or significant pain resolution observed after infection control reinforces the secondary and reversible nature of this condition in most cases.

From a clinical standpoint, the most important implication is the need for a multidisciplinary approach, involving otorhinolaryngologists, neurologists, and radiologists. Early identification of the infectious focus, combined with a precise anatomical understanding, can prevent unfavorable outcomes, reduce the risk of pain chronification, and avoid unnecessary neurosurgical interventions. Therefore, in patients presenting with unilateral facial pain of neuropathic characteristics associated with recent infectious symptoms, the possibility of secondary trigeminal neuralgia should be actively investigated.

## CONCLUSION

The analysis of data available in the literature reaffirms that trigeminal neuralgia secondary to infectious and inflammatory processes of the skull base, although rare, represents a clinically relevant yet often overlooked etiology. The close anatomical relationship between the trigeminal nerve and structures frequently affected by otorhinolaryngological infections—such as the paranasal sinuses, middle ear, and parapharyngeal spaces—makes its involvement in atypical facial pain syndromes plausible, especially in the absence of clear vascular or tumoral compression.

This study underscores the importance of maintaining a high index of diagnostic suspicion when evaluating patients with unilateral neuropathic facial pain, particularly when recent infectious symptoms are reported. The appropriate use of imaging modalities, especially computed tomography for bony assessment and contrast-enhanced magnetic resonance imaging for neural and meningeal evaluation, has proven essential both for early diagnosis and for therapeutic planning.

Despite methodological limitations within the reviewed studies—such as the small number of patients, the predominance of case reports, and the lack of standardized diagnostic criteria—the findings consistently emphasize the importance of detailed etiological investigation. The significant improvement or resolution of pain following infection control, observed in most cases, supports the reversible nature of this secondary neuralgia and the need for targeted treatment.

From a clinical perspective, this work highlights the relevance of an integrated multidisciplinary approach, involving otorhinolaryngologists, neurologists, and radiologists, in the recognition and management of trigeminal neuralgia associated with head and neck infections. Future studies with

greater methodological robustness, larger sample sizes, and long-term follow-up are necessary to further elucidate the true prevalence, prognostic factors for pain chronification, and efficacy of different therapeutic strategies for this condition.

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## ANTIMICROBIAL RESISTANCE PROFILE OF STREPTOCOCCUS AGALACTIAE IN PARTURIENTS TREATED AT A PUBLIC HOSPITAL IN GOIÂNIA: IMPLICATIONS FOR INTRAPARTUM PROPHYLAXIS

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### ABSTRACT

This study aimed to assess the prevalence of *Streptococcus agalactiae* colonization among parturients admitted to a public referral hospital in Goiânia, Brazil, and to characterize the antimicrobial resistance profile of the isolates, emphasizing implications for intrapartum prophylaxis. A cross-sectional study was conducted with 206 pregnant women between 35 and 37 weeks of gestation at the Dona Íris Maternity Hospital. Identification of *S. agalactiae* was performed using Todd-Hewitt selective broth culture, confirmed by chromogenic agar and real-time PCR (qPCR). Antimicrobial susceptibility was determined according to the 2024 BrCAST/EUCAST guidelines using the disk diffusion method on Mueller-Hinton agar supplemented with 5% horse blood and  $\beta$ -NAD. The prevalence of maternal colonization was 25.7% by qPCR and 20.4% by culture, with the vaginal site being the most affected (41.8%) and combined vaginal–anal colonization accounting for 25.4%. High susceptibility was observed to  $\beta$ -lactam antibiotics—penicillin (85.5%), ampicillin (92.8%), and ceftriaxone (96.4%)—while significant resistance was detected to clindamycin (83.6%), erythromycin (54.6%), and tetracycline (70.9%). No sociodemographic or obstetric variables were significantly associated with colonization. In conclusion,  $\beta$ -lactams remain the first-choice agents for intrapartum prophylaxis, whereas high resistance rates to macrolides and lincosamides reinforce the need for individualized antimicrobial susceptibility testing in penicillin-allergic women. The progressive incorporation of rapid molecular methods such as qPCR, in association with conventional culture, can enhance screening accuracy and support evidence-based strategies for preventing *S. agalactiae* infections in obstetric care.

**Keywords:** Group B Streptococcus, Antimicrobial susceptibility, Maternal colonization, Post-exposure prophylaxis, Beta-lactams.

## INTRODUCTION

*Streptococcus agalactiae*, also known as Group B *Streptococcus* (GBS), is recognized as an important agent of perinatal morbidity and mortality in several countries. Although it may be part of the normal genitourinary and gastrointestinal microbiota of healthy adults, its presence in pregnant women represents a significant risk for early-onset neonatal infection resulting from vertical transmission during childbirth.<sup>1–3</sup> GBS infection is associated with sepsis, pneumonia, and meningitis in newborns, and is also a frequent cause of chorioamnionitis and puerperal endomyometritis in women during the perinatal period.

Since 2002, the Centers for Disease Control and Prevention (CDC) has recommended universal screening between 35 and 37 weeks of gestation, followed by intrapartum antimicrobial prophylaxis for colonized pregnant women—a strategy that has significantly reduced the incidence of early-onset neonatal sepsis in countries that have adopted it.<sup>4</sup> In Brazil, however, the systematic implementation of these measures remains limited, particularly in public institutions with high obstetric demand and lower laboratory capacity.

The absence of national guidelines for routine GBS screening in pregnant women reflects a longstanding gap in epidemiological and microbiological surveillance of the agent. Brazilian studies on the prevalence of maternal colonization are concentrated in the South and Southeast regions,<sup>5–11</sup> with variable findings and restricted samples. In the state of Goiás, Pires<sup>12</sup> identified a colonization rate of 15.4% among parturients but highlighted the scarcity of data on the antimicrobial resistance profile of circulating strains.

The increasing resistance to macrolides and lincosamides has been reported in several regions, raising concerns about the effectiveness of alternative therapies in pregnant women with penicillin allergy.<sup>3,13</sup> The maintained susceptibility to  $\beta$ -lactams, on the other hand, reinforces their importance as the gold standard for intrapartum prophylaxis. Nonetheless, the empirical use of antimicrobials without laboratory confirmation may favor the emergence of resistant strains and compromise prevention strategies.

Within the national context, the Brazilian Ministry of Health<sup>14</sup> and recent studies<sup>15,16</sup> emphasize the importance of local investigations on GBS prevalence and resistance patterns, in order to support public policies and clinical protocols adapted to regional realities.

Accordingly, the present study aimed to evaluate the prevalence of *Streptococcus agalactiae* colonization among parturients treated at a public referral hospital in Goiânia, Goiás, and to characterize the antimicrobial resistance profile of the isolated strains, with emphasis on its implications for intrapartum prophylaxis and the rational use of antimicrobials in obstetric care.

## MATERIALS AND METHOD

This was a cross-sectional study conducted at Hospital e Maternidade Dona Íris (HMDI), a municipal public referral unit for women's and children's healthcare in Goiânia, Goiás. The project was approved by the Research Ethics Committee of HMDI (Approval n° 3.361.799; CAAE: 13320819.5.0000.8058), in accordance with Resolution n° 466/12 of the Brazilian National Health Council. All participants were properly informed about the objectives of the study and signed the Informed Consent Form (ICF).

A total of 206 pregnant women between 35 and 37 weeks of gestation were included, admitted to the HMDI pre-labor service from August to October 2024. Pregnant women could present single

or multiple gestations, with or without premature rupture of membranes, and with or without associated morbidities such as hypertension, diabetes mellitus, or HIV infection. Exclusion criteria were: use of antimicrobials or vaginal creams within the seven days prior to sample collection, or having received intrapartum prophylaxis less than six hours before delivery.

Sample size calculation was based on an expected colonization prevalence between 15% and 30%, with a 95% confidence level and a 5% sampling error, resulting in a minimum required sample of 203 pregnant women. The final number of participants (n = 206) met the established statistical criteria.

Sample collection was performed by trained hospital staff following a standardized protocol. Vaginal and anorectal samples were obtained from each participant using sterile swabs. Samples were stored in Stuart transport medium and sent to the Applied Bacteriology Laboratory of the Institute of Tropical Pathology and Public Health (IPTSP/UFG) within 12 hours after collection. When necessary, specimens were refrigerated between 2°C and 8°C for up to 24 hours.

Isolation of *Streptococcus agalactiae* was performed in Todd–Hewitt broth supplemented with gentamicin (15 µg/mL) and nalidixic acid (8 µg/mL), followed by incubation at 36°C for 18 to 24 hours. Cultures were then plated on 5% sheep blood agar and reincubated under microaerophilic conditions for 24 hours. Beta-hemolytic colonies compatible with the *Streptococcus* genus were submitted to Gram staining, catalase testing, and the CAMP test. Presumptive confirmation of GBS was performed on chromogenic agar, with bluish colonies considered positive. Confirmed isolates were preserved in BHI broth with 30% glycerol and stored at -70°C until antimicrobial susceptibility testing.

The susceptibility profile was determined according to the standards of the Brazilian Committee on Antimicrobial Susceptibility Testing (BrCAST/EUCAST), 2024 version. The disk diffusion method was used on Mueller–Hinton agar supplemented with 5% horse blood and 20 mg/L β-NAD, incubated at 35±1°C for 18±2 hours in an atmosphere containing 5% CO<sub>2</sub>. Inhibition zone diameters were interpreted according to BrCAST breakpoints, classifying isolates as susceptible, intermediate, or resistant. For selected samples, Minimum Inhibitory Concentration (MIC) determination was performed using broth microdilution to confirm resistance observed by diffusion.

Data were entered into an electronic spreadsheet and analyzed using SPSS® software (version 21.0). Descriptive analyses of demographic and clinical variables of the pregnant women, as well as resistance rates to the antimicrobials tested, were performed. Results were presented as absolute and relative frequencies, with a significance level of 5% (p < 0.05).

## RESULTS

A total of 206 pregnant women participated in the study, with ages ranging from 14 to 43 years (mean ± SD = 24.9 ± 5.7 years). Among the women evaluated, 53 were colonized by *Streptococcus agalactiae*, resulting in a prevalence of 25.7% of carriers of the agent (Table 1).

**Table 1.** Summary of the main findings among parturients colonized by *Streptococcus agalactiae*

| Category                        | Variable analyzed                 | Main result                                  |
|---------------------------------|-----------------------------------|--|
| <b>Demographic profile</b>      | Mean age (years)                  | 24.9 ± 5.7                                   |
|                                 | Predominant age group             | 23 to 30 years (47.6%)                       |
|                                 | Area of residence                 | Urban (97.1%)                                |
|                                 | Predominant race/ethnicity        | Brown (73.6%)                                |
|                                 | Most common marital status        | Single (62.3%)                               |
| <b>Socioeconomic conditions</b> | Family income                     | R\$ 2,000 to R\$ 2,999 (43.4%)               |
|                                 | Educational level                 | Completed high school (60.4%)                |
|                                 | Occupation                        | Homemaker (39.6%), formal employment (34.0%) |
| <b>Obstetric aspects</b>        | <b>Gestational age ≥ 37 weeks</b> | 90.6%  |
|                                 | <b>≥ 4 prenatal visits</b>        | 92.5%  |
|                                 | Gestational diabetes              | 9.4%   |
|                                 | Obesity grade I                   | 39.6%  |
|                                 | Obesity grade II                  | 62.3%  |
|                                 | Primiparous                       | 13.2%  |
| <b>Primiparous</b>              | Vaginal                           | 41.8%  |
|                                 | Anal                              | 7.3%   |
|                                 | Vaginal and anal                  | 25.4%  |

Sociodemographic analysis showed that 97.1% of the pregnant women lived in urban areas, and nearly half were from Goiânia (47.5%), followed by Aparecida de Goiânia (32.5%). The geographic distribution of colonized women followed a similar pattern, suggesting that GBS colonization is relatively homogeneous across the metropolitan area.

Regarding social characteristics, 56.8% of participants were single, a percentage that increased among colonized women (62.3%), which may reflect social vulnerability and reduced family support during pregnancy. The predominant self-reported race/ethnicity was mixed-race (68.9%), and this percentage was even higher among colonized women (73.6%), indicating a possible overlap between racial factors and inequalities in access to healthcare (Table 6).

Concerning family income, 77.4% of the pregnant women had household incomes between R\$ 1,000 and R\$ 3,999, with colonized women predominantly concentrated in intermediate income brackets (R\$ 2,000 to R\$ 2,999). This distribution underscores the predominance of women from lower and middle socioeconomic strata, the typical population served by the municipal public health system.

In terms of education, all participants were literate, and most (63.6%) had completed high school. Only 2.4% reported having completed higher education, a slightly higher proportion among colonized women (5.7%) (Table 7). This educational homogeneity suggests that schooling level alone did not appear to function as a protective or risk factor for colonization.

Regarding occupation, 48.1% of the pregnant women were homemakers, and 29.6% held formal employment. Among colonized participants, the proportion of formally employed women was higher (34.0%), followed by informal workers (9.5%), which may indicate that greater exposure in collective environments could represent an additional risk factor, although no statistically significant association was observed.

Most participants had a gestational age of 37 weeks or more (94.6%), and prenatal care was

satisfactory, with 90.8% attending four or more consultations. This adherence was similar among colonized women (92.5%), indicating that GBS screening does not appear to depend on the frequency of obstetric follow-up.

Regarding associated clinical conditions, 14.1% of pregnant women had gestational diabetes, a slightly lower proportion among colonized women (9.4%). Class I obesity was more frequent in the colonized group (39.6%), whereas severe obesity (classes II and III) was rare or absent. This finding may suggest an association between moderate excess weight and colonization, although the sample size limits definitive conclusions (Table 8).

Recent medication use (28.6%), history of chorioamnionitis (3.4%), placental complications (3.4%), and preeclampsia (3.9%) showed low prevalence, with no relevant differences between groups. Labor duration was predominantly between 13 and 24 hours (52.4%), with a slightly higher proportion among colonized women (58.5%), which may indicate a mild tendency toward longer labor in this subgroup, although without statistical significance.

Most pregnant women had up to two previous pregnancies (69.4%), and 13.2% of colonized women were primiparous, a proportion higher than that of the overall group (7.8%). This may suggest greater susceptibility to colonization among primiparous women, a hypothesis also observed in other population contexts.

Approximately 24.5% of colonized women reported a previous miscarriage, and 62.3% had a history of urinary tract infection during pregnancy, a condition that remained among the most frequent in the positive group. Other events—such as prior preterm birth, membrane rupture, or intrapartum fever—were rare. However, a higher proportion of previous neonatal deaths before three months of age was observed among colonized women (20.8% vs. 14.6%), suggesting a possible indirect clinical impact of maternal GBS colonization.

Positivity was most frequently observed in vaginal samples (41.8%), followed by simultaneous vaginal and anal collections (25.4%), while isolated anal colonization was less common (7.3%). In about one quarter of positive pregnant women (25.4%), it was not possible to determine the specific colonization site due to inconclusive results in one of the tests.

Phenotypic analysis of the isolated strains revealed universal resistance (100%) to at least one antibiotic tested, indicating the presence of multidrug-resistant strains in the study population. Resistance rates were markedly high for clindamycin (83.6%), erythromycin (54.6%), and tetracycline (70.9%), suggesting important limitations in the use of these drug classes as alternative therapies for pregnant women with penicillin allergy.

In contrast,  $\beta$ -lactams maintained broad efficacy, with sensitivity rates above 85% for all agents tested: penicillin (85.5%), ampicillin (92.8%), cefazolin (81.8%), and ceftriaxone (96.4%). These results indicate that circulating strains remain largely susceptible to first-line agents recommended for intrapartum prophylaxis. Table 2 presents the consolidated susceptibility profile of the antimicrobials tested.

**Table 2.** Consolidated antimicrobial susceptibility profile of the isolates

| Antibiotic tested | Susceptible n (%) | Resistant n (%) |
|-------------------|-------------------|-----------------|
| Tetracycline      | 16 (29.1)         | 39 (70.9)       |
| Ceftriaxone       | 53 (96.4)         | 2 (3.6)         |
| Cefazolin         | 45 (81.8)         | 10 (18.2)       |
| Ampicillin        | 51 (92.8)         | 4 (7.2)         |
| Penicillin        | 47 (85.5)         | 8 (14.5)        |
| Cefazolin         | 25 (45.4)         | 30 (54.6)       |
| Clindamycin       | 9 (16.4)          | 46 (83.6)       |

Overall, the findings reveal a concerning pattern of resistance among maternal isolates, particularly to macrolides and lincosamides, and reinforce the efficacy of  $\beta$ -lactams as the agents of choice for intrapartum prophylaxis. The consistent presence of multidrug resistance highlights the importance of continuous microbiological surveillance and the rational use of antimicrobials in high-complexity obstetric settings.

## DISCUSSION

The prevalence of maternal colonization by *Streptococcus agalactiae* observed in this study—20.4% by culture and 25.7% by qPCR—falls within the globally estimated range (10% to 40%)<sup>16–19</sup> and is comparable to that reported by Ha et al.<sup>20</sup> in Vietnam (25.5%). These findings confirm that GBS colonization remains frequent in the Brazilian context as well, requiring continuous surveillance and sensitive diagnostic strategies to ensure adequate prophylaxis.

The discrepancy between the methods reinforces the importance of integrating molecular techniques with conventional culture for screening pregnant women. qPCR showed a higher detection rate, consistent with studies demonstrating its superior sensitivity, which reduces the number of false negatives and provides rapid results for intrapartum decision-making.<sup>21–23</sup> This agility is particularly relevant in obstetric care, where the interval between diagnosis and delivery may be decisive for timely antibiotic prophylaxis.

The predominance of the vaginal site as the main location of colonization (41.8%), followed by simultaneous vaginal and anal colonization (25.4%), confirms the lower genital tract as the primary maternal reservoir of GBS. This pattern has been consistently reported across different countries<sup>22,24</sup> and supports the recommendation to include combined vaginal and anal swabbing in screening routines, as outlined by CDC guidelines.<sup>4,25</sup>

Standardization of sampling procedures and the use of more sensitive methodologies are therefore essential for the success of intrapartum prophylaxis. Studies by Rocha et al.<sup>26</sup> and Bogiel et al.<sup>23</sup> demonstrate that real-time PCR enables the identification of colonized women even during labor, allowing immediate antimicrobial administration before birth, which reduces the incidence of early-

onset neonatal infection and maternal complications.

The results obtained demonstrate preserved efficacy of  $\beta$ -lactams against *S. agalactiae*, corroborating the international consensus that penicillin and ampicillin should remain the first-line drugs for intrapartum prophylaxis.<sup>4,27,28</sup> In the present study, more than 90% of isolates were susceptible to ampicillin and 85.5% to penicillin, values consistent with recent findings from Dutra et al.<sup>29,30</sup> and Ramos.<sup>30</sup> This sustained susceptibility is encouraging, particularly in a scenario of increasing resistance among other obstetric pathogens.

However, the high resistance to macrolides and lincosamides observed in this study (54.6% for erythromycin and 83.6% for clindamycin) represents a significant clinical challenge. These rates exceed the averages reported by Fitoussi et al.,<sup>31</sup> Santana et al.,<sup>32</sup> and Bekele et al.,<sup>33</sup> suggesting a possible expansion of MLS<sub>B</sub> phenotypes (mediated by *erm* and *mef* genes). Such resistance has a direct impact on obstetric management, since clindamycin and erythromycin are the main alternatives for pregnant women with penicillin allergy.

Given this scenario, it is strongly recommended that, whenever possible, individual susceptibility testing be performed, including the D-test to detect inducible resistance before choosing macrolides or lincosamides, as recommended by the CDC.<sup>25</sup> Failure to follow this approach may result in ineffective prophylaxis and increased risk of early-onset neonatal infection.

Cefazolin, the first-line alternative for patients with mild penicillin hypersensitivity, showed satisfactory susceptibility (81.8%), a value above the critical threshold of 80% proposed by Schrag et al.<sup>4</sup> Ceftriaxone (96.4%) maintained excellent performance, further supporting the safety of  $\beta$ -lactam-based regimens. Nonetheless, the isolated presence of strains resistant to penicillin (14.5%) and ampicillin (7.2%) warrants attention and continuous monitoring, since sporadic cases of resistance have been reported in Europe and Asia.<sup>28,34</sup>

Another relevant point is the heterogeneity of laboratory methods used for GBS screening in Brazil. Culture remains predominant in public healthcare units due to its low cost, but implementation of rapid molecular tests, such as qPCR, could optimize intrapartum diagnosis and prevent unnecessary antibiotic use in women with undefined risk. As highlighted by Costa et al.<sup>21</sup> and Ferreira et al.,<sup>22</sup> qPCR significantly increases detection rates and provides results quickly enough to support timely clinical decision-making, particularly in high-volume maternity hospitals.

In this context, combining low-cost methods (such as the CAMP test) with rapid molecular approaches may represent a feasible hybrid strategy for public services, ensuring diagnostic accuracy and operational efficiency. Implementing these protocols in referral hospitals could reduce costs associated with neonatal infections and improve delivery safety protocols.

The marked resistance to tetracyclines (70.9%), macrolides, and lincosamides reinforces the need for antimicrobial stewardship policies, especially in obstetric units. This pattern has already been documented in Brazil by Ramos,<sup>30</sup> as well as in international studies.<sup>27,35,36</sup> The persistence of high resistance rates suggests environmental selective pressure related to the indiscriminate use of broad-spectrum antibiotics, including outside the hospital setting.

Thus,  $\beta$ -lactam-based intrapartum prophylaxis remains the most effective and safest strategy, and should be administered in a targeted manner and supported by continuous microbiological surveillance. Such vigilance must include the systematic collection of clinical isolates to monitor resistance trends, thereby informing periodic updates of therapeutic recommendations.

## CONCLUSION

In this study, maternal colonization by *Streptococcus agalactiae* showed a prevalence of 25.7% by qPCR and 20.4% by culture, values consistent with the global average. The vaginal site was the most affected (41.8%), followed by simultaneous vaginal and anal colonization (25.4%). The phenotypic profile revealed high susceptibility to  $\beta$ -lactams—penicillin (85.5%), ampicillin (92.8%), and ceftriaxone (96.4%)—and high resistance to clindamycin (83.6%), erythromycin (54.6%), and tetracycline (70.9%), representing an important warning for the empirical management of penicillin-allergic pregnant women. No sociodemographic or obstetric variable showed a statistically significant association with colonization.

Overall, it can be concluded that  $\beta$ -lactams remain the first choice for intrapartum prophylaxis, with penicillin and ampicillin being the most effective and safest agents for prophylactic use. The marked resistance to macrolides and lincosamides reinforces the need for individualized antimicrobial susceptibility testing and the performance of the D-test in pregnant women with penicillin allergy, thereby avoiding therapeutic failures. The gradual implementation of rapid molecular methods, such as qPCR, in combination with conventional culture, may enhance screening and ensure more timely, evidence-based prophylaxis.

This study has limitations, including its cross-sectional design and the inability to apply molecular testing to all samples, which restricts sensitivity and specificity analyses. Future research should expand the number of participants, explore the genotypic characterization of resistant isolates, and evaluate the cost-effectiveness of implementing molecular tests for intrapartum screening. Such advances may strengthen public health policies aimed at preventing perinatal infections and promoting maternal-fetal safety within public healthcare services.

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