

MESTRADO INTEGRADO EM MEDICINA

# **Sinogenic Intracranial Abscesses in Children – a Ten Year Experience**

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2025



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Medicina Clínica

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Sinogenic Intracranial Abscesses in Children – a ten year experience.

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## SINOGENIC INTRACRANIAL ABSCESSSES IN CHILDREN – A TEN YEAR EXPERIENCE

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### Abstract

**Objective:** To analyze the clinical course, management and outcomes of sinogenic intracranial abscesses in children over a ten-year period at a tertiary university hospital.

**Study Design:** Retrospective cohort.

**Setting:** Branch of Pediatric Otorhinolaryngology of a tertiary academic hospital center with Pediatric Neurosurgery and Pediatric Intensive Care facilities.

**Methods:** Electronic charts of 14 pediatric patients below 18 years of age admitted with intracranial abscesses secondary to acute rhinosinusitis between January 2015 and December 2024, were retrospectively reviewed. Demographics, clinical presentation, laboratory findings, radiological results, microbiology, surgical and medical management, and outcomes were analyzed.

**Results:** Males predominated (64.3%) with a mean age of 12.14 years. All patients presented with fever, and the majority had headache (92.9%) and neurological symptoms (57.1%). The frontal sinus was involved in all cases and subdural abscesses represented the most common intracranial complication. *Streptococcus anginosus* group was identified in 71.4% of positive cultures. All patients underwent surgery and broad-spectrum antibiotics, with an average of 1.8 surgeries per child. Mean length of hospitalization was 53.2 days. No mortality or significant long-term morbidity occurred in this series.

**Conclusion:** Sinogenic intracranial abscesses affect predominantly adolescent males and are predominantly related to frontal sinusitis. *Streptococcus anginosus* group strains were the predominant pathogen harvested in our series. Despite their high clinical severity, favorable outcomes without long-term sequelae can be achieved if timely surgical management and appropriate and appropriate antimicrobial therapy are provided. Careful monitoring of adolescents with acute rhinosinusitis is warranted for early detection of intracranial complications.

## **INTRODUCTION**

Acute bacterial rhinosinusitis occurs in about 7% of children with upper respiratory infections (1). Rarely, this common inflammation of the paranasal and nasal sinus mucosa can complicate and extend to the orbit and/or intracranially, especially in children.

Orbital complications (OC) are the most common and comprise around 80% of acute rhinosinusitis (ARS) complications and occur mostly in children under five years old (2-4). These complications can be classified as pre-septal or orbital cellulitis, subperiosteal abscess, orbital abscess and cavernous sinus thrombosis, as described by Chandler (5).

In contrast, intracranial complications (IC) are considerably less frequent, affecting mainly male adolescent and leading to much higher morbimortality. Before the implementation of broad-spectrum antibiotics, imaging and surgical improvements, mortality rates could reach as high as 100% depending on location. However, in recent years, diagnosis has become more precise through advanced imaging by computerized tomography (CT) and magnetic resonance imaging (MRI) and more effective and time-sensitive treatment, led to a mortality drop to around 3-12% (6,7). These life-threatening complications include intracranial abscesses (ICAbs), meningitis and dural sinus thrombosis (8). Furthermore, ICAbs can be divided into extradural, subdural and intraparenchymal.

Infection can progress intracranially either directly through sinus wall dehiscences, bony erosion necrotic areas of osteomyelitis; or indirectly, via the valveless diploic veins that connect the intracranial venous system and the vasculature of the sinus mucosa. The peak in vascularity and in relative blood supply that occurs in children during the development of the sinuses may explain why these complications are more common in children than adults (9).

This study aims to address the recent experience of a tertiary university hospital in the management of ICAbs secondary to ARS, during a period encompassing the last ten years.

## **Material and methods**

### Setting

Section of Pediatric Otorhinolaryngology of the Department of Otorhinolaryngology from a tertiary academic hospital center with Pediatric Neurosurgery and Pediatric Intensive Care facilities.

### Study design

Electronic charts from children below 18 years of age, admitted to a tertiary pediatric care hospital with a diagnosis of ICAs between January 2015 and December 2024, were retrospectively reviewed. All data available – clinical, microbiology and imaging by CT or MRI - were screened to identify ICAs of sinogenic origin.

Patients with fungal rhinosinusitis, immunosuppression, cranial dysmorphias or trauma, genetic syndromes, congenital malformations and neoplasms were excluded from this investigation.

This study was approved by the institutional Ethics Committee of ULSSJoão (Ref. CE-453-24).

### Study Variables

The following information was collected from the electronic records of each patient: age, gender, comorbidities, month and year of diagnosis, symptoms and their duration before hospitalization, antimicrobials and steroids before admission, laboratory findings (C-Reactive Protein - CRP, neutrophils, lymphocytes and leucocytes on admission, after surgery and before discharge), laterality and sinus affected by ARS, ICAs and concomitant complications, microbiology results, medical and surgical management, length of hospitalization (LOH) and duration of stay in the Pediatric Intensive Care Unit when needed.

### Data analysis

Quantitative variables were described using their means and range, whereas categorical variables were described as numbers and percentages. For statistical analysis, Fisher's Test was used to compare categorical variables like demographics and clinical presentation, Man-Whitney U Test for non-parametric continuous variables and Spearman Correlation for continuous variable associations. Significance was set at  $p \leq 0.05$ . All statistical analysis was performed with IBM SPSS Statistics Data Editor™ 30.0.

## RESULTS

### Demographics

This study included 14 pediatric patients fitting the previously defined criteria. There was a male predominance, with nine boys (64,3%), and five girls (35,7%). Mean age at diagnosis was  $12.14 \pm 3.04$  years old (range 7-17), nine (64.3%) were older than 12 years old. Thirteen patients (92.9%) were Caucasian and one child (7.1%) was of Romani ethnicity.

None had a prior diagnosis of chronic rhinosinusitis or history of rhinosinusitis exacerbations as well as no prior procedures by otorhinolaryngology or neurosurgery. Five (35.7%) children had significant comorbidities including peripheral pulmonary stenosis, intellectual difficulties, obesity, vesicoureteral reflux and median cerebral artery stroke at birth without long-term sequelae. No comorbidity was associated with likelihood to develop a specific complication.

Seasonality of presentation was as follows: Winter (n=7, 50%), followed by Spring (n=5, 35.7%) and Summer (n=2, 14.3%), and no cases presented during Autumn. No statistical differences in incidence were found in this cohort between the pre-COVID and the post-COVID eras. The average of cases per year was 1.2 from 2015 to 2019 and 1.6 from 2020 and 2024. No cases were admitted in 2020. A summary of patients' demographics, affected sinus, intracranial abscesses and concomitant complications, surgical team, type of intervention and reintervention can be found in **Table 1**.

### Clinical Presentation

All children had symptoms prior to diagnosis, lasting on average  $7.21 \pm 4.39$  days (range 1-15 days). Symptoms included fever (100%), headache (92.9%) and neurological symptoms (57.1%) such as seizures, hemiparesis/paresis and prostration (**Table 2**). Seizures were more common in children  $\geq 12$  years old ( $p = 0.049$ ).

Prior to admission, half of the patients (n=7) had at least one observation by a doctor and were prescribed antibiotics as depicted in **Table 2**. Taking antibiotics prior to hospitalization was associated with longer periods of vomiting before admission when compared with those without antibiotics ( $8.3 \pm 6.1$  days vs  $1.75 \pm 0.5$ ;  $p = 0.028$ ).

### Laboratory Findings

Most children had available blood test results from the day of admission, 1-2 days after surgery and 1 to 10 days before discharge. Only one child did not have blood work from the day after surgery. On admission the average CRP was  $202.09 \pm 103.42$  mg/L, average White Blood Cell (WBC) count  $17.47 \pm 6.80$ ,  $\times 10^9$  /L, neutrophils  $83.9 \pm 9\%$  and lymphocytes  $9.9 \pm 6.3\%$  resulting in an average Neutrophil-to-Lymphocyte Ratio (NLR) of  $12.3 \pm 7.8$ . Statistics showed a trend for higher CRP values on admission on children  $\geq 12$  years old ( $p=0.072$ ) and also that the longer the child was symptomatic the higher lymphocytes would be on admission ( $rs= 0.6$ ;  $p=0.028$ ).

When it comes to sinus involvement, cases of pansinusitis had lower neutrophil values on admission ( $p=0.014$ ); and after surgery the NLR was still lower ( $p=0.014$ ), with lower neutrophil ( $p=0.021$ ) and higher lymphocyte counts ( $p=0.014$ ).

Following surgical and medical management, CRP and NLR tended to decrease progressively and reached their lowest scores on the discharge day. This difference was significant in regard to the CRP values after surgery ( $p=0.019$ ), more noticeably in older children ( $r_s=0.718$ ,  $p=0.006$ ). Laboratory results are presented in **Table 3**.

#### Sinus involvement and concomitant complications

The frontal sinus was involved in all cases. Five (35.7%) children had pansinusitis, and extension to the sphenoid sinus occurred only in this context. Frequencies of afflicted sinuses are presented in **Figure 1** and types of intracranial and extracranial complications are described in **Table 4**.

All patients had either a CT scan and/or MRI on admission (**Figure 2**). The most common ICabs were subdural abscesses ( $n=10$ ), three were isolated and seven occurred in association with other forms of bacterial complications. Out of three cases with meningoencephalitis, two had concomitantly sagittal sinus thrombosis ( $p=0.033$ ) and all these had concomitant involvement of the sphenoid sinus ( $p=0.027$ ).

Patients with intraparenchymal cerebral abscesses presented with higher CRP levels on admission ( $p=0.048$ ), whereas in epidural abscesses the CRP on admission tended to have the lower values ( $p=0.009$ ). Osteomyelitis of the frontal bone was associated with shorter periods of fever before hospitalization ( $p=0.028$ ).

Three patients (21.4%) exhibited concomitant orbital complications on admission and all of them coincided to have subdural abscesses, with pre-admission symptoms lasting between seven and fifteen days.

#### Bacteria and antimicrobial management

Bacteria species were identified in seven children (50%) through direct sample (abscesses –  $n=5$ , 71.4%), blood culture ( $n=1$ , 14.3%), lumbar puncture ( $n=1$ , 14.3%) or molecular diagnosis ( $n=1$ , 14.3%). *Streptococcus anginosus* group was the most commonly identified species ( $n=5$ , 71.4%). Culture was polymicrobial in two (28.6%) cases. Only one case (11.1%) identified two anaerobic microorganisms. The microbiology results are shown in **Table 5**. Pre-hospitalization antibiotic therapy was not statistically associated with the microbiology results.

All patients were treated with broad-spectrum antibiotics; twelve (85.7%) were administered ceftriaxone, eleven (78.6%) metronidazole, eight (57.1%) vancomycin, two (14.3%) meropenem and one (7%) was given cefotaxime. One child had an allergic reaction to IV ceftriaxone and vancomycin and was switched to IV meropenem. Children were hospitalized until the end of intravenous broad-spectrum antibiotic administration,

averaging  $43.29 \pm 22.15$  days. Ten (71.4%) had adjunct corticotherapy. The three (21.4%) patients who had thrombosis of the sagittal or cavernous sinus were also initially administered low-weight subcutaneous heparin for an average of  $36.3 \pm 41.36$  days, and two of them later transitioned to oral warfarin, one for 9 months and the other for 12 months.

Meropenem was associated with lymphocytosis after surgery ( $p = 0.048$ ). Treatment with metronidazole led to lower lymphocyte counts ( $r=-0.586$ ,  $p=0.036$ ) and higher NLR ( $r=0.586$ ,  $p=0.036$ ) after surgery.

### Surgical management

All patients underwent otorhinolaryngology and/or neurosurgical procedures, with an average of 1.8 surgeries per child (1-5). Half of the inaugural surgical treatments were performed by both teams simultaneously. Patients' intracranial abscesses were treated with craniotomy with or without FESS. Surgical approaches can be found in **Table 6**.

### Outcomes

Length of hospitalization was  $53.2 \pm 28.1$  days on average, (range 32 to 121 days) and this parameter was statistically associated with longer periods of fever before hospitalization ( $r = 0.666$ ,  $p = 0.013$ ). No correlations were found between LOH and other factors like clinical presentation, comorbidities, sinus involvement, type of IC and concomitant complications, type of surgical or medical treatment and biochemical or microbiological results ( $p>0.05$ ).

Five patients (35.7%) needed a second surgery, and children  $\geq 12$  years old were more likely to need revision surgical interventions ( $p = 0.045$ ). Two patients had revision surgery to drain a residual abscess, one by neurosurgery and another by the otorhinolaryngology team, by frontal trephination revision. One child underwent a revision of the previous frontal trephination plus an additional neurosurgery and otorhinolaryngology combined surgery to drain a residual subdural abscess; Yet another patient required reintervention to deal with a scar dehiscence and an additional revision craniotomy. Lastly, one case needed a total of five neurosurgical reinterventions due to persistent hydrocephalus formation, which was initially managed with an external ventricular shunt and eventually with a ventriculoperitoneal shunt.

No cases of mortality were registered and morbidity rate was 7.1% derived from ventriculoperitoneal shunt placement for hydrocephaly management. All other cases are still alive and with no significant morbidity at the time of data review for this study in January 2025.

## DISCUSSION

The current study, dedicated to the recent experience in the management of pediatric sinogenic intracranial abscesses, showed that these rare complications mainly affected male adolescents with frontal ARS. Timely diagnosis and management led to a good overall outcome. This is in line with Patel et al (6) who states that given the severity of ICABs and lack of specific signs and symptoms, a high degree of suspicion is important for early detection, so that broad spectrum antibiotic administration and early surgical intervention can be successful in minimizing morbimortality and guaranteeing a positive outcome in these children.

Sex prevalence and average age were also congruent with previous studies, showing that adolescent boys are the most affected (10-12), which can be explained by their larger frontal sinuses, by the rapid development of the frontal sinus mucosa and neovascularization of the valveless diploic veins during adolescence, making them more prone to bacterial dissemination (8,13,14).

Interestingly, Bhat et al (15) described a non-statistical increase in IC in the years following the COVID pandemic, along with a change in seasonality. In our investigation, statistical differences in incidence were not found when comparing admissions before and after COVID. Year 2020 was the only period without ICABs admissions, most likely due to infection control measures implemented at the time.

Previous publications (6,11,16) described the majority of symptoms as non-specific, like fever and headache, with very few describing the typical symptoms of rhinosinusitis, like nasal discharge and facial pain, which is in line with our results. In contrast, our patients had higher rates of neurological symptoms, 57.1% upon admission, compared to other groups who described these symptoms in 18-38% of children at presentation and usually associated with longer LOH (6,10,17).

Most patients presented with leukocytosis and elevated CRP levels, as expected (10,11,18). Older children tended to present with greater CRP and Neutrophil-to-Lymphocytes Ratio (NLR), which might let us assume that adolescent's inflammatory response tends to be more intense and more similar to adults rather than to toddlers.

Surgical and medical intervention are unquestionably important in the treatment of ICABs. Our patients showed an analytical decline in CRP and NLR values immediately after surgery; this decline was even more pronounced in older children. So far, NLR has not yet been tested on its specificity to identify intracranial infections and cut-offs have not been properly defined. Yet the intervals 5 - 10 for local infections and 10 - 13 for systemic infections may be used as proposed by Buonacera et al (19). The average NLR in this study ( $12.3 \pm 7.8$ ) was above the proposed cut-off and it was interesting to observe its changes paralleling CRP values during the patients' recovery.

Similarly to previous studies (6,10,11), in which the frontal sinus was the most frequently involved, all patients in our series had frontal sinusitis. The frontal sinus begins its expansion after 2 years of age, growing rapidly between the ages of 6 and 19, explaining the rarity of frontal sinus affection and ICABs development in younger children (20).

When it comes to the proportions of ICabs, subdural (21,22) and epidural (9,10,16) collections have been described as the most commonly encountered sites. Infections in the subdural space are capable of faster dissemination when compared to epidural abscess, that spread in a slower fashion due to limited potential space between the dura and skull (9). In accordance, epidural abscesses were found to have lower CRP values on admission and discharge when compared to intraparenchymal cerebral abscesses.

In the current series, the sphenoid sinus was only involved in situations of pansinusitis and was never the sole offender, which is in concordance with previous studies which show that sphenoid rhinosinusitis is responsible for IC in a small percentage of cases (6,10). The severity of rhinosinusitis seemed to be more closely associated with cases of pansinusitis, meningitis and sagittal sinus thrombosis than to the sphenoid sinus involvement *per se*. Also, pansinusitis was associated with higher rates of lymphocytosis after surgery, potentially suggesting a change of the immune system response.

Orbital involvement should not distract from the possibility of concomitant intracranial complications in children (16), since they can be prevalent in up to 21% of children, as seen in this series.

Although, other studies obtained higher rates of positive microbiology cultures (92-94%) (6,8,10,16), only 7 (50%) of our patients had an identified pathogen. Microbiology of uncomplicated ARS tends to differ from the bacteria involved in sinogenic abscess formation. Traditionally most cases of ARS are caused by *Haemophilus influenzae*, *Streptococcus pneumoniae* and *Moraxella catarrhalis* (13). However, since the implementation of broad-spectrum antibiotics and the administration of the antipneumococcal vaccine to children it is theorized that the main responsible pathogens involved have changed (11, 23). In the current study, strains *Streptococcus anginosus* were the most frequently isolated bacteria (n=5/7, 71.4%); in fact this is a group whose pathogenicity is mainly explained by its ability to secrete hyaluronidase leading to liquefaction and abscess formation (24). We have not found polymicrobial growth to be linked to LOH as shown previously by Schupper et al (11), probably because there were only two patients with polymicrobial cultures in our study.

Third generation cephalosporins were administered to our patients for aerobic gram negative coverage, metronidazole for anaerobic coverage and its ability to penetrate the blood brain barrier and vancomycin was used to cover against methicillin-resistant staphylococcus aureus or until it was excluded by microbiology results in agreement with the work of Brook (25). Yoshikawa et al (26), advised that anaerobic bacteria play an underestimated role in subdural empyema formation. In accordance, metronidazole was administered to 11 of 14 of our children (78.6%).

No sinus involvement, type of complication or surgical procedure/intervention was statistically more likely to be associated with the need for reintervention.

The average LOH was higher than what other studies of the kind have described (10, 11, 18). On the other hand, the results may be over-estimated since after removing two outlier patients (121 and 116 days of hospitalization) the average LOH reduces to 42.3 days. One of these patients was admitted for 121 days, staying long after clinical improvement

because of social services problems that led to a potential overestimation of average length. The second longest hospitalization had a cerebellar and subdural abscess and cavernous sinus thrombosis that complicated with hydrocephalus, needing multiple neurosurgery reinterventions.

Other studies have identified polymicrobial cultures and frontal sinus involvement as potential risk factors for longer LOH (11), however, this was not the case in this series, as LOH was not influenced by presentation on admission, comorbidities, sinus involvement, type of ICAs and concomitant complications, type of surgical or medical treatment and biochemical or microbiological results.

Contrary to other studies, no patient had long term neurological sequelae on follow-up (6,8,10,16) but one child had significant morbidity due to hydrocephalus development. Whilst our study has shown very favorable outcomes, we must bear in mind other publications like the paper by Patel et al (6), whom in a systematic review of 180 patients, attributed rates of morbidity and mortality from sinogenic intracranial complications as of 27% and 3%, respectively.

The limitations of this study derive from its retrospective nature with small sample size, however, the fact that all cases were admitted and treated in the same hospital center makes its methodology congruent across all patients. On the other hand, patients have different follow-up times, ranging from ten years to six months. Lastly, microbiology results being positive in only 50% of cases makes conclusions hard to draw in this domain. Future prospective multicenter studies are certainly warranted.

## Conclusions

Our findings confirm the predominance of ICAs in adolescent males, with subdural abscesses as the most common intracranial complication associated with ARS. The frontal sinus stood out as the main culprit in the genesis of ICAs. *Streptococcus anginosus* group emerged as the predominant pathogen in our cohort.

Despite the inherited risk of significant morbidity and mortality, our series demonstrated that favorable outcomes can be achieved if early recognition, timely surgical management and appropriate antimicrobial therapy are implemented.

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## TABLES

**Table 1-** Summary demographics, affected sinus, intracranial abscesses and concomitant complications, surgical team and intervention, reintervention team

|    | Age/<br>Gender | Season,<br>Year | Intracranial abscesses and<br>concomitant complications                       | Affected<br>Sinuses | Surgical<br>Team | Surgical Intervention                                                                                                                                           | Reintervention |
|----|----------------|-----------------|-------------------------------------------------------------------------------|---------------------|------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------|
| 1  | 15/M           | W, 2015         | Ca                                                                            | E                   | ORL              | Drainage via FESS; Maxillary antrostomy; Anterior and posterior Ethmoidectomy                                                                                   |                |
| 2  | 14/M           | Sp, 2015        | Right Frontoparietal Sa; Cerebritis                                           | Fr, E, Mx           | ORL + NS         | Right parietal Craniotomy; Maxillary antrostomy via FESS; Ethmoidectomy via FESS;                                                                               |                |
| 3  | 13/M           | Sp, 2015        | Parietal Ca; Sa; SST; Men; Encephalitis                                       | Pansinusitis        | ORL              | Maxillary antrostomy; Anterior Ethmoidectomy;                                                                                                                   | ORL            |
| 4  | 12/F           | W, 2018         | Left Frontal Ea                                                               | Pansinusitis        | ORL + NS         | Left frontal craniotomy; Ethmoidectomy; Maxillary Antrostomy; Trephination of frontal sinus                                                                     |                |
| 5  | 17/F           | W, 2018         | Cerebellar Ca; Sa; CVST; Post Septal Cellulites; Hydrocephalus                | Fr, E               | ORL + NS         | Drainage via FESS; Occipital craniectomy; Maxillary Antrostomy;                                                                                                 | NS             |
| 6  | 12/M           | W, 2019         | Left Sa; SST; Men; Pre-Septal Cellulitis; Encephalitis                        | Pansinusitis        | ORL + NS         | Frontal and temporal craniotomy; Maxillary Antrostomy; Ethmoidectomy;                                                                                           |                |
| 7  | 17/M           | W, 2021         | Right Frontal Ca                                                              | Pansinusitis        | ORL              | Maxillary antrostomy via FESS; Ethmoidectomy via FESS; Trephination of frontal sinus;                                                                           | ORL + NS       |
| 8  | 8/F            | Sp, 2022        | Left Parasagittal Sa; Men                                                     | Pansinusitis        | NS               | Craniotomy                                                                                                                                                      |                |
| 9  | 12/M           | Sp, 2022        | Bilateral Frontal Sa; Osteomyelitis                                           | Fr                  | NS               | Frontal craniotomy; Trephination of frontal sinus; Maxillary antrostomy; Ethmoidectomy via FESS;                                                                | ORL            |
| 10 | 9/M            | Sm, 2022        | Left anterior Ea; Left Fronto-Lateral and Right Parafalcial Sa; Osteomyelitis | Fr                  | NS               | Craniotomy; Trephination of frontal sinus;                                                                                                                      |                |
| 11 | 7/M            | W, 2022         | Bilateral Fronto-Temporal Sa; Right Frontal Ea                                | Fr                  | ORL + NS         | Maxillary antrostomy via FESS; Ethmoidectomy via FESS;                                                                                                          |                |
| 12 | 13/F           | W, 2024         | Right Frontal Ea; Cerebritis                                                  | Fr                  | ORL + NS         | Frontal drainage via FESS; Right frontotemporal craniotomy; Trephination of the right frontal sinus; Anterior and posterior ethmoidectomy; Maxillary antrostomy | ORL            |
| 13 | 11/F           | Sp, 2024        | Right Parafalcial Sa; Right Paramedian Ea                                     | Fr                  | ORL + NS         | Frontal craniotomy; Maxillary antrostomy via FESS; Ethmoidectomy via FESS;                                                                                      |                |
| 14 | 10/M           | Sm, 2024        | Left Frontoparietaltemporal Sa; Right Paramedian frontal Sa                   | Fr                  | NS               | Frontoparietaltemporal Craniotomy;                                                                                                                              |                |

M: Male; F: Female; Fr: Frontal; E: Ethmoidal; Mx: Maxillary; S: Sphenoid; Ea: Epidural abscess; Sa: Subdural abscess; Ca: Cerebral abscess; Men: Meningitis; SST: Sagittal sinus thrombosis; CVST: Cavernous Sinus Thrombosis. W: Winter, Sp: Spring; Sm: Summer. Otorhinolaryngology: ORL. Neurosurgery: NS

**Table 2** – Symptoms on hospital admission and pre-hospitalization therapy.

|                                                | Frequency (%) | Mean duration of symptoms |
|------------------------------------------------|---------------|---------------------------|
| <i>Presenting Symptoms</i>                     |               |                           |
| Fever                                          | 14 (100)      | 6.08 ± 4.4                |
| Headache                                       | 13 (92.9)     | 8.08 ± 4.7                |
| Vomit                                          | 7 (50)        | 4.57 ± 2                  |
| Rhinorrhea                                     | 5 (35.7)      | 5.2 ± 5                   |
| Cervicalgia                                    | 2 (14.3)      | 8 ± 8                     |
| Frontal edema                                  | 2 (14.3)      | 2.5 ± 0.7                 |
| <i>Neurological Symptoms</i>                   |               |                           |
|                                                | 8 (57.1)      |                           |
| Seizures                                       | 5 (35.7)      |                           |
| Paresis                                        | 5 (35.7)      |                           |
| Prostration                                    | 3 (21.4)      |                           |
| Aphasia                                        | 2 (14.3)      |                           |
| <i>Antimicrobials prior to hospitalization</i> |               |                           |
|                                                | 7 (50)        |                           |
| Amoxicillin and Clavulanic Acid                | 5 (35.7)      |                           |
| Azithromycin                                   | 1 (7.1)       |                           |
| Not specified                                  | 1 (7.1)       |                           |
| <i>Corticotherapy prior to hospitalization</i> |               |                           |
|                                                | 2 (14.3)      |                           |

**Table 3** – Laboratory findings (mean ± sd), on admission after surgical treatment and before hospital discharge

|                               | Before admission | After surgery | Before discharge |
|-------------------------------|------------------|---------------|------------------|
| CRP (mg/L)                    | 202.09 ± 103.42  | 133.95 ± 92.2 | 9.23 ± 15.4      |
| WBC count ( $\times 10^9$ /L) | 17.47 ± 6.80     | 14.01 ± 5.57  | 7.84 ± 4.86      |
| Neutrophils (%)               | 83.9 ± 9         | 78.4 ± 10.9   | 45.96 ± 22.2     |
| Lymphocytes (%)               | 9.9 ± 6.3        | 14.5 ± 9      | 40.75 ± 17.9     |
| NLR                           | 12.3 ± 7.8       | 7.5 ± 4.3     | 2.18 ± 3.42      |

**Table 4** -Infected sinus, laterality and type of ARS complication.

|                                          | Frequency (%) |
|------------------------------------------|---------------|
| <i>Rhinosinusitis Laterality</i>         |               |
| <i>Unilateral</i>                        | 10 (71.4)     |
| <i>Bilateral</i>                         | 4 (28.6)      |
| <i>Intracranial Abscesses</i>            |               |
| <i>Subdural</i>                          | 10 (71.4)     |
| <i>Cerebral</i>                          | 4 (28.6)      |
| <i>Epidural</i>                          | 3 (21.4)      |
| <i>Other concomitant Septic IC</i>       |               |
| <i>Meningitis</i>                        | 3 (21.4)      |
| <i>Cerebritis</i>                        | 5 (35.7)      |
| <i>Encephalitis</i>                      | 2 (14.3)      |
| <i>Osteomyelitis</i>                     | 2 (14.3)      |
| <i>Sagittal Sinus Thrombosis</i>         | 2 (14.3)      |
| <i>Cavernous Sinus Thrombosis</i>        | 1 (7.1)       |
| <i>Concomitant Orbital Complications</i> | 3 (21.4)      |
| <i>Pre-Septal Cellulitis</i>             | 2 (14.3)      |
| <i>Post-Septal Cellulitis</i>            | 1 (7.1)       |

**Table 5** –Bacterial Isolates

| Species                            | N=14; Frequency (%) |
|------------------------------------|---------------------|
| <i>Positive Results</i>            | 7 (50)              |
| <i>Streptococcus intermedius*</i>  | 3 (42.9)            |
| <i>Streptococcus constellatus*</i> | 2 (28.6)            |
| <i>Streptococcus pneumoniae</i>    | 2 (28.6)            |
| <i>Staphylococcus epidermidis</i>  | 1 (14.3)            |
| <i>Fusobacterium nucleatum</i>     | 1 (14.3)            |
| <i>Dialister pneumosintes</i>      | 1 (14.3)            |

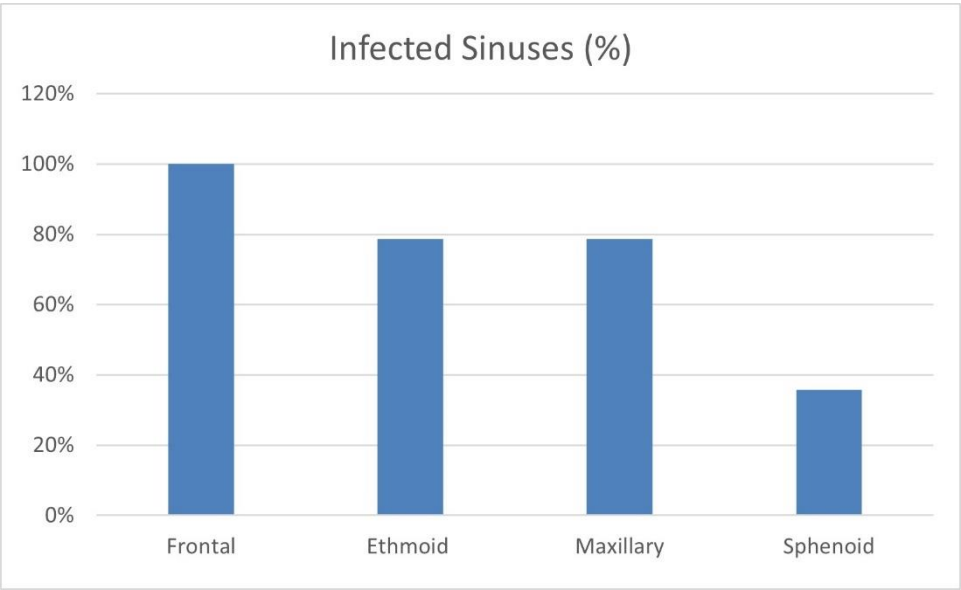
(\*belongs to the *Streptococcus anginosus* group)

**Table 6** – Surgical management

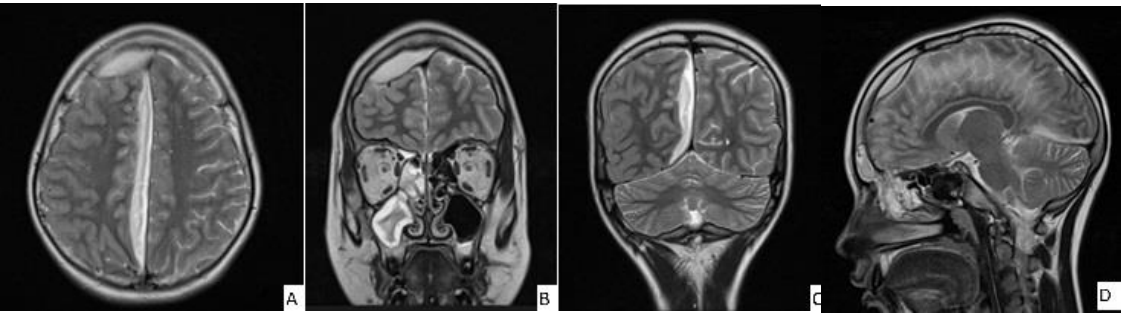
| <i>Surgical Approach</i>  |                                         | <i>Frequency (%)</i> |
|---------------------------|-----------------------------------------|----------------------|
| <i>Surgical team</i>      |                                         |                      |
|                           | <i>Otorhinolaryngology</i>              | 10 (71.4)            |
|                           | <i>Neurosurgery</i>                     | 11 (78.6)            |
|                           | <i>Neurosurgery+Otorhinolaryngology</i> | 7 (50)               |
| <i>Surgical procedure</i> |                                         |                      |
|                           |                                         | 14 (100)             |
|                           | <i>Craniotomy</i>                       | 9 (64.3)             |
|                           | <i>FESS</i>                             | 7 (50)               |
|                           | <i>Maxillary antrostomy</i>             | 11 (78.6)            |
|                           | <i>Ethmoidectomy</i>                    | 9 (64.3)             |
|                           | <i>Frontal Sinus Trephination</i>       | 5 (35.7)             |
|                           | <i>Craniectomy</i>                      | 1 (7.1)              |
|                           | <i>Frontal Sinusotomy</i>               | 1 (7.1)              |

FIGURES

**Figure 1** – Frequency of infected sinus



**Figure 2** – Axial (A), coronal (B, C) and sagittal (D) T2 weighted MRI brain images of patient 13



STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

|                           | Item No | Recommendation                                                                                                                                                                                                        | Page No                                                                                                                                                                                                                                                                                                                                                                          |
|---------------------------|---------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Title and abstract</b> | 1       | (a) Indicate the study's design with a commonly used term in the title or the abstract –<br>(b) Provide in the abstract an informative and balanced summary of what was done and what was found                       | Page 6 - "A Ten Year Experience";                                                                                                                                                                                                                                                                                                                                                |
| <b>Introduction</b>       |         |                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                  |
| Background/rationale      | 2       | Explain the scientific background and rationale for the investigation being reported                                                                                                                                  | Page 7 – "Acute bacterial rhinosinusitis occurs in about 7% of children with upper respiratory infections (1). Rarely, this common inflammation of the paranasal and nasal sinus mucosa can complicate and extend to the orbit and/or intracranially, especially in children."                                                                                                   |
| Objectives                | 3       | State specific objectives, including any prespecified hypotheses                                                                                                                                                      | Page 7 – "This study aims to address the recent experience of a tertiary university hospital in the management of intracranial abscesses secondary to acute rhinosinusitis, during a period encompassing the last ten years."                                                                                                                                                    |
| <b>Methods</b>            |         |                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                  |
| Study design              | 4       | Present key elements of study design early in the paper                                                                                                                                                               | Page 8 – "Electronic charts from children below 18 years of age, admitted to a tertiary pediatric care hospital with a diagnosis of intracranial abscesses between January 2015 and December 2024, were retrospectively reviewed. All data available – clinical, microbiology and imaging by CT or MRI - were screened to identify intracranial abscesses of sinogenic origin. " |
| Setting                   | 5       | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection                                                                                       | Page 7-8 "Pediatric Otorhinolaryngology of the Department of Otorhinolaryngology from a tertiary academic hospital center with Pediatric Neurosurgery and Pediatric Intensive Care facilities."                                                                                                                                                                                  |
| Participants              | 6       | (a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up<br><br>(b) For matched studies, give matching criteria and number of exposed and unexposed | Page 8 "children below 18 years of age, admitted to a tertiary pediatric care hospital with a diagnosis of ICabs"; "All data available – clinical, microbiology and imaging by CT or MRI - were screened to identify ICabs of sinogenic origin."                                                                                                                                 |
| Variables                 | 7       | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable                                                                              | Page 8 "The following information was collected from the electronic records of each patient: age, gender, comorbidities, month and year of diagnosis, symptoms and their duration before hospitalization, antimicrobials and steroids before                                                                                                                                     |

|                              |     |                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
|------------------------------|-----|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                              |     |                                                                                                                                                                                                                                                                                                                                               | admission, laboratory findings (C-Reactive Protein - CRP, neutrophils, lymphocytes and leucocytes on admission, after surgery and before discharge), laterality and sinus affected by ARS, ICABs and concomitant complications, microbiology results, medical and surgical management, length of hospitalization (LOH) and duration of stay in the Pediatric Intensive Care Unit when needed.”                                                                                                                                                                                                                                                    |
| Data sources/<br>measurement | 8*  | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group                                                                                                                                                          | Page 8 “collected from the electronic records of each patient”                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| Bias                         | 9   | Describe any efforts to address potential sources of bias                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| Study size                   | 10  | Explain how the study size was arrived at                                                                                                                                                                                                                                                                                                     | Page 8 “clinical, microbiology and imaging by CT or MRI - were screened to identify ICABs of sinogenic origin.”                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| Quantitative variables       | 11  | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why                                                                                                                                                                                                                  | Page 8 “Quantitative variables were described using their means and range”                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| Statistical methods          | 12  | <p>(a) Describe all statistical methods, including those used to control for confounding</p> <p>(b) Describe any methods used to examine subgroups and interactions</p> <p>(c) Explain how missing data were addressed</p> <p>(d) If applicable, explain how loss to follow-up was addressed</p> <p>(e) Describe any sensitivity analyses</p> | <p>Page 8 “Quantitative variables were described using their means and range, whereas categorical variables were described as numbers and percentages. For statistical analysis, Fisher’s Test was used to compare categorical variables like demographics and clinical presentation, Man-Whitney U Test for non-parametric continuous variables and Spearman Correlation for continuous variable associations. Significance was set at <math>p \leq 0.05</math>. All statistical analysis was performed with IBM SPSS Statistics Data Editor™ 30.0.”</p> <p>Non applicable</p> <p>Non applicable</p> <p>Non applicable</p> <p>Non applicable</p> |
| <b>Results</b>               |     |                                                                                                                                                                                                                                                                                                                                               | Pages 9 - 11                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| Participants                 | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially                                                                                                                                                                                                                                                               | Page 9 “This study included 14 pediatric patients fitting the previously defined criteria”                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |

|                   |     |                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
|-------------------|-----|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                   |     | <p>eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed</p> <p>(b) Give reasons for non-participation at each stage</p> <p>(c) Consider use of a flow diagram</p>                                                                                                                                                                                               | Non applicable                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| Descriptive data  | 14* | <p>(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders</p> <p>(b) Indicate number of participants with missing data for each variable of interest</p> <p>(c) Summarise follow-up time (eg, average and total amount)</p>                                                                                                                | <p>Page 9 “male predominance, with nine boys (64,3%), and five girls (35,7%). Mean age at diagnosis was <math>12.14 \pm 3.04</math> years old (range 7-17), nine (64.3%) were older than 12 years old. Thirteen patients (92.9%) were Caucasian and one child (7.1%) was of Romani ethnicity”</p> <p>“Seasonality” “All children had symptoms prior to diagnosis”</p> <p>Non applicable</p> <p>Page 11 “Length of hospitalization was <math>53.2 \pm 28.1</math> days on average” “On the other hand, patients have different follow-up times, ranging from ten years to six months”</p> |
| Outcome data      | 15* | Report numbers of outcome events or summary measures over time                                                                                                                                                                                                                                                                                                                                                               | Page 11 “Length of hospitalization”; “needed a second surgery”; “No cases of mortality were registered and morbidity rate was...”                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| Main results      | 16  | <p>(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included</p> <p>(b) Report category boundaries when continuous variables were categorized</p> <p>(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period</p> | <p>Page 8 “Significance was set at <math>p \leq 0.05</math>”</p> <p>Non applicable</p> <p>Non applicable</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| Other analyses    | 17  | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses                                                                                                                                                                                                                                                                                                                               | Non applicable                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| <b>Discussion</b> |     |                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| Key results       | 18  | Summarise key results with reference to study objectives                                                                                                                                                                                                                                                                                                                                                                     | Page 12 “these rare complications mainly affected male adolescents with frontal ARS. Timely diagnosis and management led to a good overall outcome.”;                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| Limitations       | 19  | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias                                                                                                                                                                                                                                                                   | Page 14 “The limitations of this study derive from its retrospective nature with small sample size, however, the fact that all cases were admitted and treated in the same hospital center makes its                                                                                                                                                                                                                                                                                                                                                                                     |

|                          |    |                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                               |
|--------------------------|----|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                          |    |                                                                                                                                                                            | methodology congruent across all patients. On the other hand, patients have different follow-up times, ranging from ten years to six months. Lastly, microbiology results being positive in only 50% of cases makes conclusions hard to draw in this domain. Future prospective multicenter studies are certainly warranted.” |
| Interpretation           | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | Page 12 - 14                                                                                                                                                                                                                                                                                                                  |
| Generalisability         | 21 | Discuss the generalisability (external validity) of the study results                                                                                                      | Non applicable                                                                                                                                                                                                                                                                                                                |
| <b>Other information</b> |    |                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                               |
| Funding                  | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based              | Non                                                                                                                                                                                                                                                                                                                           |

\*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at <http://www.strobe-statement.org>.

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- **A title page**, including the manuscript title and all authors' full names, academic degrees (no more than three), institutional affiliations, locations, and ORCID iD. Designate one author as the corresponding author. Also indicate where the paper was presented, if applicable.
- **A structured abstract** of up to 250 words with the headings: Introduction, Objective, Methods, Results, and Conclusion.
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### Systematic Reviews (including Meta-analyses)

Critical assessments of literature and data sources on important clinical topics in otolaryngology-head and neck surgery. Systematic reviews that reduce bias with explicit procedures to select, appraise, and analyze studies are highly preferred over traditional narrative reviews. The review may include a meta-analysis, or statistical synthesis of data from separate, but similar, studies leading to a quantitative summary of the pooled results. The components of a systematic review are:

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- **A structured abstract** of up to 250 words with the headings: Introduction, Objectives, Data Synthesis, and Conclusion.
- **The Manuscript body** should be divided as: introduction; review of a particular subject; discussion; final comments; references.

- *Manuscript length* of no more than 15 pages (exclusive of the title page and abstract).

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The manuscript is an update that explores a particular subject, developed from current data, based on recently published works.

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Huttenhower C, Gevers D, Knight R, et al. Structure, function and diversity of the healthy human microbiome. *Nature* 2012;486(7402):207-214
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Baldwin KB. An exploratory method of data retrieval from the electronic medical record for the evaluation of quality in healthcare [dissertation]. Chicago: University of Illinois at Chicago, Health Sciences Center; 2004:116
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Valente M, Hosford-Dunn H, Roeser RJ. *Audiology Treatment*. 2nd ed. New York: Thieme; 2008
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Vilkman E. A survey on the occupational safety and health arrangements for voice and speech professionals in Europe. In: Dejonckere PH, ed. *Occupational Voice: Care and Cure*. Hague: Kugler Publications; 2001:129-137
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## Declaração

Para os devidos efeitos declaro que o estudo 'Intracranial Complications of Pediatric Rhinosinusitis', apresentado a esta Comissão de Ética por Maria Francisca de Almeida Marques Queirós Ribeiro, no âmbito do Mestrado Integrado em Medicina da FMUP, foi submetido com a referência CE-453-24, e que o mesmo foi avaliado e aprovado na reunião de 20 de dezembro de 2024.

Porto e Unidade Local de Saúde de São João, 20 de março de 2025

Pedro Brito, Secretário da CE da ULS de São João

