

# Anatomical Variation of the Frontal Sinus Outflow Tract in the Pediatric Population in KwaZulu-Natal: A Cause for Complicated Sinusitis with Intracranial Complications?

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## Abstract

**Objective:** The objective of this study was to compare the anatomical variations in the frontal sinus outflow tract (FSOT) of pediatric patients with sinogenic intracranial complications to those without and determine if the bone density of the frontal bone contributed to intracranial disease progression.

**Methods:** This study was carried out at a quaternary hospital in Durban, South Africa between January 2018 and August 2020. Multi-detector computed tomography (MDCT) scans of pediatric patients who presented with sinogenic intracranial complications were used to trace the anatomy of the FSOT and compared to patients without complicated sinusitis. The patients were divided into three groups. Group A: control group, Group B: patients with sinusitis, but no intracranial complications and Group C: patients with sinusitis complicated by intracranial spread. The specific parameters observed the presence of frontal cells and agger nasi cell, the diameter of the frontal sinus ostium and the bone density of the frontal sinus.

**Results:** A total of 83 patients met the inclusion criteria (53 males and 30 females). Important findings included disease involvement of the frontal sinus in all patients in group C. Frontal cells were found to occur in higher proportions in the groups with sinusitis (groups B and C) with the overall prevalence of frontal cells being 88%. Preventative measures implemented against the spread of the SARS CoV-2 virus was observed to influence the number of patients with this disease.

**Conclusions:** This study highlights the anatomical variations that the otorhinolaryngologist managing patients with complicated sinusitis be aware of especially when surgery is being considered.

**Keywords:** Frontal cells, frontal sinus, intracranial complications, sinusitis

## INTRODUCTION

Sinusitis is defined as inflammation of the mucosa of the paranasal sinuses and in the majority of cases is the result of a bacterial or viral infective process.<sup>1</sup> It is termed complicated sinusitis when the progression of the disease extends outside of the paranasal sinuses with complications divided into orbital, bony, and intracranial.<sup>1,2</sup>

Intracranial complications range from meningitis to intracranial abscesses and venous sinus thrombosis.<sup>3</sup> Spread is hematogenic via the rich supply of valveless diploic veins that penetrate the dura mater.<sup>4</sup> Intracranial complications are usually a result of frontal sinus disease.<sup>5</sup>

The frontal sinus, located between the anterior table (AT) and posterior table (PT) of the frontal bone,<sup>6</sup> is pyramidal in shape and is divided into 2 cavities by the intersinus septum.<sup>3</sup> The AT is composed of thick cortical bone whereas the PT is thin and forms part of the anterior cranial fossa and is separated from the frontal lobes of the brain by the dura.<sup>3</sup>

In children, the paranasal sinuses are present at birth but start to pneumatize from around the age of 7 and then undergo rapid growth up until the age of 18.<sup>7-9</sup>

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Each frontal sinus is drained by its own frontal sinus outflow tract (FSOT).<sup>6</sup> The FSOT has an hourglass shape when viewed in the sagittal plane with the narrowest point at the frontal sinus ostium (FSO).<sup>1</sup>

The superior portion of the hourglass is the frontal sinus infundibulum and the inferior portion is the frontal recess.<sup>1</sup> The FSO is found at the most medial and inferior aspect of the frontal sinus cavity and leads into the frontal recess.<sup>6</sup> The drainage pattern, shape, and width of the frontal recess are influenced by the following boundaries, that is, medially is the middle turbinate, laterally the lamina papyracea and lacrimal bone, the agger nasi cell anteriorly, and the ethmoidal bulla and anterior ethmoidal cells are posterior. The inferior boundary is determined by the attachment of the uncinate and the agger nasi.<sup>3</sup> The presence of frontal cells has shown to cause obstruction of the FSOT and can push the drainage pathway anteriorly or posteriorly depending on their location.<sup>10</sup>

Bone mineral density development differs with age in cranial bones.<sup>11</sup> A study by Takahashi et al<sup>11</sup> investigated this by measuring the bone mineral density of the mastoid bone and how this affected the spread of acute mastoiditis. They found that the regional differences in bone maturation could partly account for the spread of acute mastoiditis in different age groups and also suggested that this may be applicable to the different patterns of spread of complicated sinusitis in children.

Risk factors for complicated sinusitis with intracranial complications include children over the age of 7 as the frontal sinuses begin to develop from this age.<sup>5,7,9</sup> There is also usually a preceding history of a viral upper respiratory tract infection (URTI).<sup>1,3</sup> Other factors which influence the development of complicated sinusitis include poor socioeconomic status, seasonal variation with a higher incidence in the winter months, and anatomical variations in the drainage pathway of the paranasal sinuses.<sup>5,7,9,12</sup>

The aim of this study was to compare the anatomy of the FSOT in patients with complicated sinusitis to those without, in order to determine the influence of anatomic variations of the FSOT on the development of complications and if the bone density of the frontal bone contributed to intracranial disease progression.

## METHODS

### Setting

This was a prospective comparative study carried out on pediatric patients with complicated sinusitis and intracranial complications seen at the Inkosi Albert Luthuli Central Hospital (IALCH) in Durban, South Africa. The province of Kwa Zulu Natal has a population of 11.5 million people (Statistics SA 2020) with only 15% on medical insurance (Council for Medical Schemes report, 2020) leaving approximately 9.8 million people dependent on state

### Main Points

- *This study highlights the anatomical differences in patients who have complicated sinusitis with intracranial complications and the importance of addressing them to prevent further morbidity and mortality.*
- *The presence of frontal cells contributes to the narrowing of the frontal sinus outflow tract and was found to occur more often in patients with complicated sinusitis.*
- *Mucosal edema, secondary to acute inflammation, appears to contribute more to obstruction of the frontal sinus ostium than just bony narrowing alone.*
- *The bone density of the frontal bone did not appear to affect the spread of disease to the brain.*

healthcare services. Inkosi Albert Luthuli Central Hospital is the only quaternary hospital in this sector, and as it offers otorhinolaryngology (ENT) and neurosurgical services, it is the single center of referral for these cases.

### Computed Tomography Scan

Patients referred with symptoms of complicated sinusitis underwent a contrast-enhanced multi-detector computed tomography (MDCT) scan as a standard of care. This confirmed the presence of intracranial sepsis, delineated which sinuses were diseased and assisted with neurosurgical and ENT surgical planning.

To ensure uniformity, all paranasal sinus scans for patients with complicated sinusitis were requested to be scanned at 1.0 mm irrespective of age, using the Siemens Definition AS (Siemens, Malvern, Pa, USA). Consent for undertaking the procedure as well as administration of contrast material was obtained prior to the MDCT being conducted. Each patient also had to give assent to be a part of the study. The study was approved by the Biomedical Research and Ethics Council (BE502/18) as well as the Kwa Zulu Natal department of Health.

### Patient Selection

The study population consisted of male and female patients, below the age of 18 that were found to have clinical and radiological evidence of complicated sinusitis between January 2018 and August 2020.

Patients or their guardians were required to give assent (in the case of minors) and consent was taken for study participation.

### Exclusion Criteria

Patients who had sustained previous nasal or facial trauma or had undergone previous sinus surgery. The selected patients were then compared to 2 other groups to allow for more meaningful analysis, as shown below:

Group A: control group—no clinical evidence of complicated sinusitis. These were patients, below the age of 18, who had presented to the ENT clinic at IALCH with conditions that required an MDCT of the internal auditory meatus. With similar acquisition protocols, these images were used as an anatomical reference if confirmed to be devoid of any paranasal sinus disease.

Group B: This group consisted of patients who presented with features of complicated sinusitis (e.g., peri-orbital cellulitis/abscess) but with no intracranial complications detected on the MDCT scan.

Group C: This group included all patients with complicated sinusitis and intracranial complications confirmed on the MDCT scan.

The scans were analyzed and the anatomical factors that were recorded included the presence of an agger nasi cell and the presence of frontal cells. The bone density of the AT and PT of the frontal sinus using the axial slices was measured bilaterally. The scans were scrolled through until both frontal sinuses and inter-sinus septum was in view and measurements of the AT and PT were then taken. Bone density measurements were also taken of the nasion on the sagittal slices to use as a control, as this is hard bone. The bone density was measured in Hounsfield using the pixel tool found on the radiology viewing software used by IALCH, that is, Siemens Syngo.plaza (Siemens).

The anteroposterior and medial-lateral diameter of the FSO was measured in centimeters using the sagittal (for anteroposterior measurements) and

the coronal slices (for medial-lateral measurements). The FSOT was identified using the infundibulum and following the FSOT pathway into the nose on the sagittal slices first, the axial and coronal scans were then viewed side by side with the cross-referencing tool and the subsequent measurements were taken.

### Statistical Analysis

The statistical data analysis was conducted in R Statistical computing software of the R Core Team, 2020, version 3.6.3. The results are presented in the form of descriptive and inferential statistics. The descriptive statistics of numerical measurements were summarized as the means and standard deviation. On the other hand, the categorical variables were described as counts as well as simple and multiple bar charts were used to visually display the categorical variables. To assess the mean difference of numerical measurements across 3 levels of a categorical variable, analysis of variance test were used for normally distributed measurements and Kruskal-Wallis for assessing the median difference of the non-normally distributed measurements. In the case of significant mean difference, post hoc tests were conducted using Tukey's honestly significant difference single-step multiple comparison procedure and similarly with Dunn's test for a significant difference in the medians. Significance was set at  $P < .05$ .

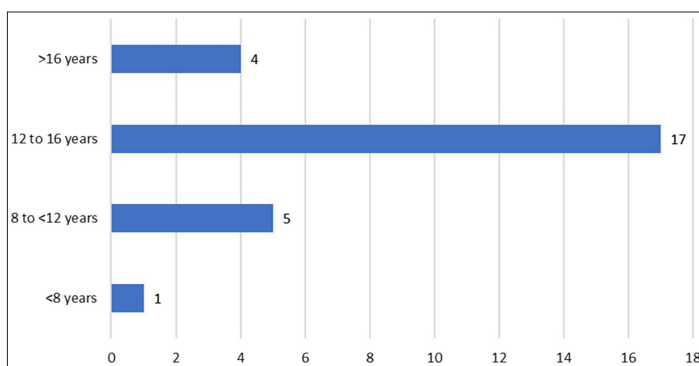
### RESULTS

The 83 patients who were included were split into the following groups: groups A (control) and B had 28 patients each and group C had 27 patients. There was an overall male predominance with a total of 53 males and 30 females ( $P = .5$ ), with the male to female distribution per group being: A: 20 males and 8 females, B: 16 males and 12 females, and C: 17 males and 10 females. There was no significant difference in mean age (Table 1).

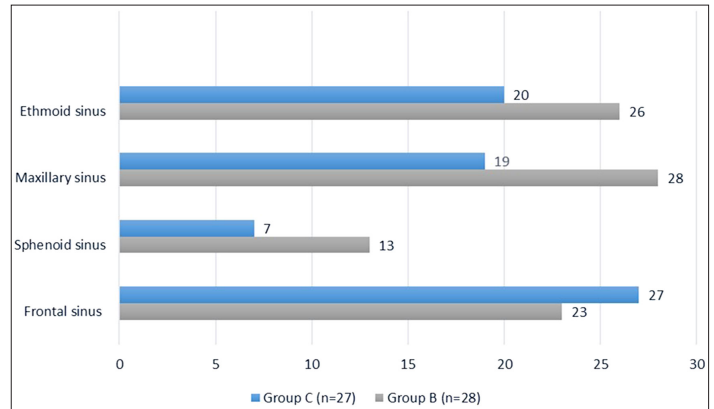
With age further stratified, those between 12 and 16 were found to have the highest risk of complicated sinusitis with intracranial complications while children below 8 years had the lowest (Figure 1).

**Table 1.** Mean Age  $\pm$  Standard Deviation (SD) in Years Between the 3 Groups

Group	A n=28	B n=28	C n=27	P	Overall n=83
Mean $\pm$ SD (years)	11.9 $\pm$ 4.39	10.8 $\pm$ 3.63	12.7 $\pm$ 3.11	.160	11.8 $\pm$ 3.80



**Figure 1.** Graph demonstrating the number of patients with complicated sinusitis and intra-cranial complications according to age.



**Figure 2.** Graph demonstrating the individual sinuses involved in all patients with complicated sinusitis.

The frontal sinus was found to be diseased in all patients with intracranial complications (100%,  $n = 27$ ) as opposed to those without (82%,  $n = 28$ ); however, this was not statistically significant ( $P > .05$ ) (Figure 2).

### Anatomical Variants in the Frontal Sinus Outflow Tract

#### Frontal Cells

In this study, the overall prevalence of frontal cells was found to be 88%, with a higher proportion in groups B (92.9%) and C (92.6%) compared to group A (78.6%) but was not significant ( $P > .05$ ).

#### Other Variants

The presence of a pneumatized middle turbinate (concha bullosa) was observed to have a higher prevalence in the group with intracranial complications (group C = 33%) compared to the control groups (group A = 25% and group B = 11%), but this was not statistically significant,  $P > .05$ .

#### Drainage Pattern of Frontal Sinus Outflow Tract

The presence of an agger nasi cell was 84% overall with no significant difference across the 3 groups (group A = 89%, group B = 79%, and group C = 85%),  $P > .05$ .

The exact position of the superior attachment of the uncinate process could not be accurately determined in the majority of scans due to mucosal edema and partial volume artifact.

### Narrowing of the Frontal Sinus Ostium

There was no statistically significant difference in the anteroposterior diameter of the FSO between the 3 groups; however, the bilateral medial-lateral diameter was found to be larger in group C compared to the other 2 groups (Tables 2 and 3). Analysis of variance showed that when frontal cells were present, the FSO diameter could decrease by 23%.

### Bone Density

There was no statistical difference in the bone density at the AT and PT of the frontal sinus among the 3 groups. This was also found to have no difference when compared among different age groups (Tables 4 and 5).

**Table 2.** Mean  $\pm$  Standard Deviation (SD) Values of the Medial-Lateral Right Frontal Sinus Ostium Between the 3 Groups

Group	A	B	C	P
Mean $\pm$ SD (mm)	0.271 $\pm$ 0.0867	0.232 $\pm$ 0.0612	0.326 $\pm$ 0.890	<.001

**Table 3.** Mean  $\pm$  Standard Deviation (SD) Values of the Medial-Lateral of the Left Frontal Sinus Ostium Between the 3 Groups

Group	A	B	C	P
Mean $\pm$ SD (mm)	0.242 $\pm$ 0.0905	0.257 $\pm$ 0.116	0.300 $\pm$ 0.0898	.013

**Table 4.** Mean  $\pm$  Standard Deviation (SD) of the Bone Density Measurements in Hounsfield units Between the 3 Groups

	Right AT	Left AT	Right PT	Left PT
Group A	833 $\pm$ 351	967 $\pm$ 335	821 $\pm$ 302	911 $\pm$ 251
Group B	848 $\pm$ 330	885 $\pm$ 286	851 $\pm$ 311	937 $\pm$ 282
Group C	843 $\pm$ 287	875 $\pm$ 285	710 $\pm$ 219	818 $\pm$ 261
P	.983	.466	.157	.225

AT, anterior table; PT, posterior table.

**Table 5.** Mean  $\pm$  Standard Deviation (SD) of the Bone Density Measurements in Hounsfield Units Between the Different Age Groups

	Right AT	Left AT	Right PT	Left PT
<8 years	765 $\pm$ 356	925 $\pm$ 461	805 $\pm$ 387	871 $\pm$ 292
8 to <12 years	823 $\pm$ 288	828 $\pm$ 243	783 $\pm$ 279	951 $\pm$ 254
12 to <16 years	855 $\pm$ 305	971 $\pm$ 253	797 $\pm$ 258	874 $\pm$ 269
>16 years	902 $\pm$ 404	849 $\pm$ 337	790 $\pm$ 298	844 $\pm$ 272
P	.763	.316	.997	.658

AT, anterior table; PT, posterior table.

## DISCUSSION

Sinusitis with intracranial complications carries a significant risk of morbidity and mortality risk with a high incidence in developing countries.<sup>9</sup> Anatomical variations of the frontal sinus have been noted to contribute to obstruction of its outflow tract in patients with chronic sinusitis as well as acute sinusitis, but the investigators wanted to determine if it played a role in causing intracranial complications.<sup>13</sup>

The study showed a teenage male predominance, which was expected as it is an established feature of the disease.<sup>5,7,9</sup> Complicated sinusitis with intracranial spread is uncommonly found in children below the age of 7 as the frontal sinuses are hypoplastic and only begin to pneumatize from the age of 7 and upwards, which was evidenced by this study having the lowest number of patients in the study group below the age of 8.

### Frontal Cells

The presence of frontal cells may contribute to significant narrowing of the frontal ostium diameter in the diseased state and may represent a risk factor for developing frontal sinusitis with intracranial complications. It is well known that these cells are a cause for frontal sinus outflow obstruction and are a cause for surgical failure in patients undergoing endoscopic sinus surgery (ESS).<sup>10,14</sup> Velasquez et al<sup>13</sup> found that pediatric patients with acute frontal sinusitis had a higher prevalence of frontal cells and a more complicated anatomical pattern of the FSOT. This was in keeping with the results of this study, where although the type of frontal cell was not investigated, the presence of frontal cells was noted to occur more

often in those patients with complicated sinusitis. This highlights the role that frontal cells play as a predisposing factor in developing complicated sinusitis.

### Narrowing of the Frontal Sinus Ostium

The size of the FSO and FSOT is affected by the degree of pneumatization (rather than the presence) of the agger nasi air cells and the presence of frontal cells. The finding of an increased medial to lateral diameter of the FSO in patients with intracranial complications perhaps speaks to the concept that it is the 3-dimensional FSOT volume that is more relevant to obstruction.

The narrowest part of the ostium ranges from between 0.2 and 0.3 mm in diameter, and the results may be affected by inaccuracies in the reconstruction and reformatting of the scans which were done at 1.0 mm.

This may also highlight the obstructive role of inflammatory mucosal edema of the sinus outflow tract. This finding was also noted by Thorp et al<sup>12</sup> in their study on the frontal sinus.

### Bone Density Measurements

The pattern of spread of the intracranial complication was not determined by the bone density of the surrounding bony boundaries. Takahashi et al<sup>11</sup> in their study on the pattern of spread of infection in acute mastoiditis found that the spread was dependent on the bone density of the temporal bone in children of different ages. They postulated that this could be applied to children with complicated sinusitis; however, the results we obtained revealed no significant difference in the bone density of the frontal sinus boundaries when compared among the different sample groups. This finding suggests that hematogenous spread via diploic veins or along natural bony foramina are the more likely routes of spread of infection outside the sinuses.<sup>1,9</sup>

The high degree of mucosal edema was a limiting factor in tracing and identifying the superior attachment of the uncinat process as well as measuring the exact ostium of the FSOT. As a result, the superior attachment of the uncinat cannot be reliably used as a predisposing anatomical variant for developing acute complicated sinusitis in this study. This may be improved with better imaging quality, that is, ultra-thin MDCT slice thickness (<0.5 mm).

We were not able to control variables such as scan quality as many patients presented to us with inadequate scans from other health facilities and led to exclusion from the study. It would have been impractical to expose the patient to unnecessary radiation from a repeat CT exclusively for the purposes of this study.

The ongoing COVID-19 pandemic led to South Africa entering a lockdown period on March 26, 2020, with mandatory mask-wearing in public and hand-washing practices being enforced. The number of patients presenting to IALCH with complicated sinusitis in the 12 months prior to the implementation of these public health measures was 39 cases and this decreased by 40% in 2020 to 17 cases. This is supported by international data showing there was a significant decrease in the number of patients presenting with viral URTIs since the start of the pandemic.<sup>15</sup> Even though this was not an objective of the study it is an important observation, as URTIs are described as a preceding factor in the pathogenesis of complicated sinusitis.<sup>1,3</sup>

This study highlights the frontal cell and its intimate relationship with the FSOT as well as the effect of frontal sinusitis on developing intracranial

complications. These cells in conjunction with mucosal edema that occurs in diseased sinuses contribute to frontal sinus obstruction. The hypothesis that the pattern of intracranial spread could be influenced by the bone density of the frontal bone did not hold in this study and suggests that the spread is more likely from hematogenous pathways. The managing ENT surgeon should look for these anatomic variants in patients presenting with complicated sinusitis so that they are addressed at the time of primary surgery. Further research considerations include evaluating how the different types of frontal cells contribute to the narrowing of the FSOT by employing the use of cone beam CT, as this allows for improved scan reconstruction and optimal visualization of fine anatomical detail.

## CONCLUSION

Complicated sinusitis with intracranial complications is still a highly prevalent disease in our population and should not be taken lightly. The key is early identification of the disease by adopting a high degree of suspicion to allow timely diagnosis, preferably before the progression of intracranial spread. Surgical treatment of the sinuses is often employed as first-line treatment in our setting, and identification and understanding of the anatomical variations and how they affect the outflow tract are imperative. As shown in this study, frontal cells should be actively searched for, especially in patients with frontal sinus disease as they are a pre-disposing factor for developing frontal sinusitis. This will allow for them to be addressed at the time of surgery and contribute to decreasing the morbidity associated with this disease.

It is also interesting to note the public health implications that the simple measures of mask-wearing and hand hygiene have on decreasing the spread of URTIs, specifically during winter months when the rate of influenza is at its peak. It potentially has a knock-on effect in decreasing the progression of the disease, in this case, to complicated sinusitis.

**Ethics Committee Approval:** This study was approved by the Biomedical Research Ethics Council (BREC) (Reference number: BE502/18).

**Informed Consent:** Written informed consent was obtained from the patients who participated in this study.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept – T.N., C.R., K.S.; Design – T.N., C.R., K.S.; Data Collection and/or Processing – T.N.; Analysis and/or Interpretation – T.N.; Writing Manuscript – T.N., C.R., K.S.; Critical Review – C.R., K.S.

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**Declaration of Interests:** The authors declare that they have no competing interest.

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## REFERENCES

1. Benninger M, Chapter 113. Rhinosinusitis. In: Gleeson M, ed. *Scott-Brown's Otolaryngology and Head and Neck Surgery*. 7th ed; 2008:1439-1448.
2. Giannoni C, Chapter 38: Complications of rhinosinusitis Johnson J, Rosen C, eds. *Bailey's Head and Neck Surgery- Otolaryngology*. 5th ed. Philadelphia: Lippincott Williams and Wilkins; 2013:573-585.
3. Schick B, Draff W. The frontal sinus. In: Kountakis S, Senior BA, Draff W, eds. *Rhinology and Facial Plastic Surgery*. Berlin: Springer; 2009:567-573.
4. Germiller JA, Monin DL, Sparano AM, Tom LWC. Intracranial complications of sinusitis in children and adolescents and their outcomes. *Arch Otolaryngol Head Neck Surg*. 2006;132(9):969-976. [\[CrossRef\]](#)
5. Oxford LE, McClay J. Complications of acute sinusitis in children. *Otolaryngol Head Neck Surg*. 2005;133(1):32-37. [\[CrossRef\]](#)
6. D'Antoni AV. Gray's anatomy. The anatomical basis of clinical practice [internet]. In: Standing S, ed. *Clinical Anatomy*. 41st ed. 2016:556-571. Available at: <http://ebooks.cambridge.org/ref/id/CBO9781107415324A009%0Ahttp.wiley.com/10.1002/ca.22677>.
7. Tshifularo M, Monama GM. Complications of inflammatory sinusitis in children: institutional review. *S Afr Fam Pract*. 2006;48(10):16-16c. [\[CrossRef\]](#)
8. Ahmed A. Imaging of the paediatric paranasal sinuses. *South African J Radiol*. 2013;17(3). Available at: <http://www.sajr.org.za/index.php/sajr/article/view/273/346>.
9. Schlemmer KD, Naidoo SK. Complicated sinusitis in a developing country, a retrospective review. *Int J Pediatr Otorhinolaryngol*. 2013;77(7):1174-1178. [\[CrossRef\]](#)
10. Wormald PJ, Hoseman W, Callejas C, et al. The International Frontal Sinus Anatomy Classification (IFAC) and classification of the extent of endoscopic frontal sinus surgery (EFSS). *Int Forum Allergy Rhinol*. 2016;6(7):677-696. [\[CrossRef\]](#)
11. Takahashi K, Morita Y, Ohshima S, Izumi S, Kubota Y, Horii A. Bone density development of the temporal bone assessed by computed tomography. *Otol Neurotol*. 2017;38(10):1445-1449. [\[CrossRef\]](#)
12. Thorp MA, Roche P, Nilssen EL, Mortimore S. Complicated acute sinusitis and the computed tomography anatomy of the ostiomeatal unit in childhood. *Int J Pediatr Otorhinolaryngol*. 1999;49(3):189-195. [\[CrossRef\]](#)
13. Velasquez N, Strober W, Shaffer A, Stapleton A. Clinical and radiologic characterization of frontal sinusitis in the pediatric population. *Ann Otol Rhinol Laryngol*. 2021;130(8):923-928. [\[CrossRef\]](#)
14. Bent JP, Cuijly-Siller C, Kuhn FA. The frontal cell as a cause of frontal sinus obstruction. *Am J Rhinol*. 1994;8(4):185-192. [\[CrossRef\]](#)
15. Olsen SJ, Azziz-Baumgartner E, Budd AP, et al. Decreased influenza activity during the COVID-19 pandemic — United States, Australia, Chile, and South Africa, 2020. *MMWR Morb Mortal Wkly Rep*. 2020;69(37):1305-1309. [\[CrossRef\]](#)