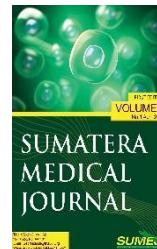




SUMEJ

Sumatera Medical Journal

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Research Article

Factors Contributing to Sphenoid Sinus Volume and Its Relation to Isolated Fungal Sphenoid Sinusitis

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ARTICLE INFO

Article history:

Received 19 September 2025

Revised 2 December 2025

Accepted 3 December 2025

Available online 1 January 2026

E-ISSN: 2622-1357

P-ISSN: 2622-9234

How to cite:

Jasmine Pei Ying Kho, Chae-Seo Rhee, "Factors Contributing to Sphenoid Sinus Volume and Its Relation to Isolated Fungal Sphenoid Sinusitis", SUMEJ, Vol. 09, No. 01, January 2026.



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<http://doi.org/10.32734/sumej.v9i1.22475>

ABSTRACT

Background: Isolated Sphenoid Sinus disease is an uncommon entity, with fungal sinusitis being identified as its most common cause. **Objective:** We investigate factors affecting sphenoid sinus volume (SSV), its pneumatization type, aeration path to the SS ostium, and its relation to isolated fungal sphenoid sinusitis (IFSS). **Methods:** A total of 43 patients with a mean age of 66.6 years, histopathologically diagnosed with IFSS, were included in this study. Demographics recorded were age and gender, parameters affecting sinus volume, obstruction of the pathway to the SS ostium, and types of SS pneumatization. The SSV of the pathological and normal sides of the patients was compared. Parameters affecting the incidence of IFSS were evaluated.

Results: Presence of lateral recess pneumatization (LRP) and post-sellar type of SS pneumatization significantly increases SSV($p<0.05$). There is no significant correlation between SSV and the incidence of IFSS ($p=0.815$). Obstruction of the airway path to the SS ostium and post-sellar type of SS pneumatization significantly increases the incidence of IFSS (OR = 21.021, $p = 0.014$; OR = 13.59, $p=0.02$). **Conclusion:** SSV increases in the presence of LRP, sellar, and post-sellar type of pneumatization. Incidence of IFSS is independent of SS volume. Post-sellar type of SS pneumatization and an obstructed path to the SS ostium increase incidence of IFSS.

Keywords: computed tomography, endoscopic sinus surgery, isolated fungal sphenoid sinusitis, sphenoid sinus volume

1. Introduction

Sphenoid sinusitis is a clinically rare entity with an estimated incidence of 1-2% [1]. Fungal sinusitis frequently affects the maxillary sinus, followed by the sphenoid sinus (SS), with a reported incidence of 4.5% to 26.8% [2]. Diagnosis of fungal sphenoid sinusitis is often delayed due to non-specific clinical symptoms such as headache. Surgical resection is the recommended treatment for sphenoid mycetoma; however, invasive fungal infections require additional systemic antifungal therapy [3]. The etiology and pathogenesis of sphenoid fungal sinusitis are not clearly identified. Few studies proposed the possible pathologic mechanism of sphenoid fungal sinusitis. One hypothesis is that aeration of the sinus could be playing a major role in the development of fungal infection [3]. A study in 2020 suggested that a large sphenoid sinus volume

is prone to fungal infection [4]. They found that the sphenoid sinus volume in a pathological sphenoid sinus with isolated fungal sinusitis was significantly higher than the healthy side ($p<0.05$).

Our study aims to investigate the role of SS pneumatization type and aeration pathway to the sphenoid sinus in developing sphenoid fungal sinusitis. This study evaluates the factors that may contribute to SS volume (SSV) and ultimately, its relation to the incidence of isolated fungal sphenoid sinusitis (IFSS). To the best of our knowledge, this is the first study evaluating the aeration pathway to the sphenoid sinus ostium and its association with IFSS.

2. Methods

A retrospective study was carried out in Seoul National University Hospital, Korea, with data collection from October 2021 until October 2023. All Paranasal Sinuses Computed Tomography (PNS CT) of patients who underwent sphenoidotomy were retrieved. CT scans with preexisting traumatic sinus fracture, tumors, or previous sinus surgery were excluded from the study. Scans of patients with histologically proven fungal SS infection were added to the study. Among the 48 patients with fungal sphenoid sinusitis, five were excluded due to invasive fungal infection. Patient's demographics, such as age and gender, were recorded. This study was approved by the Institutional Review Board of Seoul National University Hospital (IRB No. 2403-110-1523).

Image analysis

All PNS CTs were performed using Siemens SOMATOM Force, which produces 196 slices of images per rotation. Images are reconstructed into multiplanar slices, 1mm thickness, axial, coronal, and sagittal cuts, and reviewed using INFINITT PACS software in bone window. The type of SS pneumatization was defined into four categories in the sagittal view [Figure. 1] [5].

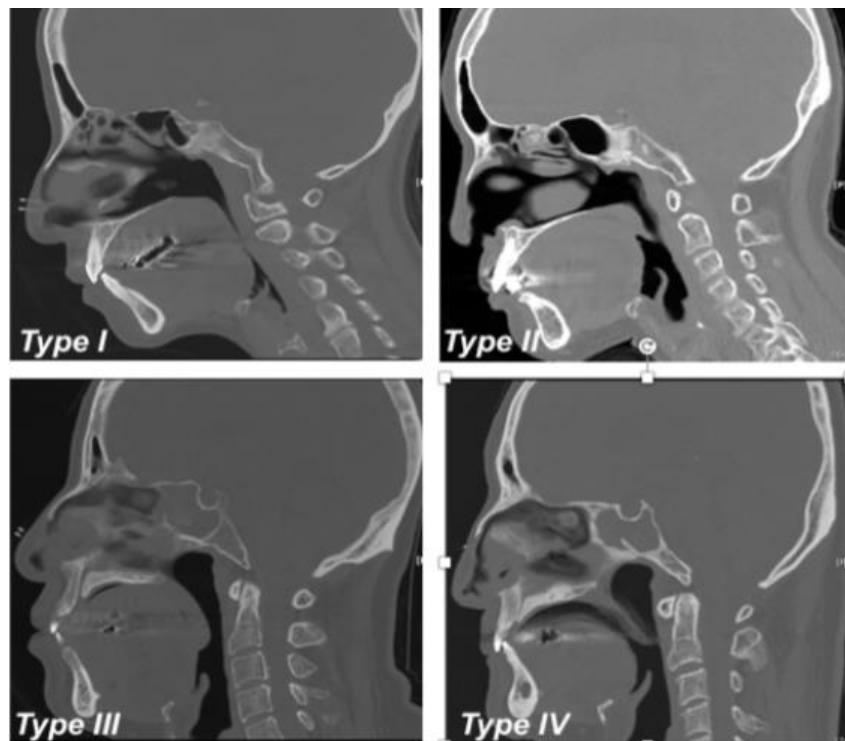


Figure 1. Types of Sphenoid Sinus Pneumatization

Type I (Conchal): Incomplete or minimal extension of the sinus.^[5,6]

Type II (Presellar): The posterior border of the sphenoid sinus is in front of the anterior wall of the sella turcica.

Type III (Sellar): The sinus is located between the anterior and posterior walls of the sella.^[5,6]

Type IV (Post-sellar): The posterior wall of the sinus has passed the posterior border of the sella.

All PNS CTs were further evaluated for the presence of Onodi cells (OC), anterior clinoid pneumatization (ACP) and lateral recess pneumatization (LRP). LRP is defined as a pneumatized area

between the foramen rotundum and vidian canal [6]. The SS volumes of the healthy versus the pathological side were measured manually twice and compared. Anatomical obstruction of the pathway to the SS ostium was assessed. It is defined as any bend touching the nasal septum (by the superior turbinate, pneumatized posterior ethmoid, or middle turbinate) in 3 or more consecutive CT cuts (Figure 2).



Figure 2. Coronal and axial images showing a blocked aeration path to the SS ostium (blue arrow)

Statistical analysis

Statistical analysis was conducted using SPSS Version 26 software. Descriptive data were expressed in numbers, percentages, and means. The Mann-Whitney U test was used to compare ordinal variables to the increment of SS volume. The Pearson Chi-square test was used to examine the association between variables and the incidence of IFSS. Logistic regression was employed to evaluate factors affecting IFSS. A p-value of <0.05 was considered statistically significant with a 95% confidence interval.

3. Results

Data from a total of 43 patients (18 male, 25 female) with a mean age of 66.7 years (ranging 40-84 years) were collected. The majority of subjects presented with post-sellar type pneumatization 35, followed by sellar 33, presellar 15, and conchal 3 (Figure 3).

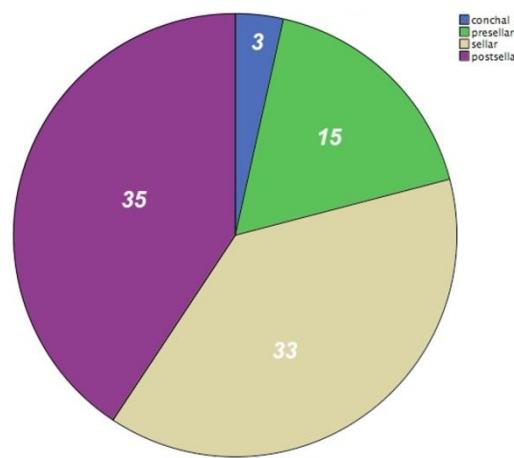


Figure 3. Pie chart exhibiting the number of sphenoid sinuses grouped according to their pneumatization type

The LRP and ACP were present in 65.1% and 18.6% of sphenoid sinuses, respectively, while 37.2% of subjects had the presence of OC (Figure 4). The obstruction of the pathway to the SS ostium was observed in 12.8% (Figure 4).

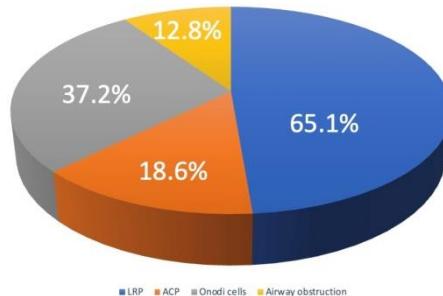


Figure 4. Pie chart depicting the percentage of LRP, ACP, OC, and obstructed aeration pathway to SS identified

The SS volume ranged from 0.69cm^3 to 16.8 cm^3 , with the mean volume of $5.32\text{cm}^2 \pm 3.25$. Presence of OC and ACP does not significantly affect SSV (Table 1). Presence of LRP significantly increases SSV (Table 1). A variant of SS pneumatization (sellar and post-sellar) also affects SSV. There is no significant difference in SSV in terms of gender when compared with non-pathological IFSS (Table 1).

Table 1. Factors affecting Sphenoid Sinus Volume

Variable	U	n1	n2	p
<i>ACP</i>	418	70	16	<i>0.05</i>
OC	724.5	54	32	0.213
<i>LRP</i>	361	30	56	<i><0.05</i>
MF Volume	715	36	50	0.105
The SS ostium path is obstructed	402.5	75	11	0.897
IFSS	893	40	46	0.815
<i>Pneumatisation (Sellar/postsellar)</i>	286	33	35	<i><0.05</i>

*ACP = Anterior Clinoid Pneumatization , LRP = Lateral recess pneumatization, MF = Difference between gender, IFSS= Isolated fungal sphenoid sinusitis, SS = sphenoid sinus, OC = Onodi cell, U=Mann-Whitney U test, p= p value

**Bolded* is statistically significant

Chi-square statistics were used to examine the association between gender, ACP, LRP, and the presence of OC and the incidence of IFSS. There is no significant association found at 5% significance level [Table 2].

Table 2. Factors in relation to the incidence of Isolated Fungal Sphenoid Sinusitis

Variable	Chi-square	df	p	r
Gender	0.13	1	0.911	
ACP	0.642	1	0.423	
LRP	0.785	1	0.376	
Onodi cells	1.943	1	0.163	

*ACP = Anterior Clinoid Pneumatization , LRP = Lateral recess pneumatization, SS = sphenoid sinus
p= p value, r = effect size

Table 3 summarizes the variables in relation to IFSS. The prevalence of ACP, LRP, OC, sellar type of pneumatization, and SSV did not show any statistical significance to the incidence of IFSS. Using logistic regression, we found Post-sellar type of SS pneumatization and an obstructed passage to SS ostium were significantly associated with the occurrence of IFSS; $OR_{PS} = 13.59$, $p=0.02$, with a 95% CI of 2.522 to 73.222, and $OR_{OBS} = 21.021$, $p=0.014$, with a 95% CI of 1.84 to 240.14, respectively.

Table 3. Factors affecting the incidence of Isolated Fungal Sphenoid Sinusitis

Variable	Odds ratio	95% CI range	p value
ACP	0.569	0.137 -2.353	0.436
LRP	3.067	0.936 - 10.053	0.064
OC	2.313	0.809 - 6.614	0.118
<i>SS ostium obstruction</i>	21.021	<i>1.84 - 240.14</i>	<i>0.014</i>
Sellar pneumatization	3.055	0.755 - 12.353	0.117
<i>Post-sellar pneumatization</i>	13.59	<i>2.522 - 73.222</i>	<i>0.02</i>
SS volume	0.838	0.688 - 1.020	0.079

*ACP = Anterior clinoid pneumatization, LRP = Lateral recess pneumatization, OC = Onodi cells, SS = Sphenoid sinus, p= p value,

**Bolded* is statistically significant

4. Discussion

Isolated SS disease is uncommon, with vague to no symptoms, occasionally citing headache as the most commonly reported finding. It accounts for 1 to 3% of all sinus diseases and is not unusual to be discovered incidentally, during radiological examination for unrelated purposes.⁷ CT findings suggestive of a fungal ball have been classically described as having a “double-density” appearance due to calcifications or metallic densities within the sinus cavity [8,9]. In our series, CT scans had a mixture of homogeneous to heterogeneous opacification. One study found that a majority of scans were heterogeneous; 83%, 61% had metallic densities within the sinus, while 17% presented with homogenous opacification [8]. Other features of PNS CT reported in fungal sinusitis include lateral wall sclerosis, bony wall defects, irregular bony surface, or irregular lobulated protruding lesion [9,10,11]. CT scans are the gold standard prior to embarking on any sinus surgery. They allow preoperative planning to avoid any complications to vital structures such as the orbit, optic nerve, and carotid artery surrounding the SS. Due to its inherently rare nature, few studies have explored fungal infection in SS. To the author's knowledge, only one study has looked into the relevance of SSV to fungal ball, and this is the first study analyzing the association between obstruction of the pathway to the SS ostium and IFSS.

The sphenoid sinus is present at birth. Its pneumatization begins around the age of 3, and reaches its adult size by the age of 9-14 years [12]. The SSV can be affected by its pattern of pneumatization, and a larger volume has been suggested to influence the formation of IFSS [4]. To the author's knowledge, no studies at present have investigated whether a reciprocal correlation exists between the presence of IFSS and a higher SSV, though SSV is suggested to be affected by age, gender, and race. Other factors postulated to increase SSV include pneumatization of anterior clinoid processes, pterygoid processes, and dorsum sellae [13]. In our study, the mean SSV is $5.32\text{cm}^2 \pm 3.25$; the mean SSV according to gender in comparison with other studies is listed in Table 4.

Table 4. Mean Volume of Sphenoid Sinus in comparison with other authors [4, 5, 13, 14, 15]

Author	Year	Country	Mean Volume (cm ³):		
			Male	Female	Range
Gibelli	2017	France	10.005 ± 5.101	7.920 ± 3.176	1.43 - 8.43
Baser	2021	Turkey	4.5 ± 2.6	5.1 ± 2.3	0.38 -11
Serindere	2022	Turkey	10.61 ± 4.15	8.89 ± 3.05	N/A
<i>*Kho</i>	2024	<i>Korea</i>	<i>6.37 ± 4.27</i>	<i>4.56 ± 1.98</i>	<i>0.69 - 16.8</i>
	Year	Country	Right side	Left side	
Orhan	2019	Turkey	5.00 (0.90–8.10)	3.70 (0.70–6.80)	1.8 - 9.6
Tuang	2023	Malaysia	5.66 ± 3.38	6.1 ± 3.43	

*our result

Presence of ACP did not significantly contribute to SSV ($U_{ACP}=418$ n₁=70 n₂=16; p=0.05). LRP is more prevalent in non-diseased SS than in those with IFSS (70% vs 60.9%). We found that pneumatization of the lateral recess statistically increased SSV ($U_{LRP}=361$ n₁=30 n₂=56, p<0.05). One study theorized that LRP

plays a role in the formation of a fungal ball in SS, as LRP is associated with a larger SSV [6]. However, we did not confirm a significant correlation between SSV and the incidence of IFSS ($U= 893$ $n_1 = 40$ $n_2 = 46$; $p= 0.815$). Some studies report a higher SSV in males versus females [14], but this did not hold true in our population, similarly disputed by other studies [12,16,17].

There exist different classifications for SS pneumatization. Some authors distinctly divide SS into three categories, namely conchal, presellar, and sellar [11,18], while others opt to differentiate the SS pneumatization into four categories: conchal, presellar, sellar or incomplete sellar, and post-sellar or complete sellar, as is used in our study [4,5,19]. We found that the majority of subjects presented with a post-sellar type of SS pneumatization, similar to other existing studies (Table 5).

Table 5. Types of Sphenoid Sinus Pneumatization in comparison with other authors [4,5,18]

Author	Year	Country	Conchal	Presellar	Sellar	Post sellar
Hiremath[1]	2018	India	0	1.2	22.2	76.6
Baser[2]	2021	Turkey	3.8	30.8	11.5	53.8
Serindere[3]	2022	Turkey	2.66	5.33	33	69.99
*Kho	2024	Korea	3	15	33	35

*Our data

Post-sellar type (52.2%) is frequently seen in IFSS, whilst sellar type (42.5%) is more common in the non-pathological side of SS. We noted that sellar and post-sellar types of pneumatization significantly increased SSV (Table 1), which is logical considering a more pneumatized sinus would have a larger surface area. Post-sellar type of pneumatization also increased the incidence of IFSS ($OR_{PS} = 13.59$; 95% CI, 2.522 to 73.22; $p < 0.05$) compared to other types of SS pneumatization. One study reported that sellar type of SS pneumatization had significantly higher odds of SS fungal ball ($OR = 10.00$; 95% CI, 1.87 to 53.48; $p < 0.01$) [6]. They hypothesized that, in contrast to conchal and presellar types, sellar type had a larger volume, which might be related to fungal ball formation; however, post-sellar classification of sphenoid sinus was not used in this study [6]. We propose that, post-sellar type of SS pneumatization similarly has a larger volume, which may support this hypothesis, leading to IFSS. According to the aerogenic theory, inhaled fungal spores that deposit in the paranasal sinuses may become pathogenic when conditions within the sinuses are relatively anaerobic [20,21]. Poor ventilation reduces pH, which is ideal for fungal growth [20]. An obstructed functional pathway to the sphenoid ostium may affect SS ventilation. We speculate that a larger sinus volume would equate to a larger surface area requiring more ventilation. The subsequent domino effect of poorer ventilation may then contribute to fungal growth.

There exist multiple theories for the pathogenesis of fungal sinusitis. The favored hypothesis is odontogenic infection, where dental sealants in the maxillary sinus have been identified as the culprit that induces inflammation and necrosis, which creates a conducive environment for fungal growth [8,19,26]. The aerogenic theory has been contested, elucidating that direct aero-contamination through the sinus ostium would place the sphenoid sinus as the most frequently infected due to the position of the ostium [8]. However, in multiple literature, the sphenoid sinus is second to the maxillary sinus in frequency of fungal infection. It has been proposed that the presence of a complete accessory septum in the SS may impact the ventilation of the SS and predispose it to fungal infection, but the author was unable to support this assumption through a multivariate logistic regression analysis [6].

A third theory suggests that functional blockage of the sinus ostium could act as an inductive factor for fungal growth, due to its favorable hypoxic conditions [20]. A blocked sinus ostium may contribute to poor air flow, leading to less aeration, which favours fungal growth. To add, poor ventilation diminishes pH, further supporting fungal proliferation [20]. Our study identified that when the air passage to the SS ostium is blocked, it statistically increased the incidence of IFSS ($OR = 21$; $p = 0.014$). No other study to date has investigated this factor. We speculate that an impeded airway to the SS ostium contributes to reduced ventilation within the sinus, thus encouraging fungal growth.

Fungal sinusitis frequently affects elderly women, with a female-to-male ratio of 2:1 [8,11,22]. Similarly seen in our series is a female predilection, with a mean age of 64.7 ± 9.7 years. Few studies have inferred that a longer life expectancy of females may contribute to the gender predominance [23,24,25]. As of 2023, according to Worldometer, South Korean demographics reported that the life expectancy of females is more than that of males, where the average female lifespan is 86.2 years, whilst the male lifespan is 79.8 years.

The ratio of elderly women to men is 1:0.6 for those aged 65 years old and above, which may be one of the reasons why there is a larger number of elderly females diagnosed with fungal sinusitis.

Isolated Fungal Sphenoid Sinusitis tends to be insidious, with mild or no symptoms being reported, making it easily evade detection. The close relationship of the SS to vital adjacent structures renders any spread of infection dangerous. Fungal infection of SS has been reported to cause devastating orbital complications [27,28]; thus, prompt diagnosis and treatment are crucial. Our study aims to comprehend the pathogenesis of IFSS and to identify any correlation between SSV and IFSS. The limitation of our study is its retrospective nature, small number of subjects, and the lack of comparison to other causes of sphenoid sinus infection.

5. Conclusion

Lateral recess pneumatisation and post-sellar variant of pneumatization significantly increase SSV. There is no significant correlation between the sphenoid sinus volume and the incidence of IFSS. Post-sellar type of pneumatization may contribute to the incidence of IFSS. Anatomical obstruction of the airway passage to the sphenoid sinus ostium plays a role in an increased incidence of fungal sphenoid sinusitis. Further future studies need to be conducted to objectively assess blockage of the airway path to the sphenoid sinus ostium.

6. Data Availability Statement

The datasets generated and analyzed during the current study are not publicly available due to privacy and ethical considerations, but are available from the corresponding author upon reasonable request. The original contributions presented in the study are included in the article/supplementary material; further inquiries can be directed to the corresponding author.

7. Ethical Statement

This study was approved by the Institutional Review Board of Seoul National University Hospital (IRB No. 2403-110-1523).

8. Author Contributions

All authors were involved in the design and data interpretation of this research. JKPY was involved in data collection, statistical analysis, and manuscript writing. CSR was responsible for reviewing and editing the manuscript.

9. Funding

No funding was received for this research.

10. Acknowledgements

We would like to thank Seoul National University Hospital, Korea, for providing the facilities and support for this research.

11. Conflict of Interest

The authors have no conflicts of interest to declare.

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