Original Article Ann Med Res 2024;31(1):71–76

Current issue list available at AnnMedRes

Annals of Medical Research

journal page: www.annalsmedres.org

The role of paranasal sinuses in the mysterious etiopathogenesis of idiopathic scoliosis

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ARTICLE INFO

Keywords:
Paranasal sinus
Nitric oxide
Idiopathic scoliosis
Magnetic resonance

Received: Dec 07, 2023
Accepted: Jan 12, 2024
Available Online: 26.01.2024

DOI:
10.5455/annalsmedres.2023.12.325

Abstract

Aim: The paranasal sinuses play a role in maintaining postural balance and synthesizing neurotransmitters such as nitric oxide (NO). Although the etiopathogenesis of idiopathic scoliosis (IS) is not fully known, it is known that hormonal and neurosensory mechanisms play a role. In this study, the possible effects of paranasal sinuses on the etiology of IS were investigated.

Materials and Methods: In this cross-sectional planned study, 38 individuals with IS (28 women and 10 men) and 39 healthy individuals (28 women and 11 men) were included. The right and left maxillary, sphenoid and frontal-ethmoid sinus volumes of the groups were calculated from magnetic resonance images. In addition, the entire head volume of each participant was calculated and the volume ratios occupied by all paranasal sinuses were calculated.

Results: In the IS group, the right maxillary sinus mean volume decreased by 16% and the left maxillary sinus volume value decreased by 14% compared to the control group ($p<0.01$). No significant difference was detected between the groups in the sphenoid and frontal-ethmoid sinus parameters ($p>0.05$). It was observed that the values of left maxillary sinus volume, frontal-ethmoid sinus volume, right maxillary sinus ratio, left maxillary sinus ratio and frontal-ethmoid sinus ratio were lower in male individuals in the IS group than in healthy individuals ($p<0.01$).

Conclusion: In the presented study, it appears that the paranasal sinuses may have a role in the development of IS.

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Introduction

Idiopathic scoliosis (IS) was defined in 1922 as scoliosis whose cause or origin is not fully known and can develop due to many possible factors. Idiopathic scoliosis constitutes 65-75% of structural scoliosis and occurs especially in any period of growth [1]. Although the etiopathology of IS is not fully known, it is suggested that it is a multifaceted process involving hormonal, neurosensory, and biomechanical mechanisms [2]. The spaces in some bones around the nasal cavity are called paranasal sinuses. These are four pairs and are called sinus frontalis, cellulae ethmoidales, sinus sphenoidalis, and sinus maxillaris [3]. Although the growth mechanism of the paranasal sinuses is not clear, it is suggested that many factors such as airflow, brain growth, muscle traction, development of the facial structure, and permanent dentition are effective [3,4]. There are multiple theories about the basic function of the paranasal sinuses. These include providing resonance to our voices [5,6], lightening the weight of the skull to maintain the balanced posture of the head on the spine [5,7], and producing nitric oxide (NO) [8]. There is evidence that synthesised NO serves as a neurotransmitter in the central and peripheral nervous systems [9-11]. In addition, NO, which also plays a role in nociceptive processes in the central nervous system, causes a decrease in central sensitivity and pain sensitivity as its level decreases. [12,13]. There is a relationship between paranasal sinus volumes and functions [14]. It has been proven that the anatomical dimensions of the paranasal sinuses can be measured from magnetic resonance image (MRI) or computed tomography images [15].There are no studies in the literature investigating the possible effects of paranasal sinuses on the aetiology of IS.

The relationship between postural balance, initial lack of pain sensitivity, and vision problems in individuals with IS and the paranasal sinuses discussed in the light of objective data. For this purpose, by calculating the paranasal sinus volumes of IS and healthy individuals from the mag-

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netic resonance images of the head, possible differences between the groups revealed, and the effect of paranasal sinus volume on the etiology of IS investigated.

Materials and Methods

Ethical approval was received for this study from Kayseri City Hospital with the decision numbered 910 dated 19/09/2023. This study, planned as a single-center and cross-sectional group, was conducted within the framework of the Declaration of Helsinki. Written consent was obtained from the participants before participating in the study.

Participants and study groups

The sample of the study was determined in the GPower programme, assuming an error level probability of 0.05 and a statistical power of 95%. As a result of the analysis, it was decided that there would be at least 35 participants in each group. IS group (n = 38): It consists of 38 individuals with IS, 28 women and 10 men. Control group (n = 39): Consists of 39 healthy individuals, 28 women and 11 men, who did not have scoliosis or any spinal deformity as determined by the scoliometer and postural analysis methods.

- *Inclusion criteria:* Individuals who had no lesions detected on head MRI, no missing molars, no history of trauma or surgery affecting the neurocranium and viscerocranium bones, and no disease affecting the musculoskeletal system were included in the study.
- *Exclusion criteria:* Individuals with any scoliosis other than IS, a history of trauma or surgery affecting the neurocranium and viscerocranium bones, pathological conditions affecting the paranasal sinuses, and missing molars were not included in the study.

Obtaining brain magnetic resonance images

The MRI procedures of the volunteers participating in the study were performed with a 3T (Tesla) Siemens Magnetom Skyra, a Dutch-brand MRI device. On MRI; T1 magnetization-prepared rapid acquisition with gradient echo (MPRAGE) sequence was performed to evaluate anatomical structures, and a fluid attenuated inversion recovery (FLAIR) sequence was performed to evaluate brain anomalies. The MRI and DTI sequences of the participants were set as follows:

- T1-weighted MPRAGE sequence: Sagitial, repetition time (TR)=2300ms, echo time (TE)=3.4ms, FOV=250mm, matrix:256x256, slice thicknes=1mm.

The resulting images were converted to DICOM format and saved.

Calculation of paranasal sinus volumes

The 3D Slicer programme was used for segmentation of paranasal sinuses. 3D Slicer, a free, open source software, is a medical image calculation and visualization software [16]. The segmentation process of the paranasal sinuses started by loading the MRI data into the 3D Slicer software. “Segment Editor” was selected using the “Modules” option in the 3D Slicer program. After these operations, new segmentation tabs were opened via the "Segmentation" tab. In this process, "Threshold Range" was adjusted via "Threshold" to cover the anatomical boundaries of the paranasal sinuses. After these steps, raw images of the paranasal sinuses were obtained with the “Apply” and “Show 3D” options. Using the raw images, the anatomical boundaries of the paranasal sinus to be measured were determined on the axial, sagittal and coronal planes with the help of the "Islands" tab and the "add selected island" tab of the software (Figure 1, Figure 2). When overflow or deficiency was observed at the anatomical border of the selected paranasal sinus, necessary corrections were made using "Erase", "Scissors" and "Paint". Volume (mm^3)

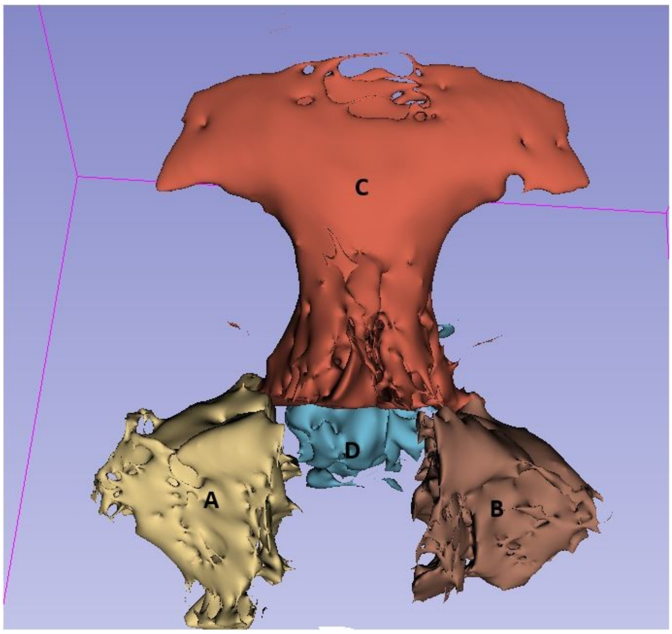

Figure 1. Three-dimensional representation of the volumes of the paranasal sinuses in the coronal plane. (A): The right maxillary sinus (B): The left maxillary sinus (C): The frontal-ethmoid sinuses (D): The sphenoid sinus.

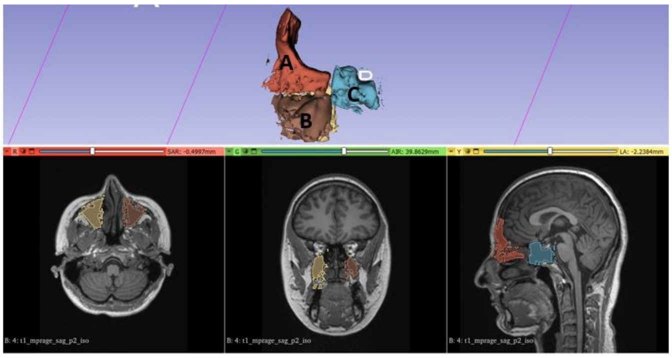

Figure 2. Three-dimensional representation of the volumes of the paranasal sinuses in the sagital plane. (A): The frontal-ethmoid sinuses (B): The left maxillary sinus (C): The sphenoid sinus.

and superficial area (mm^2) information of the paranasal sinuses were accessed through the "Quantification" tab under the "Modules" tab. Finally, the total volume and superficial area of the head region located on the basis mandible and the 3rd cervical vertebra were calculated. Using this information, the volume and superficial area ratios of each paranasal sinus relative to the entire head region were calculated. The data obtained were compared between groups.

Statistical analysis

The data in this study were analysed for normal distribution using five parameters (Skewness-Kurtosis, Std/Mean, Q-Q plots, histogram, and Shapiro-Wilk test). Parameters with a score above 3 and sufficient number of data were considered parametric and presented as Mean±Std and Independent Samples T-test was used for pairwise comparisons. Parameters not showing a normal distribution or with insufficient data were considered non-parametric and presented as median (minimum-maximum), and the Mann-Whitney U test was applied for pairwise comparisons. In the study, α=0.05 and p<α were considered significant. The IBM SPSS 28.00 package was used for statistical analysis.

Results

Thirty-eight individuals with idiopathic scoliosis with moderate to severe curvature size (35°-50°) and 39 healthy individuals participated in the study. Descriptive characteristics about the participants are given in Table 1. There was no significant difference between the groups in terms of descriptive characteristics (p˃0.05).

When the volum of the paranasl sinuses data were compared between groups, in the IS group, the mean volume of the right maxillary sinuses decreased by 16% and the mean volume of the left maxillary sinuses decreased by 14% compared to the control group. There is a statistically significant difference between the groups in the right and left maxillary sinus volume parameters (p<0.01). There was no statistically significant difference between the groups in sphenoid and frontal-ethmoid sinus parameters (p>0.05). There was no statistically significant difference between the groups in the whole head volume parameter (p>0.05). When the ratios of paranasal sinus volumes to the whole head volume were compared between groups, the volume fraction of the maxillary sinus in the head region decreased by 20% and 17% on the right and left sides, respectively, in the IS group (Table 1). There was a statistically significant difference between the groups in the ratio of the right and left maxillary sinus covering the entire head region (right maxillary sinus ratio=right maxillary sinus volume (mm^3) * 100/whole head volume (mm^3) parameters) (p<0.01). When data are compared between groups according to male gender, it was seen that the parameters of left maxillary sinus volume, frontal-ethmoid sinus volume, right maxillary sinus ratio, left maxillary sinus ratio, and frontal-ethmoid sinus ratio are lower in the IS group (p<0.01). In male individuals, the left maxillary sinus volume was found to be 19% smaller in the IS group compared to the control group. When data on female individuals are compared between groups according to gender, there is a difference between the control and IS groups only in the right maxillary sinus volume and ratio data (p<0.01), (Table 2).

Discussion

Although the etiopathogenesis of IS remains unclear, the decrease in the volume of the paranasal sinuses, especially the maxillary sinus, suggests that the paranasal sinus may have a role in the development of scoliosis. In the study, the volumes of the paranasal sinuses and the volume ratio they occupy in the entire head region were calculated separately and compared between the IS and control groups. As a result, significant differences were detected in sinus volume and ratio data between the IS group and the control group.

There are multiple hypotheses in the literature regarding the function of the paranasal sinuses [5,6]. It is assumed that the main purpose of the paranasal sinuses is to relieve the weight of the skull in order to maintain the balanced posture of the head on the spine, thereby preventing fatigue of the posterior cervical musculature and supporting the sense of balance [5,7].

Studies have shown that postural balance problems are very common in individuals with IS [17,18]. In the present study, especially the volume of the maxillary sinus and the volume it occupies in the entire head region were found to be lower in the IS group. Low maxillary sinus volume causes an increase in the weight of the head bones. This may be one of the factors causing the postural balance problem seen in individuals with IS.

In their study, Batin et al. found that individuals with IS had asymmetry in the right and left visual fields compared to healthy individuals. They suggested that the asymmetry in the visual fields would be caused by balance problems in the head [19]. In the study, the paranasal sinus volume and ratio of individuals with IS were found to be lower than those of healthy individuals, which may have led to impaired head balance and asymmetry between visual fields.

Studies in healthy adults show that NO is produced mainly in the epithelial cells of the nasal cavity, especially in the paranasal sinuses [20-22]. It has been determined that the rate of NO production decreases in cases affecting sinus volume and is directly related to sinus volume [14]. It is known that synthesised NO has more than one function. There is evidence that NO acts as a neurotransmitter in the central and peripheral nervous systems [9-11].

NO also plays a role in nociceptive processes in the central nervous system; increasing NO levels plays a role in the sensitization of pain pathways in the spinal cord; and NO synthesis inhibition reduces central sensitivity and sensitivity of pain pathways [12,13]. Studies have reported that pain from the onset of curvature is less common than expected in individuals with IS [23,24].

In the study, paranasal sinuses volume and the area covered in the head area were found to be low in individuals with IS. Low paranasal sinuses volume causes a decrease in NO synthesis. Low levels of NO in the body may have a negative effect on the sensitivity of nociceptors and the pain reaching the pain centre in the brain. The reason why

Table 1. Analysis of data between Control and Scoliosis groups.

	Control (n=39)	Scoliosis (n=38)	Sig. (p)
Height (cm)	163.15±10.53	160.18±12.47	0.262
Weight (kg)	55.94±12.86	52.23±12.83	0.209
Age (years)	17.97±3.69	17.44±3.08	0.499
Right maxillary sinus (mm^3)	23885.05±6981.33	20093.88±5273.38	**0.009**
Left maxillary sinus (mm^3)	22310.21±6444.15	19291.24±4921.33	**0.024**
Sphenoid sinus (mm^3)	17918 (10761.30-31647.60)	16342.30 (9971.72-30806.90)	0.589
Frontal-ethmoid sinuses (mm^3)	42257.43±9619.08 3	39181.66±11507.33	0.207
Whole head volume (mm^3)	374590 (2727810-3942080)	3388245 (2179310-4588840)	0.485
Right maxillary sinus ratio (%)*	0.73 (0.43-1.12)	0.59 (0.30-0.86)	**0.002**
Left maxillary sinus ratio (%)*	0.66±0.18	0.55±0.13	**0.007**
Sphenoid sinus ratio (%)*	0.52 (0.32-0.92)	0.51 (0.31-0.91)	0.521
Frontal-ethmoid sinuses ratio (%)*	1.25±0.26	1.14±0.35	0.115

Parametric data were presented as Mean±Standard Deviation (MEAN±STD) and Independent Samples T Test was used for statistical analysis.
Non-parametric data were shown as Median (Minimum-Maximum) and Mann Whitney U Test was applied for pairwise comparisons.
*(X sinus ratio= X sinus volume (mm^3) * 100/whole head volume (mm^3) parameters).

Table 2. Analysis of gender data between Control and Scoliosis groups.

	Control (n=11)	Male Scoliosis (n=10)	Sig. (p)	Control (n=28)	Female Scoliosis (n=28)	Sig. (p)
Height (cm)	173 (162-190)	173.50 (149-180)	0.809	159.17±8.72	156.75±11.36	0.374
Weight (kg)	60 (55-84)	57 (48-95)	0.426	52.67±12.66	48.25±8.58	0.131
Age (years)	18 (15-23)	18.50 (15-22)	0.756	17.60±4.01	17.00±3.12	0.530
Right maxillary sinus (mm^3)	27336.70 (19100.60-44166.60)	25025.70 (9792.20-29463.40)	0.114	21897.99±5731.29	19252.04±4731.61	0.065
Left maxillary sinus (mm^3)	27402.00 (18342.70-36384.20)	22365.65 (10362-27239)	**0.013**	20311.90±5699.99	18689.22±4852.92	0.256
Sphenoid sinus (mm^3)	201314.50 (13062.50-31647.60)	17430.00 (3318.10-30806.90)	0.426	17086.76±3913.59	17348.41±4411.72	0.815
Frontal-ethmoid sinuses (mm^3)	50156 (33214.30-60305.10)	41608.60 (24362.60-52830.20)	**0.013**	38862.04±8001.68	38763.41±12512.15	0.972
Whole head volume (mm^3)	3497520 (3022990-3942080)	4034835 (3246370-4588840)	0.061	3312625 (2727810-39334330)	3346120 (2179310-3916980)	0.611
Right maxillary sinus ratio (%)*	0.80 (0.55-1.12)	0.56 (0.30-0.86)	**0.004**	0.67 (0.43-0.99)	0.54 (0.36-0.77)	**0.046**
Left maxillary sinus ratio (%)*	0.77 (0.52-0.98)	0.54 (0.32-0.76)	**0.001**	0.62±0.19	0.57±0.14	0.235
Sphenoid sinus ratio (%)*	0.55 (0.43-0.92)	0.48 (0.31-0.82)	0.173	0.50 (0.32-0.83)	0.51 (0.94-0.91)	0.173
Frontal-ethmoid sinuses ratio (%)*	1.46 (0.97-1.72)	0.98 (0.75-1.30)	**0.001**	1.18±0.25	1.18±0.38	0.990

Parametric data were presented as Mean±Standard Deviation (MEAN±STD) and Independent Samples T Test was used for statistical analysis. Non-parametric data were shown as Median (Minimum-Maximum) and Mann Whitney U Test was applied for pairwise comparisons.
*(X sinus ratio= X sinus volume (mm^3) * 100/whole head volume (mm^3) parameters).

individuals with IS experience pain below the expected level at the beginning of the curve may be due to low NO synthesis due to the decrease in paranasal sinus volume.

NO has also been associated with central nervous system sensitization [25]. Payas et al. In their study, found that the connection between the regions of the central nervous system responsible for the sensory and motor systems of individuals with IS was lower than in healthy individuals [18]. More than one factor may have an impact on this phenomenon, but the effect of decreased NO synthesis due to the decrease in paranasal sinus volume should not be forgotten.

There have been a number of studies suggesting that NO plays an important role in various neuronal-mediated responses, including relaxation of vascular and non-vascular smooth muscles [26]. On the other hand, excess NO synthesised in the tissue is a pro-inflammatory and pro-apoptotic factor [27-29].

Ulusoy et al. In their study, found that the thickness of the choroidea layer, which constitutes the majority of the vascular layer in the eye, was thinner in IS individuals compared to healthy subjects. They found that low choroideal layer thickness was associated with an increasing scoliosis angle [30].

The thickness of the choroidea layer in the eye is provided by the smooth muscles and becomes thinner when the smooth muscles contract. This situation may be affected by the decreased synthesis of NO due to the volumetric difference in the paranasal sinuses of individuals with IS. There are some limitations to the study. It is known that there is a direct relationship between the volume of the paranasal sinuses and NO synthesis. However, in the study, the level, functionality, and receptor-level relationship of NO in individuals with IS could not be evaluated in terms of biochemistry. Another limitation is that the study was conducted in a single centre and by creating a sample from a specific region. It was not a multicenter study.

Although the effect of the paranasal sinuses on the etiopathogenesis of IS was investigated while planning this study, the possibility of predicting IS according to the volume of the paranasal sinuses was also discussed. However, it may be possible with detailed, prospective, large-sample, multi-centre, and multi-regional scoliosis screening of individuals with a longer follow-up period.

While there was no difference in the prontal+ethmoid sinus parameter between the groups in female individuals, there was a highly significant difference in male patients. Regarding the coincidence of this difference, we see a similar difference in the parameter (% frontal-ethmoid) in which we proportion the frontal-ethmoid sinus according to the entire head circumference. In the comparison between genders in the study, it is seen that the frontal-ethmoid sinus volume is reduced in the male scoliosis group compared to healthy individuals.

Conclusion

The aetiology and pathogenesis of IS remain a mystery despite dozens of studies. Although the studies mainly highlight certain issues, it is a fact that there is more than one factor in the aetiology of IS. We believe that studies conducted with individuals with IS are of indisputable importance in further elucidating the etiopathogenesis of IS. In the presented study, it appears that the paranasal sinuses may have a role in the development of IS. More comprehensive and detailed molecular studies will be useful in unravelling the pathogenesis of IS.

Ethical approval

The Kayseri City Training and Research Hospital Clinical Research Ethics Committee granted approval for this study (date: 19.09.2023, number: 910).

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