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RESEARCH ARTICLE

Age and Sex-Related Changes in Corpus Callosum Morphometry: A Magnetic Resonance Imaging Study

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Abstract

Aim: This study evaluates the morphometric data of the corpus callosum (CC) in a healthy Turkish population and aims to provide a benchmark to help identify relevant pathologic conditions.

Materials and Methods: The study designed retrospectively has been conducted by using brain Magnetic Resonance images (MRI's) of 360 individuals between the ages of 25-55 years who were admitted to the clinic with headache complaints. The anteroposterior diameter of the CC (CCAPD), the genu thickness of the CC (CCGT), the splenium thickness of the CC (CCST), the body thickness of the CC (CCBT), the CC height (CCH), the distance between the anterior end of the CC and the vertex (DAV), the distance between the posterior end of the CC and the vertex (DPV), the distance between anterior end, inner end, and vertex of the CC (DAIV), the distance between posterior end, inner end, and vertex of the CC (DPIV), the angle between DAV-DPV (AI), and the angle between DAIV-DPIV (AII) variables were measured in the study. Statistics were performed by RStudio (2023.12.1) program.

Results: In the analysis of the CC sections, the difference between the groups classified according to age was found to be statistically significant. Additionally, CCBT, DAV and DAIV variables in the 1st group, CCAPD, CCGT, CCBT and DAV variables in the 2nd group and DAV variables in the 3rd group show sex-related changes.

Conclusion: The study results are in accordance with the extant literature, which emphasises that gender and age group are significant factors in the morphology of CC segments.

Keywords: Corpus callosum, MRI, morphometry, age groups, gender.

INTRODUCTION

The corpus callosum (CC) connecting the right and left hemispheres in the midsagittal plane is a white matter network indicated as the largest commissural region in the brain (1, 2). The main function of the CC is to provide interhemispheric integration and information transfer by establishing the connection between the hemispheres (3). Comprising rostrum, genu, trunk, and splenium, CC morphometry has been shown to differ in relation with the circumstances such as age (4), gender (5), population (6), hand preference and prematurity (7). In addition, an explicit decrease has been documented in the CC size of the people diagnosed with neurological (12, 13) and psychiatric diseases (14), leading to the suggestion that CC morphometry may reflect pathologic processes. Previous studies examining CC morphometry in necropsy specimens, also have reported postmortem changes (15). Again, research has documented a decrease at the CC dimensions with aging due to brain atrophy (4, 8, 9). However, studies investigating the effect of gender on the morphometry of the CC and its parts in different populations have not yielded a persuasive result (5, 9-11). Nowadays, MRI devices perfectly reflecting soft tissues have become the gold standard in morphometric studies of the body parts just like the CC in this research (16). Furthermore, it is noteworthy to indicate that the number of studies conducted in different populations including healthy individuals as the sample group is limited (10, 11). With this information given above in mind, this study aims to present the age- and sex-related changes in the angular and linear variables of the CC using brain MRI's in a healthy adult Turkish population, and to compare them with the existing literature.

MATERIALS and METHODS

This cross-sectional retrospective study was initiated after obtaining the permission of the Clinical Research

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Ethics Committee numbered 2024/118. The images filed in the Picture Archiving and Communication Systems (PACS) archive of Bolu Abant Izzet Baysal University Training and Research Hospital have been used in the study. Brain MRI's taken in the midsagittal plane were selected between January and June 2024. The sample group consisted of 180 healthy male and 180 female aged 25-55 years. Those with a history of head trauma, degenerative, cerebrovascular, neurologic and psychiatric diseases, and CC anomalies such as hypoplasia or dysplasia were excluded from the study. Age of the participants has been divided into three groups: 25-34, 35-44 and 45-55 years old. For each group, images of 60 female and 60 male participants have been utilized. Standardized brain MRI'staken in Dicom format in the PACS archive of the participants were transferred to MicroDicom 2024.1 (64 bit) on a personal workstation. MRI's were taken with 1.5 T Signa Explorer MRI Scanner (GE Medical Systems, Milwaukee, Wisconsin, USA). The variables of the CC measured were; anteroposterior diameter (CCAPD), genu thickness (CCGT), splenium thickness (CCST), body thickness (CCBT), height (CCH), distance between the anterior edge and the vertex (DAV), distance between the posterior edge and the vertex (DPV), distance between the anterior and inner edges and vertex (DAIV), distance between the posterior and inner edges and vertex (DPIV), angle between DAV-DPV (AI), and angle between DAIV-DPIV (AII). The measurements were performed by one person to avoid inter-observer error. The variables were shown in figure 1.

Statistical analysis

The statistical analyses were performed with the open-source software program RStudio (2023.12.1). All variables were assigned to two-factor analysis of variance and the normal distribution of residual values were analyzed. Compliance with normal distribution was tested with anderson darling test, and nonparametric

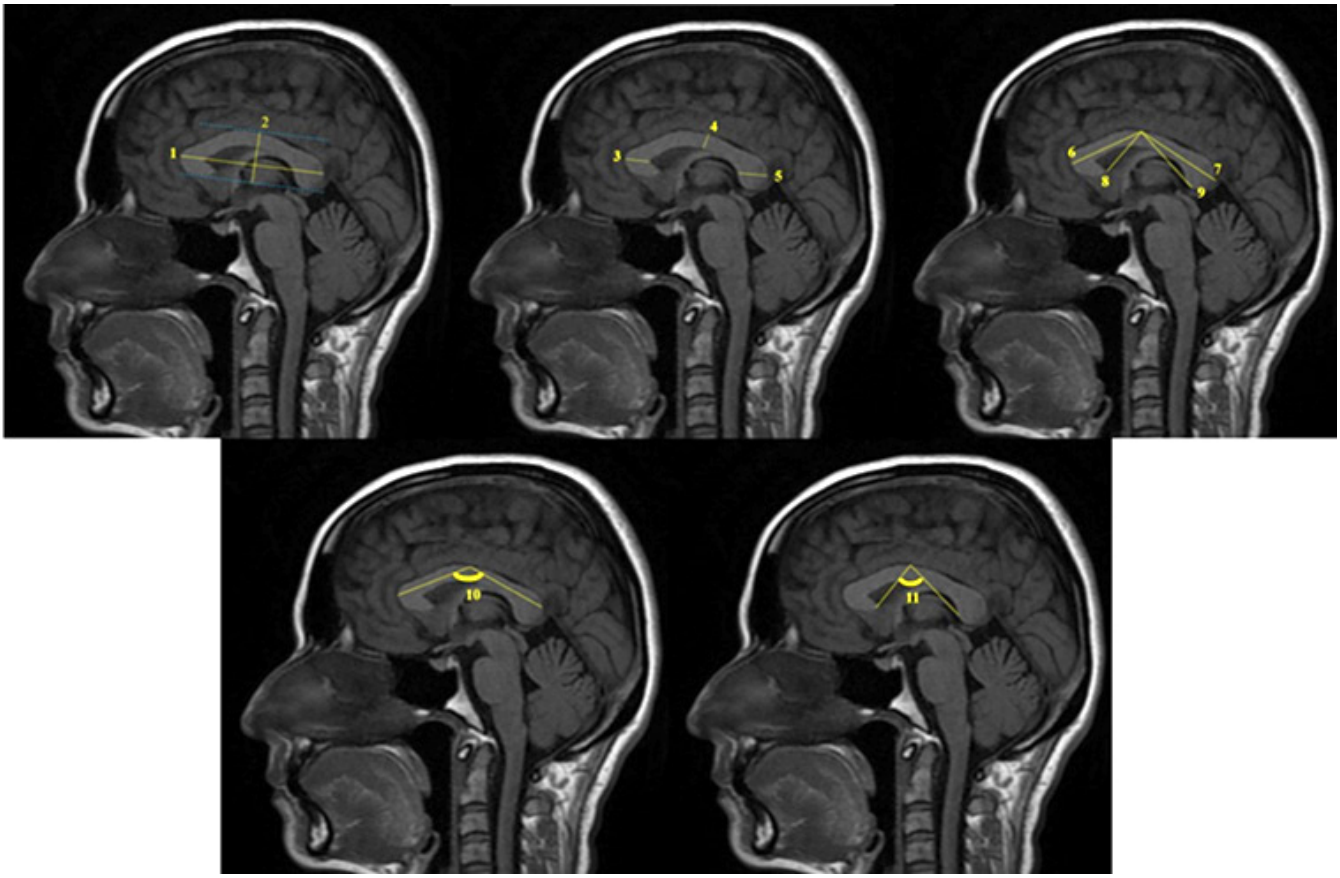

Figure 1. 1- CCAPD, 2- CCH, 3- CCGT, 4- CCBT, 5- CCST, 6- DAV, 7- DPV, 8- DAIV, 9- DPIV, 10- DAV-DPV, 11- DAIV-DPIV. (CCAPD: CC anteroposterior diameter, CCH: CC height, CCGT: CC genu thickness, CCBT: CC body thickness, CCST: CC splenium thickness, DAV: distance between the anterior end of the CC and the vertex, DPV: distance between the posterior end of the CC and the vertex, DAIV: distance between anterior end, inner end and vertex of CC, DPIV: distance between posterior end, inner end and vertex of CC, AI: angle between DAV-DPV, AII: angle between DAIV-DPIV).

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variables were tested for difference between groups by applying Kruskall-wallis test. The Mann-Whitney test was applied for the variables for which the difference between the groups was significant as a result of Kruskall-wallis test. The difference between the individuals forming the groups in terms of sex was analyzed by independent t test for parametric variables and Mann-Whitney test for nonparametric variables. Mean and standard deviation values for parametric variables and median, minimum and maximum values for nonparametric variables were analyzed. Logarithmic and square root transformation was applied to variables that did have non-normal distribution. The transformation resulted in a normal distribution for the CCAPD variable, then mean and 95% confidence intervals were calculated for this variable.

RESULTS

The median values of the age variable were determined as 26 for male and 27 for female in the first group, 40 for male and 38 for female in the second group, and 51 for male and 50 for female in the third group. For the age variable, the difference among the three groups was statistically significant. Likewise, the CCGT variable differed significantly between the first and third groups while no significant difference was seen between the first and second group. Boxplot graph of the variables with significant differences is depicted in Figure 2. For the first group, CCBT, DAV and DAIV variables have been found to be statistically significant. For the second group, the CCAPD, CCGT, CCBT, and DAV variables were statistically significant.

For the third group, a statistically significant result was found only in terms of gender among the individuals on the DAV variable. In terms of intergroup differences, there is no statistically significant difference between the first and second groups in the CCBT variable, while there is a statistically significant difference between the third group and the other groups. There is a statistically significant difference between the first and second groups in the CCGT variable. The results of the analysis and descriptive statistics of the variables are given in table 1 and table 2.

Table 1 | Table showing the analysis results and descriptive statistics of age, CCAPD, CCGT, CCST, CCBT, CCH, and DAV variables.

	G1 (N=120)		G2 (N=120)		G3 (N=120)		p-value
	M	F	M	F	M	F	
Age	26 (25-34)	27 (25-32)	40 (35-44)	38 (35-44)	51 (45-56)	50 (43-55)	p<0.001#
p-value	0.593≠		0.100≠		0.244≠		
CCAPD	68.7 (67.7-69.7)	67.3 (66.3-68.3)	69.4 (68.3-70.5)	67.3 (66.3-68.4)	68.5 (68.3-69.8)	67.9 (66.7-69.0)	0.002* 0.820**
p-value	0.06†		0.007†		0.432†		0.444***
CCGT	11.6 (6.9-15.0)[a]	11.3 (8.3-16.0)[a]	11.7 (6.6-15.9)[ab]	10.7 (6.6-15.4)[ab]	10.5 (5.7-17.3)[b]	10.7 (3.6-14.8)[b]	0.016#
p-value	0.302≠		0.011≠		0.760≠		
CCST	12.4 (7.5-16.5)	12.2 (6.1-14.8)	12.8 (8.0-15.6)	11.9 (8.5-16.1)	12.5 (7.5-16.6)	12.3 (4.7-16.2)	0.867#
p-value	0.209≠		0.399≠		0.358≠		
CCBT	6.9 (4.1-11.8)[a]	6.4 (4.5-10.2)[a]	6.7 (3.9-10.6)[a]	6.5 (3.7-8.1)[a]	6.2 (3.1-8.6)[b]	6.3 (3.6-9.0)[b]	0.006#
p-value	0.04≠		0.029≠		0.355≠		
CCH	24.6 (16.6-44.1)	24.4 (6.4-30.5)	24.4 (16.6-35.8)	24.2 (17.6-32.9)	25.6 (19.8-38.1)	25.5 (20.7-30.9)	0.059#
p-value	0.179≠		0.803≠		0.947≠		
DAV	41.2±3.1	38.5±2.9	40.9±3.0	39.2±3.6	41.0±3.2	39.3±2.8	<0.001* 0.737**
p-value	<0.001†		0.008†		0.003†		0.372***

*# The p value of the Kruskal-Wallis test result, * The p value showing the significance of the difference between sexes in the two-factor analysis of variance ** The p value showing the significance of the difference between the groups in the two-factor analysis of variance *** The p value showing the group and sex interaction in the two-factor analysis of variance ≠ p value of Wilcoxon signed-rank test, † p value of two simple t test result.*

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Table 2 | Table showing the results of the analyses and descriptive statistics of DPV, DAIV, DPIV, A1, and A2 variables.

	G1 (N=120)		G2 (N=120)		G3 (N=120)		p-value
	M	F	M	F	M	F	
DPV	34.93±3.75	35.13±2.91	34.84±3.48	34.7±3.56	34.8±3.71	35.41±3.34	0.540*
							0.734**
p-value	0.752†		0.833†		0.346†		0.707***
DAIV	30.6 (26.1-46.22)	29.8 (23.3-35.2)	30.3 (24.4-43.5)	30.2 (20.9-39.9)	30.7 (24.8-41.1)	30.0 (23.7-38.8)	0.855#
p-value	0.02≠		0.298≠		0.104≠		
DPIV	30.9 (22.5-44.8)	30.2 (26.9-37.8)	30.8 (23.1-40.9)	29.7 (24.5-93.9)	30.8 (23.4-37.2)	31.1 (25.4-37.6)	0.365#
p-value	0.327≠		0.104≠		0.205≠		
Angle1	85.3±8.8	85.5±7.0	84.2±6.5	85.0±7.0	83.5±6.7	83.3±6.6	0.740*
							0.097**
p-value	0.890†		0.529†		0.876†		0.870***
Angle2	124.6 (100.6-138.8)	125.5 (116.2-137.2)	125.7 (113.4-139.9)	126.6 (110.9-138.3)	124.0 (111.3-135.3)	125.8 (112.9-137.7)	0.268#
p-value	0.232≠		0.508≠		0.170≠		

*# The p value of the Kruskal-Wallis test result, * The p value showing the significance of the difference between sexes in the two-factor analysis of variance ** The p value showing the significance of the difference between the groups in the two-factor analysis of variance *** The p value showing the group and sex interaction in the two-factor analysis of variance ≠ p value of Wilcoxon signed-rank test, † p value of two simple t test result.*

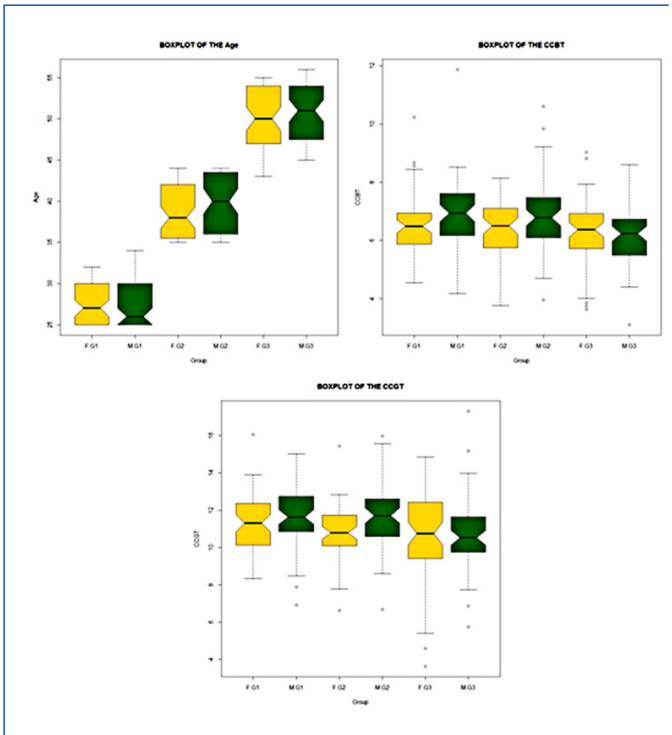

Figure 2. Boxplot graph showing the difference of Age, CCBT, and CCGT variables in terms of group and sex.

DISCUSSION

Interconnecting similar cortical regions in the two cerebral hemispheres, the CC is the largest commissural network of the nervous system. It may be affected by several diseases producing symptoms characterized by visual, auditory, kinesthetic and complex functional impairment occur in diseases (17). In the literature, studies examining the changes in diseases such as multiple sclerosis (19), anorexia nervosa (20), Alzheimer's disease (17), migraine (21), and alcohol use (22) have also been frequently encountered. Enlargement in the CC area has been found in children diagnosed with autism (17) whereas a reduction in this area has been observed in major depression (18). Additionally, changes in CC morphometry have been observed at different stages of human development (23,24) and in old age (25). Although cadaveric (26,27) or radio-anatomical (28) methods have been used in brain studies, MRI is preferred for diagnosis and treatment follow-up. The present study has been conducted on brain MRI's of a healthy adult Turkish population to show the changes in CC morphometry in age and sex stratified groups. Having analyzed the results of the study, differences were observed for CCGT and CCBT variables within the groups classified according to age. In addition, sex-related changes were found to be statistically significant in CCBT, DAV and DAIV variables in group 1, CCAPD, CCGT, CCBT and DAV variables in group 2, and DAV variable in group 3. Ultimately, the average results of the CC sections in male were higher.

A study conducted in Türkiye to determine the morphometry of CC segments and intracranial

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structures using MRI's, and to present their relationship with hand and foot dominance (29), has shown a relationship between dominance and some segments of the CC, additionally, as in the present study, indicating a significant difference between the CC morphometry and sex. In another study carried again in Türkiye (28), the same variables have been evaluated on MRI and cadaveric materials, and the correlation between the results has been analyzed. The correlation was high, and the results were similar to those of the present study. Another study (30) also aiming to reveal CC morphometry during normal aging period in healthy adult Turkish individuals by considering sex differences, revealed similar mean values. Likewise, a similar study (9) analyzed CC morphometric measurements in relation with age and gender using MR brain images of healthy participants, revealing similar results as compared to those of the present research, and particularly indicating the fact that the CCST variable was larger in male. Another study (21) which included both a sample group of healthy individuals and those diagnosed with migraine, focused on the correlation between CC and white matter lesions and migraine characteristics, presenting no correlation between migraine and CC morphologic structure, and the variables related to CCAPD and CC sections of the control group had similar averages with the current study.

In contrast to the present study, a research report that was designed to examine the correlation between CC shape and size on brain MRI's in a healthy adult Indian population (31) has documented no sex difference in variables including CC segments and has obtained higher mean values of the variables, as compared to the findings of the present study. This may be due to the population difference and unequal number of the male and female used in the study. One cross-sectional study (32), which has examined CC morphometry and possible variations in a North Indian population using MRI's, evaluated length, height, minimum and maximum thicknesses, has shown, in parallel with the present study, higher values of CCAPD and CCST variables in males, and has reported age-related variation in CC variables. In addition, CCAPD and CCH variables measured in this research have had higher mean values than those of the current study while CCST and CCBT variables have been measured lower. This suggests that CC morphometry may vary depending on the population. Again, the results of a study (33) evaluating CCAPD and CC sections on brain MR images in different age groups have emphasized that the morphometry of CC sections varies with age, just as the findings of the present study. It has also been reported that the CCAPD variable is longer in the elderly. It is of valuable to mention hereby that such age group has not been used in the present study.

A research report (34) focused on age- and sex-related analysis of CC dimensions in the Polish population, has aimed to provide reference values related to the healthy population, dividing participants into ten different groups, including pediatric and geriatric ages. It has reported that CC morphometry has varied in all age groups and sex-related differences have been observed. The results are similar to the findings obtained in the present study despite the use of an age-restricted sample group. On the other hand, another similar study (35) conducted on the CC reference values of the adult population in Nigeria, has interestingly measured higher CCAPD and CCH variables while the CC sections have been shown lower mean values.

Some findings also suggest that there has been no correlation between sex and the variables. The reason for the different results from the present study is thought to be due to the different population, different age groups, and unequal sex distribution. A study presenting age- and sex-based CC reference values in healthy individuals from the Jordanian population (7) has classified participants as children, adolescents and adults. The study findings have shown a significant increase in CC morphology in both sexes starting from childhood. In parallel with the present study, it has been reported that CC angular variables reflect sexual dimorphism.

According to a study investigating the sex-dependent change of CC morphology in thirty healthy individuals living in the South Korean population (10), the CC has been found, through using a 3D MRI device, as sexually dimorphic in parallel with the present study. The sample group in a study designed to report CC measurements and reference values, and to make racial comparisons in a Middle Eastern Arab population (8) has included healthy pediatric and adults and pediatric group diagnosed with autism spectrum disorder. This study has found that the CCAPD, CCGT, and CCBT variables are lower in the healthy adults than those in the current study while the CCST is higher. In addition, higher values have been reported in males, very similar to the findings of the current study.

An investigation designed to assess CC morphometry in stroke survivors (36) using the brain MRI's of patients and control group participants, has shown that diameter measurements of the CC are lower in stroke patients.

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On the other hand, the results of the control group of the study have lower mean values than the values of the present study, but higher results have been observed in males, just as the case in the present study. In another study performed on the patients with major mental disorders and healthy controls (37), it was emphasized that CC morphology was affected in patients with obsessive-compulsive disorder and schizophrenia. The results of the control group of this study were again in parallel with the present study.

The main results of the present study conducted to assess the angular and linear variables of the CC in healthy adults using brain MRI's showed that the morphometry of the CC segments changed with age and the angular and linear variables of the CC were significantly higher in males. Whilst the present research has demonstrated analogous results to those of studies conducted in Turkey to a limited extent, it has also indicated discrepancies that are of significant value to emphasise and report. Consequently, the present research contributes to clinicians by providing reference data on disease diagnosis and treatment follow-up.

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Ethical Approval: This cross-sectional retrospective study was initiated after obtaining the permission of the Clinical Research Ethics Committee numbered 2024/118.

Author Contributions: Idea/Concept: A.R., I.K., M.Y.; Design: A.R., I.K., M.Y.; Supervision: I.K., M.Y.; Resources: A.R., M.Y.; Materials: G.R., A.R., M.Y.; Data Collection and/or Processing: G.R., A.R.; Analysis and/or Interpretation: G.R., A.R., M.Y.; Literature Review: G.R., A.R.; Written by: G.R., A.R.; Critical Review: I.K., M.Y.

Conflict of Interest: There is no conflict of interest between the authors.

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RESEARCH ARTICLE

Evaluation of Anatomy Education in Health-Related Programs in Vocational Colleges

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Abstract

Aim: Anatomy is one of the core courses of health sciences education and plays an important role in providing students with professional skills. This study aims to determine the opinions of students studying in health programs towards anatomy education and to examine the level of contribution of anatomy teaching to professional development and practical training opportunities.

Materials and Methods: The study was based on survey data from 527 students. The questionnaire consisted of questions about the adequacy of anatomy course hours, the contribution of anatomy education to professional life, anatomy laboratory training, cadaver use, and organ donation. Descriptive analyses were applied to the data and the results of the analysis are given as median, minimum (min), and maximum (max).

Results: The findings of the study revealed that students thought that anatomy education contributed significantly to their professional development, but anatomy education hours were insufficient in some departments and they did not have enough access to anatomy laboratory training. In addition, the rate of students stating that cadaveric training is not provided is quite high. Students' attitudes toward organ and cadaver donation show variation across programs.

Conclusion: This study demonstrates that anatomy education holds a significant place in health programs, but practical training opportunities are inadequate. It emphasizes that students need greater access to anatomy laboratories and cadaver training to improve their academic success.

Keywords: Anatomy, education, vocational school.

INTRODUCTION

Depending on the developments in the field of science and technology in recent years, academics and students, who are among the dynamics of education, have had to improve themselves. The relationship between academics and students is a relationship that includes mobility in its structure and is in constant interaction (1).

Academicians transfer knowledge and skills to students that they will use in their lives (2). Anatomy is a branch of science that briefly examines the organs that make up the human structure and the systems formed by these organs coming together. Anatomy is a fundamental medical science course offered in health-related programs within Faculties of Medicine, Faculties of Health Sciences, and Vocational Schools. It is delivered in theoretical, practical, or combined theoretical and practical formats. It is also offered as a compulsory or elective course in various faculties, including the Faculties of Fine Arts, Sports Sciences, Education, Engineering, and Architecture (3). This course is essential for all healthcare professionals whose roles involve intervention in or care of the human body throughout their professional practice. Therefore, anatomy education, which offers an in-depth study of the human body, must be provided in a complete and effective manner by competent instructors to healthcare personnel serving in disciplines where human life is directly involved (4). Extensive research has been conducted both in our country and in the world on how anatomy education should be delivered, and various studies have been conducted asking students, who are the main elements of education, to give feedback on this subject (5-8). Based on these feedback, instructors have tried to make the anatomy course more efficient by updating their course programs and curricula (9).

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This study aimed to determine the opinions of students studying in health programs about the anatomy education, to examine the level of contribution of anatomy education to professional development and practical training opportunities. The findings of this study are expected to guide instructors in making necessary curricular adjustments to maximize students' benefit from the course, and it is anticipated that the study will also contribute to the existing body of literature.

MATERIALS and METHODS

In this study, 527 students who were currently taking anatomy classes and those who had previously taken them participated. Those who signed the informed consent form and were students in the relevant health programs of vocational schools were included in the study. This study was approved by the decision of the local non-interventional ethics committee of Düzce University dated 05.05.2025 and numbered 2025/125.

Participants were requested to fill out a sociodemographic questionnaire comprising items related to their gender, age, and the academic programs in which they were enrolled. Then, they were asked to answer "yes", "no", and "undecided" to the questionnaire consisting of 8 questions.: 'Do you find the duration of the Anatomy course hours you have taken sufficient?', 'Do you enjoy studying Anatomy?', 'Do you think that the Anatomy education you have received will contribute to your professional life?', 'If you complete your undergraduate degree, would you like to do postgraduate education in Anatomy afterwards?', 'Have you received Anatomy laboratory training?', 'Have you been lectured on cadavers during your Anatomy education? ', 'Would you like to donate your body as a cadaver after death?', 'Would you like to donate your body as a cadaver after death?', 'Have you donated organs or do you plan to donate organs?', 'Yes, I have donated organs, no, I have not donated organs, I plan to donate my organs, I do not plan to donate my organs'.

To increase the efficiency and ensure the safety of the study, the names and surnames of the students were not collected.

Statistical Analysis

Descriptive analyses were applied to the data. Analysis results were given as median, minimum (min), and maximum (max). SPSS 21 package program was used in statistical analyses and a 95% confidence interval was selected.

RESULTS

In our study, participants included 30 male and 187 female students from the Department of Physiotherapy / Disability Care and Rehabilitation with a median age of 20 years (range: 17–48). From the Department of Elderly Care, 29 male and 102 female students participated, with a median age of 20 (range: 17-53).

The Department of Occupational Therapy contributed 13 male and 78 female students, with a median age of 20 (17-26). Additionally, 10 male and 78 female students from the Department of First and Emergency Aid participated, with a median age of 19.5 (range: 17-45) (Table 1).

Table 1 | Median (min-max) values of number and age of participants by departments

Section	Male (N)	Female (N)	Age (min-max)
Physiotherapy / Disabled Care and Rehabilitation	30	187	20 (17-48)
Elderly Care	29	102	20 (17-53)
Occupational Therapy	13	78	20 (17-26)
First and Emergency Aid	10	78	19,5 (17-45)

For the questions on the adequacy of anatomy course hours and the contribution of anatomy education to professional life, the most common response across departments was 'Yes'. For the item 'Do you enjoy studying anatomy?', the most common response was 'Yes' in Physiotherapy/Disabled Care and Rehabilitation (n=129), Occupational Therapy (n=71), and First and Emergency Aid (n=55), whereas in Elderly Care (n=60) the most frequent response was 'No'. For the items on willingness to pursue postgraduate anatomy education, receiving anatomy laboratory training, cadaver-based teaching, and donating one's body as a cadaver, the most common response across all departments was 'No'. For the item on organ donation, the most frequent response across all programs was 'No, I have not donated organs.' The percentage distributions of responses to each question by department were presented in Table 2.

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Table 2 | Responses to questions by departments

Questions	Responses	Department 1	Department 2	Department 3	Department 4
Do you find the duration of the Anatomy course hours you take sufficient?	Yes	74.7%	67.2%	87.9%	44.3%
	No	13.4%	19%	6.6%	42%
	UD	11.9%	13.8%	5.5%	13.7%
Do you enjoy studying anatomy?	Yes	59.4%	28.2%	78%	62.5%
	No	24.4%	45.8%	6.6%	25%
	UD	16.2%	26%	15.4%	12.5%
Do you think the anatomy education you received will contribute to your professional life?	Yes	79.7%	66.4%	92.3%	80.7%
	No	10.15%	23.7%	3.4%	7.8%
	UD	10.15%	9.9%	4.3%	11.5%
If you complete your undergraduate degree, would you like to do postgraduate education in Anatomy afterwards?	Yes	32.2%	17.6%	31.8%	18.2%
	No	37.8%	64.1%	35.2%	54.5%
	UD	30%	18.3%	33%	27,3%
Have you received anatomy laboratory training?	Yes	12%	2.3%	6.6%	0
	No	88%	97.7%	93.4%	100%
	UD	0	0	0	0
During your anatomy education, were you lectured on cadavers?	Yes	27.6%	10.7%	37.4%	3.4%
	No	72.4%	89.3%	62.6%	96.6%
	UD	0	0	0	0
Have you been an organ donor or do you plan to be an organ donor?	Yes, I have	0.48%	0	2.2%	0
	No, I'm not	47.5%	49.6%	36.3%	47.7%
	I plan	30.4%	34.4%	28.5%	33%
	I do not plan	21.7%	16%	33%	19.3%
Would you like to donate your body as a cadaver after death?	Yes	6.9%	7.6%	8.8%	5.7%
	No	64.1%	67.9%	76.9%	70.5%
	UD	29%	24.5%	14.3%	23.8%

*UD: undecided; Department 1: Physiotherapy / Disabled Care and Rehabilitation; Department 2: Elderly Care; Department 3: Occupational Therapy; Department 4: First and Emergency Aid.

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DISCUSSION

Anatomy education is considered the cornerstone of every profession in the health sciences, providing not only fundamental knowledge but also a critical foundation for developing clinical skills (10). In this context, the study findings suggest that revisions to the anatomy curriculum by academic staff may be necessary, and students should be better informed about organ donation.

The findings assess the impact of anatomy education on health sciences students from a broad perspective. The percentage of students who believe that anatomy courses contribute to their professional lives (79.7% or higher in programs such as Physiotherapy, Disability Care, and Occupational Therapy) is quite high. This result suggests that many students perceive anatomy not merely as a subject but as a fundamental source of knowledge for the health professions. Estai and Bunt emphasized that anatomy education is not limited to theoretical knowledge but also plays a crucial role in providing students with the necessary knowledge to acquire clinical skills (11). The high percentage of students in our study who stated that anatomy education contributed to their professional development supports this perspective.

However, the students' responses regarding the adequacy of anatomy course hours make us think that there may be some deficiencies in the education process. The fact that 74.7% of students in the Physiotherapy program reported the course duration as sufficient may indicate that the content and delivery of anatomy education were effective for this group. However, students in other programs (e.g., 19% of students in the Aged Care program and 42% of students in the First and Emergency Aid program) responded that they found the duration of anatomy courses insufficient. This finding highlights the need to allocate more time to anatomy education and reflects that the educational needs may vary significantly across different departments. Drake and Pawlina emphasized that anatomy education should be carried out with a multifaceted approach and explanation, both theoretically and practically (12). In this context, it is clear that students should be provided with sufficient time and various teaching methods.

Another noteworthy finding of the study relates to anatomy laboratory training and the use of cadavers. In our study, most of the students (especially most of the students from Aged Care, First and Emergency Aid, Physiotherapy programs) stated that they did not receive anatomy laboratory training (rates ranging between 88-100%). Likewise, the percentage of students who stated that they did not receive lectures on cadavers was quite high. These findings indicate that practice in anatomy education, especially practice on cadavers, is lacking. It is well established that practical training, which is one of the most effective ways to recognize anatomical structures, plays a critical role in deepening students' knowledge of anatomy(5,7,12,13). However, it is frequently emphasized in the literature that anatomy education should be enriched through practical and applied methods (5,7,12,13). The study conducted by Harmon et al. in 2021 during the Covid-19 pandemic emphasizes the importance of theoretical education while also stating how effective practical education and elements such as the use of cadavers are in reinforcing students' anatomy knowledge. It is clear that cadaveric education helps students to better understand biological structures and is also an important tool in developing clinical skills (15, 16). Lack of anatomy laboratory training may be directly related to educational failure. When students are unable to support their theoretical knowledge with concrete and real-world observations, their ability to apply their knowledge correctly may be weakened (17).Therefore, it is clear that more practical opportunities and laboratory applications should be offered in education. Student perspectives on organ and cadaveric donation also hold a significant place in this study. Their attitudes toward organ donation provide insight into their ethical awareness and personal values within the healthcare field. While a significant proportion of Physiotherapy and Occupational Therapy students (around 30-34%) stated that they were willing to donate organs, this rate was relatively lower among students in the Elderly Care program. In particular, the diversity of student responses to ethical questions regarding organ and cadaveric donation highlights the connection between anatomy education and ethical understanding (18,19). These findings suggest that ethics-related discussions and awareness-raising content should be more extensively integrated into educational curricula to help students better comprehend their ethical responsibilities in healthcare. Chen et al. (2024) emphasized that ethics education significantly shapes the decisions and attitudes of health science students, playing a crucial role in raising awareness about organ donation (20). Similarly, the study conducted by Kezmezacar found that theoretical anatomy education positively influenced students' perspectives on cadaver donation (18).The use of technology in anatomical education is an important factor in contributing to students' learning processes and ethical values (21). In recent years, the use of technologies such as three-dimensional printers

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and virtual reality in anatomy education offers students a more interactive and concrete learning experience (22). Our study supports the need to utilize technological advances in addition to laboratory and cadaver training in anatomy practical applications in order to increase students' interest in anatomy courses and their academic success. In particular, the increased use of anatomical models and digital simulations is believed to facilitate the reinforcement of theoretical knowledge through practical application. Incorporating technological tools into the learning environment enables students to visualize complex concepts, thereby improving learning efficiency (10). In this context, the multimodal approach in education and the widespread use of digital resources may contribute to greater student engagement and academic success in the field of anatomy.

CONCLUSION

Students are generally satisfied with anatomy class hours. They generally enjoy studying anatomy and think that anatomy education will contribute to their professional lives in the future. When looking at the answers given by the students, most of them have not seen cadavers. For this reason, in addition to theoretical classes, classes should also be taught using models or cadavers in a laboratory environment. Students generally gave negative responses to organ donation. Instructors need to provide information about the importance of organ donation.

As a result, in this study, anatomy education was evaluated from the perspective of students and it was determined that some improvements should be made. Instructors need to increase the efficiency of students in anatomy classes by making some improvements in the anatomy course program and curriculum.

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Ethical Approval: This study was approved by the decision of the local non-interventional ethics committee of Düzce University dated 05.05.2025 and numbered 2025/125.

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RESEARCH ARTICLE

YouTube as a Patient Education Tool: Assessing the Quality and Engagement of Dental Implant Videos

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Abstract

Aim: With >1.5 million implants placed annually and patients increasingly relying on YouTube, this study evaluated the quality, reliability, and engagement of English-language videos on implant therapy.

Materials and Methods: On 15 July 2025, two YouTube searches ("dental implant," "tooth replacement") were run with default relevance. The first 100 results per query were screened (English; 2–15 min; uploaded ≤5 years; ≥5,000 views). After excluding duplicates, lectures, promotions, and off-topic videos, 80 remained. Two reviewers extracted metadata (views, likes, comments, upload date, duration), uploader type, and content features (pre-op assessment, surgical steps, complications, prosthetics, maintenance, cost, diagrams/animations, references). Quality was rated using DISCERN (0–75), Global Quality Scale (GQS, 1–5), and JAMA Benchmarks; inter-rater agreement used Cohen's κ. Engagement included view ratio (views/day), like ratio, and Video Power Index (VPI).

Results: Videos averaged 38,450 ± 21,300 views, 1,250 ± 840 likes, 85 ± 60 comments, and 7.8 ± 3.2 minutes. Uploaders were mainly dentists/clinics (52.5%); narration by professionals in 67.5%. Coverage was uneven: surgical steps (60%), complications (40%), references (6.3%). Mean DISCERN 46.2 ± 13.7; GQS 3.1 ± 0.9. Dentist-narrated videos scored higher on DISCERN than others (49.8 ± 12.5 vs. 37.4 ± 13.9; $p < 0.001$). Discussing complications was linked to higher VPI (45.8 ± 20.3 vs. 32.5 ± 17.2; $p = 0.012$). Animations associated with more likes and higher view ratios ($p < 0.05$). DISCERN modestly negatively correlated with view ratio ($\rho = -0.228$; $p = 0.041$). Inter-rater reliability was substantial.

Conclusion: English-language implant videos show moderate, variable quality. Clinician-led narration and discussion of complications, supported by visual aids, are associated with higher quality and stronger engagement. Professional involvement and standardized guidance could improve patient education.

Keywords: YouTube, dental implants, video quality, DISCERN, patient education.

INTRODUCTION

Dental implants have become the treatment of choice for replacing missing teeth, with survival rates exceeding 95% at 10 years and over 1.5 million implants placed worldwide each year (1). As implant therapy grows, so does patient demand for accessible information on indications, surgical techniques, complications, and long-term maintenance. In parallel, YouTube has emerged as the second-largest search engine globally, with over two billion monthly users who frequently consult videos for health-related queries .

Several cross-sectional studies have highlighted considerable variability in the accuracy and completeness of YouTube videos on dental-implant topics. For instance, Abukaraky et al. systematically reviewed the first 100 "dental implant" videos, finding that many lacked critical details on implant failure modes and decision-making (1), while Özkan et al. demonstrated that videos addressing "dental implant failure" scored poorly on a 10-point content scale and Global Quality Scale (GQS)(2). Moreover, specific concepts such as the All-on-4 protocol and zygomatic implants have likewise been shown to exhibit low content quality and questionable reliability in recent appraisals (3,4).

Despite these insights, there remains no comprehensive evaluation of YouTube videos covering the full spectrum of standard implant procedures—including pre-operative assessment, surgical steps, prosthetic restoration, and postoperative care—using validated instruments such as DISCERN and GQS. To address this gap, we aimed to systematically assess the content quality, reliability, and viewer engagement of English-language YouTube videos on dental implant therapy,

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applying standardized scoring tools and quantitative engagement metrics.

MATERIALS and METHODS

Study Design and Data Source

We conducted a cross-sectional content analysis of English-language YouTube videos on dental implant therapy. YouTube searches were performed on 15 July 2025 at 10:00 UTC using the platform's default "relevance" sorting. Two independent searches were run with the keywords "dental implant" and "tooth replacement," following the approach of Abukaraky et al. (1). No additional filters were applied at the time of search to best simulate a patient's natural information-seeking behavior. Since the data of this study are completely publicly available, it does not require ethics committee approval.

Eligibility Criteria and Video Selection

From each search, the first 100 videos were screened. We included videos that:

1. Were presented in English
2. Had a duration between 2 and 15 minutes
3. Were uploaded within the past five years (sinceJuly 2020)
4. Had ≥5,000 views

We excluded videos that were duplicate uploads, conference lectures, purely promotional content (e.g., advertisements without educational commentary), or unrelated to standard implant procedures. After title and description screening, full-length videos were reviewed for final eligibility, yielding a sample of 80 videos for analysis. Example of dental implant video was presented in Figure 1.

Data Extraction

For each included video, we recorded:

- Metadata: title, URL, upload date, duration, viewcount, likes, and comment count
- Uploader type: dentist/clinic, commercial entity, patient testimonial, or other
- Content topics: surgical steps, pre-operative assessment, prosthetic restoration, complications, maintenance, and cost information
- Reference citation: presence or absence of scientificor clinical references

Figure 1. Example of dental implant video.

Two trained reviewers independently extracted data using a standardized Excel form. Discrepancies were resolved by consensus.

Quality and Reliability Assessment

We assessed each video's informational quality using three validated instruments:

1. DISCERN tool: 16-item questionnaire for evaluatingreliability and quality of health information (5).
2. Global Quality Scale (GQS): 5-point Likert scalerating overall educational value (6).
3. JAMA Benchmark Criteria: four-domain checklist (authorship, attribution, disclosure, currency)(5).

Each video was scored independently by bothreviewers. Inter-rater agreement was calculated usingCohen's kappa coefficient, with $\kappa > 0.75$ indicatingexcellent agreement.

Statistical Analysis

We computed descriptive statistics (mean ± SD, median [IQR]) for continuous variables and frequencies for categorical variables. Group comparisons (e.g., uploader type vs. DISCERN score) were performed using one-way ANOVA or Kruskal–Wallis tests, as appropriate. Spearman's rho was used to examine correlations between quality scores and engagement metrics (views, likes). All analyses were conducted in SPSS v26. A two-tailed $p < 0.05$ was considered statistically significant.

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RESULTS

A total of 80 English-language YouTube videos on dental implant therapy met our inclusion criteria and were analyzed.

Video Sources and Presenters

• Uploader type:

- Dentists/clinics: 42 videos (52.5 %)
- Commercial entities (implant manufacturers, product distributors): 15 videos (18.8 %)
- Patient testimonials: 12 videos (15.0 %)
- Other (e.g., health-bloggers, news channels): 11 videos (13.8 %)

• Narrator:

- Dentist or oral surgeon: 54 videos (67.5 %)
- Patient: 18 videos (22.5 %)
- Other presenter (e.g., industry representative): 8 videos (10.0 %)

The 80 videos in our sample averaged 38.450 views (SD 21.300), with individual counts ranging from 5.200 to 125.800. On average, they received 1.250 ± 840 likes (range 120–4.500) and 85 ± 60 comments (range 0–320). Video lengths averaged 7.8 ± 3.2 minutes, spanning from 2.1 to 15.0 minutes, and had been online for a mean of 950 ± 420 days (range 45–1,820 days). The daily view ratio averaged 40.5 ± 22.1 views per day (range 2.8–200.4), while the like ratio (likes as a percentage of total reactions) was 92.1 ± 8.3 %, with a minimum of 75.0 % and a maximum of 100.0 %. Finally, the Video Power Index (VPI)—a composite engagement metric—had a mean of 37.3 ± 19.5, ranging from 2.1 to 180.8 (Table 1).

Qualitative Content Features

- Pre-operative assessment described: 60 videos (75.0%)
- Surgical steps detailed: 48 videos (60.0 %)
- Complications discussed: 32 videos (40.0 %)
- Prosthetic restoration covered: 55 videos (68.8 %)
- Maintenance and follow-up guidance: 44 videos(55.0 %)
- Cost or financing information: 18 videos (22.5 %)
- Use of diagrams or animations: 25 videos (31.3 %)
- Citations or references provided: 5 videos (6.3 %)

Table 1 | Quantitative Characteristics

Metric	Mean ± SD	Range
Views	38.450 ± 21.300	5.200 – 125.800
Likes	1.250 ± 840	120 – 4.500
Comments	85 ± 60	0 – 320
Duration (minutes)	7.8 ± 3.2	2.1 – 15.0
Days since upload	950 ± 420	45 – 1,820
View ratio (views/day)	40.5 ± 22.1	2.8 – 200.4
Like ratio (likes/(likes+dislikes))	92.1 ± 8.3 %	75.0 – 100.0 %
Video Power Index (VPI)	37.3 ± 19.5	2.1 – 180.8

Video Quality Metrics

- DISCERN score (0–75): 46.2 ± 13.7 (range 18–72)
- Global Quality Scale (1–5): 3.1 ± 0.9 (range 1–5)

DISCERN categories (Figure 2)

- Very poor (15–26): 8 videos (10.0 %)
- Poor (27–38): 20 videos (25.0 %)
- Moderate (39–50): 28 videos (35.0 %)
- Good (51–62): 16 videos (20.0 %)
- Excellent (63–75): 8 videos (10.0 %)

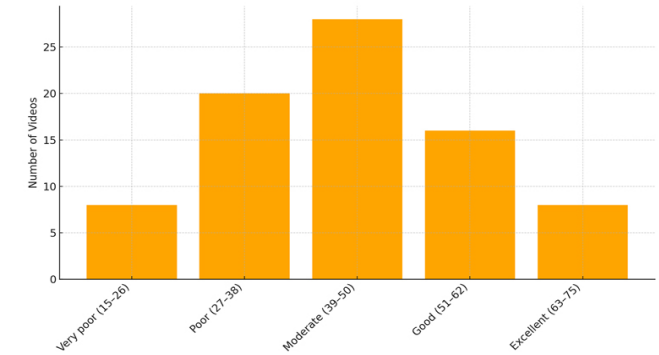

Figure 2. DISCERN category distribution.

Associations Between Content and Engagement

- Videos detailing complications achieved highermean VPI (45.8 ± 20.3 vs. 32.5 ± 17.2; p = 0.012).
- Videos including animations or diagrams had significantly greater numbers of likes (1,480 ± 900 vs. 1,110 ± 820; p = 0.034) and view ratios (48.7 ± 25.1 vs. 35.2 ± 18.4; p = 0.021).
- Dentist-narrated videos scored higher on DISCERN (49.8 ± 12.5) compared to patient-narrated videos (37.4 ± 13.9; p < 0.001)(Table 2).

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Table 2 | Impact of Video Content Features on Viewer Engagement

Content Feature	Comparison	Values	p-value
Videos detailing complications	VPI (detailed vs. non-detailed)	45.8 ± 20.3 vs. 32.5 ± 17.2	0.012
Videos including animations or diagrams	Likes (with vs. without)	1.480 ± 900 vs. 1,110 ± 820	0.034
Videos including animations or diagrams	View ratio (with vs. without)	48.7 ± 25.1 vs. 35.2 ± 18.4	0.021
Dentist-narrated vs. patient-narrated videos	DISCERN score	49.8 ± 12.5 vs. 37.4 ± 13.9	< 0.001

- A modest negative correlation was observed between DISCERN score and view ratio (Spearman's $\rho = -0.228$, $p = 0.041$), suggesting that higher-quality videos did not always attract the highest daily view rates.

DISCUSSION

Our analysis of 80 English-language YouTube videos on dental implant therapy revealed overall moderate quality (mean DISCERN 46.2 ± 13.7) but considerable variability, with 35% scoring in the "moderate" range and 35% in the "poor" or "very poor" categories. These findings mirror those of Gaikwad et al., who reported an average DISCERN of 35.0 ± 6.3 for peri-implant disease videos, with 77% rated "poor" quality (3), and Abukaraky et al.'s 2018 study, which found that most "dental implant" videos lacked comprehensive, evidence-based information (e.g., only 8% referenced scientific sources) (1).

Videos uploaded by dentists or clinics in our sample scored significantly higher on DISCERN and GQS than patient-testimonial or commercial videos, reflecting Özkan et al.'s observation that "dental implant failure" videos from professional sources achieved better content scores than those from laypersons (mean CS = 4.8 vs. 2.7 on a 10-point scale; $p < 0.001$)(2). Nonetheless, even clinician-led content often omitted key details: only 40% discussed complications and just 6% provided citations. Similarly, Osman's systematic review of YouTube health videos noted widespread deficits in reference attribution and completeness across medical topics (6).

Interestingly, we observed a modest negative correlation between DISCERN score and view ratio ($\rho = -0.228$; $p = 0.041$), indicating that higher-quality videos did not necessarily attract more viewers per day. This "quality–popularity" gap has been documented across surgical and general health content: Javidan et al. found that high-quality perioperative videos often garnered fewer views than lower-quality ones, suggesting that algorithmic visibility favors engagement cues over informational rigor (7).

Together, these results underscore the urgent need for standardized guidelines and proactive involvement of professional bodies to improve YouTube's dental implant content. Prior reviews recommend adopting peer-reviewed checklists (e.g., the JAMA benchmarks, DISCERN) during video production and embedding clear authorship, date, and reference details in descriptions to enhance reliability (8). Future work should explore interventions—such as professional-society–curated playlists or YouTube's enhanced tagging for certified content—to bridge the gap between viewer demand and evidence-based education.

Our finding of a mean DISCERN score of 46.2 ± 13.7 for general dental implant videos is notably higher than Gaikwad et al.'s 2024 analysis of peri-implant disease content (mean DISCERN 35.0 ± 6.3), where over 75% of videos were rated "poor" quality (3,9). This suggests that broader-scope implant videos may offer more comprehensive information than niche peri-implant topics, possibly reflecting creators' awareness of wider patient interests and the competitive imperative to produce higher-quality content.

Consistent with Madathil et al.'s 2015 systematic review, which highlighted pervasive variability and a lack of standardization in health-related YouTube videos (6,8), our data demonstrate that metrics driven by popularity (views, likes) are unreliable proxies for informational quality. Osman et al. similarly concluded that YouTube's algorithm prioritizes engagement over accuracy, advocating for integration of expert reviews into ranking algorithms (6).

Videos focusing on specialized techniques like the All-on-4 concept exhibited a mean DISCERN of 47.7 ± 9.9 and GQS of 3.41 ± 0.95 in Gaikwad et al.'s 2024 study, paralleling our moderate scores but underscoring persistent content gaps—particularly in discussing patient selection criteria and long-term outcomes (3). This alignment across studies indicates that even focused technical topics benefit from the same methodological rigor (e.g., standardized checklists) applied to general implant content.

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Provider presence within videos was a strong determinant of quality: Ioschpe et al. found that inclusion of a healthcare professional significantly improved both DISCERN and PEMAT understandability scores ($p < 0.05$) (10). Our observation that dentist-narrated videos outperformed patient testimonials (mean DISCERN 49.8 vs. 37.4; $p < 0.001$) reinforces the value of expert involvement, suggesting that collaborations between clinicians and experienced medical communicators could further elevate content standards.

In light of these findings, Pavuloori et al.'s 2025 systematic review advocates for surgeon- and institution-endorsed content, recommending the use of validated educational frameworks and transparent authorship disclosures to guide both creators and viewers (11). Implementing such guidelines—and potentially developing a "YouTube Health Seal" for certified videos—could mitigate misinformation and empower patients with reliable, evidence-based dental implant information.

Our study has several limitations that should be considered when interpreting the findings. First, because we captured YouTube content at a single time point (15 July 2025), our snapshot may not reflect the platform's rapidly changing video landscape, where new uploads and algorithmic shifts can alter content visibility almost daily. Second, by restricting our analysis to English-language videos on YouTube, we may have overlooked high-quality implant information available in other languages or on alternative social media platforms, limiting the generalizability of our results to non-English-speaking audiences. Third, our reliance on YouTube's default "relevance" sorting, without additional filtering, mirrors typical user behavior but introduces algorithmic bias: individual search histories and geographic location can influence the videos retrieved. Fourth, although we used validated instruments (DISCERN, GQS, and the JAMA benchmarks) and achieved strong inter-rater reliability ($\kappa > 0.75$), scoring inherently involves subjective judgment; future work might benefit from larger rater panels or automated content-analysis tools to further reduce potential bias. Fifth, while we examined broad engagement metrics such as views, likes, and Video Power Index, we did not evaluate deeper user-behavior measures like watch time or audience retention, nor did we assess the impact of external promotion strategies; this constrains our understanding of why some lower-quality videos achieve high popularity. Finally, our focus on standard implant procedures led us to exclude highly technical or niche topics-such as zygomatic implants or grafting protocols-so our conclusions may not extend to specialized surgical content intended for professional training.

CONCLUSION

In summary, YouTube videos on dental implant therapy demonstrate moderate but highly variable informational quality and engagement, highlighting the urgent need for standardized, evidence-based, clinician-led content to better support patient education.

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RESEARCH ARTICLE

Determining the Academic Self-Efficacy of Health Services Vocational School Students Taking Physiology Course

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Abstract

Aim: The study aimed to determine the academic self-efficacy (ASE) levels of students enrolled in the Health Services Vocational School (HSVS) taking the mandatory Physiology course. Given the foundational importance of physiology to the health professions, understanding students' self-belief in mastering this complex subject is critical for educational interventions.

Materials and Methods: This descriptive, cross-sectional study included 245 volunteer students (out of a population of 312). Data were collected via the Descriptive Characteristics Form and the Academic Self-Efficacy Scale (ASE) (33 items, three dimensions; min: 33, max: 165), which was adapted into Turkish by Ekici (2012). The reliability coefficient (Cronbach's Alpha) for the overall scale in this study was high (0.88). Data analysis used descriptive statistics, an Independent Samples t-test, and a One-way ANOVA.

Results: The mean ASE total score was 89.90±17.58, indicating a moderate level, slightly below the theoretical midpoint of99.Students demonstrated high self-efficacy in basic learning (90.2% believed they could learn key concepts), but confidencewas lower for complex tasks (53.9% felt partially sufficient to explain complex processes). Crucially, ANOVA revealedstatistically significant differences ($p < 0.05$) in ASE scores across students' programs, class attendance, average weekly studytime, confidence in using study strategies, and belief in recovery from failure. The most significant finding was the strongcorrelation between self-efficacy and active learning behaviors.

Conclusion: HSVS students exhibited a moderate level of ASE, with higher confidence in basic knowledge acquisition but lower confidence in applying complex physiological concepts and problem-solving. Educators should implement problem-based learning methods to boost self-efficacy regarding complex skills. The strong link between ASE and study behaviors suggests that fostering effective learning strategies is paramount for enhancing.

Keywords: Academic Self-Efficacy (ASE), Health Services Vocational School, Physiology Course, Vocational Education.

INTRODUCTION

Introductory science courses offered at health services vocational schools(HSVS)play a critical role in developing students' professional knowledge and skills. Among these courses, physiology is a fundamental learning area aimed at understanding the structure and functions of the human body. Students who do not sufficiently grasp the physiology course may experience difficulties in professional practice in the future and encounter inadequacies in clinical decision-making processes (1,2). Therefore, students' learning processes, academic motivation, and self-efficacy perceptions regarding physiology courses are considered an important area in educational research (1).

The concept of self-efficacy, as defined in Bandura's (1997) social cognitive theory, refers to an individual's belief that they can successfully perform a specific task (1). Academic self-efficacy is closely related to students' perceptions of success in learning tasks during the educational process (3). Students with high academic self-efficacy not only succeed in their courses but also increase their motivation to learn, use more determined and effective strategies in the learning process, and cope more resiliently with the conceptual difficulties of the course (4). In contrast, students with low self-efficacy perceptions may show a tendency to give up more quickly in challenging courses, experience anxiety, and be unable to use learning strategies effectively (4, 5).

The literature shows that health sciences students' academic self-efficacy is positively related not only to academic achievement but also to many educational

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and psychosocial factors such as class participation, attitude toward learning, self-discipline, and professional development (6). Particularly in courses such as physiology, which require a heavy information load and conceptual depth, students' perceptions of self-efficacy are seen as one of the most important psychological variables determining course success (7).

The physiology course aims to help students understand the functional systems of the human body, comprehend the interactions between these systems, and appreciate the importance of homeostatic regulation as one of the fundamental components of health-related programs (3, 8). As a fundamental science in the health field, physiology provides students with a solid theoretical foundation to better interpret the problems they will encounter in clinical practice. The conceptual intensity and information load of the course require students to effectively use their analytical thinking, problem-solving, and information synthesis skills (1). The literature emphasizes that the necessity for students to relate abstract concepts to concrete examples in their first year of university education can make the learning process challenging both mentally and cognitively (9).

In this context, determining the academic self-efficacy levels of HSVS students taking physiology courses is expected to contribute to revealing their strengths and weaknesses in the learning process. The findings will pave the way for reorganizing educational programs according to students' learning needs, developing more effective guidance and support strategies for teaching staff during the course, and adapting course content to facilitate learning.

Research Questions

- What are the academic self-efficacy levels of students taking physiology courses at the VocationalSchool of Health Services?
- Is there a meaningful relationship between students' sociodemographic characteristics and their academic self-efficacy levels?

MATERIALS and METHODS

Type of Research

This study is a descriptive and cross-sectional design.

Population and Sample of the Study

The study population consisted of students studying in the Vocational School of Health Services who were taking the Physiology course (n=312). The sample consisted of 245 students who voluntarily agreed to participate in the study. The sample size was determined based on the willingness of students to participate, aiming for the highest possible participation rate, which yielded a response rate of 78.5% (245/312) of the target population.

Ethical Aspects of the Study

The study was conducted in accordance with the principles of the Declaration of Helsinki. The study was approved by the Ethics Commission of the University (Date/number: 09-2025/146). All students were informed of the research purpose and procedure, and verbal consent was obtained from those who agreed to participate.

Data Collection Tool and Data Collection

Data were collected using the Descriptive Characteristics Form and the Academic Self-Efficacy Scale.

The Descriptive Characteristics Form was developed by the researchers based on the literature (1,2,3,5,7). It includes 20 questions covering students' sociodemographic characteristics such as age and gender, as well as variables considered likely to affect their academic self-efficacy perceptions regarding the physiology course. To ensure the content validity of the questions, the opinions of two nursing/health sciences experts in the field were consulted, and the form was finalized after necessary adjustments.

The Academic Self-Efficacy Scale was developed by Owen and Froman (1988) (10) and adapted into Turkish by Ekici (2012) (11). The scale consists of a total of 33 items with a five-point Likert-type grading: "Quite a Lot" (5 points), "A Lot" (4 points), "Partially A Lot" (3 points), "Little" (2 points), and "Quite Little" (1 point). The total possible score ranges from 33 (lowest) to 165 (highest), with a higher score indicating a higher level of positive academic self-efficacy attitudes and behaviors.

The scale consists of three dimensions, although it can also be used as a single dimension, as indicated.

These dimensions are the social status dimension, the cognitive applications dimension, and the technical skills dimension. The social status dimension consists of 10 items (items 2, 3, 4, 11, 14, 15, 16, 17, 25, and 27). The

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cognitive applications dimension consists of 19 items (items 1, 5, 6, 7, 8, 9, 10, 12, 13, 18, 19, 20, 21, 22, 24, 30, 31, 32, and 33). The technical skills dimension consists of 4 items (items 23, 26, 28, and 29).

The Academic Self-Efficacy Scale, consisting of a total of 33 items, has a five-point Likert-type grading: "Quite a Lot" (5 points), "A Lot" (4 points), "Partially A Lot" (3 points), "Little" (2 points), and "Quite Little" (1 point). The highest possible score that can be obtained from the scale overall is 165, and the lowest is 33. A high score means that academic self-efficacy attitudes and behaviours are positive and at a high level.

As in the original scale, the Turkish form consists of three dimensions (social status, cognitive applications, and technical skills) and 33 items. The Cronbach's Alpha reliability coefficient for the overall scale is 0.86; for the social status dimension, 0.88; for the cognitive applications dimension, 0.82; and for the technical skills dimension, 0.90 (11). In our study, Crombach's alpha value is 0.88 for the overall scale; 0.85 for the social status dimension, 0.83 for the cognitive applications dimension; and 0.87 for the technical skills dimension.

Data Collection: The data were collected through face-to-face surveys by the researchers. Participants were asked to complete the sociodemographic form and the Academic Self-Efficacy Scale. The application lasted approximately 15–20 minutes.

Evaluation of Data

The data obtained from the study were analyzed using the SPSS version 25.0 (Statistical Package For Social Sciences IBM, USA) software package. Descriptive statistics including number, percentage, mean, and standard deviation values were used to summarize the data.

The Shapiro-Wilk test (for sample sizes n < 50) and the Kolmogorov-Smirnov test (for sample sizes n > 50) were used to test the normality of the data distribution, along with an examination of skewness, kurtosis, and histograms. Based on the results, which indicated a normal distribution (p > 0.05 for the ASE total score), parametric tests were chosen for inferential analysis.

An Independent Samples t-test was performed to compare the Academic Self-Efficacy scores across two independent groups, and a One-way ANOVA test was used to compare the scores across three or more independent groups (e.g., Department/Program).

RESULTS

Table 1 presents the descriptive characteristics of the students participating in the study. The mean age of the students participating in the study was 19.31±3.59. % 61.2% of the students were female, % 24.5% were in the Home Health Care program, 93.5% continuously attended the Physiology course and % 53.1% stated that they studied for the physiology course for 1-2 hours weekly. Regarding self-efficacy beliefs,90.2% of the students believed they could learn theimportant concepts of the Physiology course and69.8% expressed confidence in their ability to applythe course material effectively in exams.

Additionally a large portion of the students indicated that their self-efficacy was only "partially" sufficient for specific areas; 51.4% for the ability to solve a complex physiology topic independently after understanding it, 46.9% for having the necessary study strategies for success in the Physiology course, 53.9% for the ability to explain complex physiology processes (e.g.. homeostasis. nerve conduction) step-by-step, 59.2% for the feeling of competence in physiology problem-solving tasks; and 59.6% for the ability to quickly grasp new concepts related to physiology.

It was determined that 57.1% of the students believed they could contribute to physiology in group work. 69.0% were confident in linking the course teachings with clinical practices, 70.6% were able to find and use appropriate resources when sensing a new learning need in the Physiology course and 64.1% would seek additional support if necessary to increase their success level in the Physiology course.

Table 2 presents the students' Academic Self-Efficacy Scale scores and sub-dimension scores. The total mean score for the Academic Self-Efficacy Scale among students was 89.90±17.58. When examining the scale's sub-dimensions; the students scored 53.06±10.30 on the cognitive applications dimension, 23.31±5.53 on the social status dimension and 11.25±2.90 on the technical skills dimension.

Table 3 presents the mean scores on the Academic Self-Efficacy Scale for students according to selected descriptive characteristics. A statistically significant difference was found between the mean Academic Self-Efficacy scores and the students' Department/ Program, Attendance at the Physiology Course, Average Weekly Study Time for Physiology Course, Belief in the Ability to Learn Important Concepts in the

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Table 1 | Students' Demographic Characteristics (n=245)

Descriptive Characteristics	X ±SD	Min-Max
Age	19.31±3.59	17–61
Gender	n	%
Female	150	61.2
Male	95	38.8
Department/Program		
Home Health Care Program	60	24.5
Elderly Care Program	40	16.3
Operating Room Services	49	20
First Aid and Emergency Care	43	17.6
Audiometry	53	21.6
Attendance at the Physiology Course		
Always	229	93.5
Generally	16	6.5
Average Weekly Study Time for Physiology Course		
Less than 1 Hour	30	12.2
1-2 hours	130	53.1
2-3 hours	57	23.3
3 hours or more	28	11.4
Belief in the Ability to Learn Important Concepts in the Physiology Course		
Yes	221	90.2
No	3	1.2
Partially	21	8.6
Belief in the Ability to Effectively Use Information in Exams in the Physiology Course		
Yes	171	69.8
No	10	4.1
Partially	64	26.1
Ability to Solve a Difficult Physiology Topic Independently After Understanding It		
Yes	96	39.2
No	23	9.4
Partially	126	51.4
Having Necessary Study Strategies to Succeed in a Physiology Course		
Yes	108	44.1
No	22	9
Partially	115	46.9
Ability to Quickly Grasp New Concepts Related to Physiology		
Yes	70	28.6
No	29	11.8
Partially	146	59.6
Self-Confidence in Solving Questions Accurately and Timely in the Physiology Course		
Yes	123	50.2
No	27	11
Partially	95	38.8
Belief in the Ability to Try Again and Fix the Situation After Failure in the Physiology Course		
Evet	209	85.3
No	9	3.7
Partially	27	17–61

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Table 1 | continues

	n	%
Ability to Effectively Utilize Resources (book. notes. video) in Physiology Course		
Yes	210	85.7
No	8	3.3
Partially	27	11
Belief in the Ability to Effectively Prepare for Physiology Exams		
Yes	193	78.8
No	5	2
Partially	47	19.2
Ability to Explain Complex Physiology Processes (e.g.. homeostasis. nerve conduction) Step-by-Step		
Yes	51	20.8
No	62	25.3
Partially	132	53.9
Feeling of Competence in Physiology Problem-Solving Tasks		
Yes	62	25.3
No	38	15.5
Partially	145	59.2
Belief in the Ability to Contribute to Physiology in Group Work		
Yes	140	57.1
No	15	6.1
Partially	90	36.7
Confidence in Linking Course Teachings with Clinical Practices		
Yes	169	69.0
No	6	2.4
Partially	70	28.6
Ability to Find and Use Appropriate Resources When Sensing a New Learning Need in Physiology		
Yes	173	70.6
No	8	3.3
Partially	64	26.1
Seeking Additional Support if Necessary to Increase Success Level in Physiology Course (faculty. friend)		
Yes	157	64.1
No	16	6.5
Partially	72	29.4

$\bar{X}$±S.D.. mean ± standard deviation

Table 2 | Distribution of Students' Mean Scores on the Academic Self-Efficacy Scale (n=245)

Academic Self-Efficacy Scale and Sub-dimensions	$\bar{X}$±S.D.	Min.	Max.
The social status dimension	23.31±5.53	13	36
The cognitive applications dimension	53.06±10.30	27	76
The technical skills dimension	11.25±2.90	4	16
Academic Self-Efficacy Scale	89.90±17.58	51 (33)	132 (165)

$\bar{X}$±S.D.. mean ± standard deviation

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Table 3 | Distribution of Academic Self-Efficacy Scale Mean Scores According to Students' Certain Descriptive Characteristics (n=245)

Descriptive Characteristics	Mean Scores on the Academic Self-Efficacy Scale
Department/Program	
Home Health Care Program	94.13±19.65
Elderly Care Program	90.00±16.89
Operating Room Services	91.26±19.89
First Aid and Emergency Care	92.18±15.65
Audiometry	82.54±14.30
Statistical Analysis	**F=3.395 p=0.010***
Attendance at the Physiology Course	
Always	90.53±17.96
Generally	80.87±5.81
Statistical Analysis	**t=4.575 p=0.033***
Average Weekly Study Time for Physiology Course	
Less than 1 Hour	84.22±15.09
1-2 hours	89.84±16.76
2-3 hours	91.73±17.01
3 hours or more	99.75±22.29
Statistical Analysis	**F=5.275 p=0.002***
Belief in the Ability to Learn Important Concepts in the Physiology Course	
Yes	101.02±12.46
No	89.12±17.43
Partially	92.47±13.76
Statistical Analysis	**F=8.322 p=0.000***
Belief in the Ability to Effectively Use Information in Exams in the Physiology Course	
Yes	102.21±19.85
No	83.27±12.22
Partially	93.55±18.14
Statistical Analysis	**F=36.276 p=0.000***
Having Necessary Study Strategies to Succeed in a Physiology Course	
Yes	93.07±21.57
No	87.21±12.37
Partially	88.36±17.29
Statistical Analysis	**F=3.238 p=0.041***
Belief in the Ability to Try Again and Fix the Situation After Failure in the Physiology Course	
Yes	105.00±23.23
No	89.31±17.65
Partially	89.90±17.58
Statistical Analysis	**F=3.513 p=0.031***
Ability to Effectively Utilize Resources (book. notes. video) in Physiology Course	
Yes	109.75±21.00
No	88.69±16.58
Partially	93.44±20.67
Statistical Analysis	**F=6.411 p=0.002***
Ability to Explain Complex Physiology Processes (e.g.. homeostasis. nerve conduction) Step-by-Step	
Yes	103.56±18.69
No	85.04±18.55
Partially	86.90±17.58
Statistical Analysis	**F=23.26 p=0.000***

$\bar{X}$ ±S.D.; mean ± standard deviation; t: Student t-test; F: one-way ANOVA; p < 0.05.*

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Physiology Course, Belief in the Ability to Effectively Use Information in Exams in the Physiology Course, Having Necessary Study Strategies to Succeed in a Physiology Course, Belief in the Ability to Try Again and Fix the Situation After Failure in the Physiology Course, Ability to Effectively Utilize Resources (book, notes, video) in Physiology Course, and Ability to Explain Complex Physiology Processes (e.g., homeostasis, nerve conduction) Step-by-Step ($p<0.05$).

DISCUSSION

In the literature, the self-efficacy levels of students were determined to be moderate in the study conducted by Yüzer Alsaç and Öztaş (2023) (6) on nursing students, and in the study conducted by Yorulmaz (2019) (12) on health management students. Similarly, in this study, the mean total score on the Academic Self-Efficacy Scale for students taking physiology courses was found to be moderate (89.90±17.58). This common trend suggests that, despite their theoretical potential, students in the early years of professional higher education have not yet maximized their self-efficacy due to complexities in their learning experiences, the adaptation process, or uncertainties regarding the educational process.

This situation may be related to the fact that the mastery experiences described in Bandura's Social Cognitive Theory have not yet fully consolidated, or to difficulties in generalizing previous academic achievements (from the high school period) to the university environment (3).

On the other hand, researches in the literature highlights the importance of cognitive self-efficacy in academic success (7,14). Similarly, the high score students received on the Cognitive Applications Dimension, one of the self-efficacy sub-dimensions (53.06±10.30), suggests high confidence in their cognitive competencies (comprehension and recall). This finding reveals that students feel competent in basic learning tasks; the 90.2% firm belief that they can learn the course's important concepts suggests they have a strong belief in exam success and conceptual learning in a fundamental course such as Physiology (7, 13). However, this confidence is likely to be directed only towards low-level cognitive goals such as comprehension and recall. This distinction indicates that while students are confident in acquiring theoretical knowledge, their self-efficacy in more complex processes, such as analyzing, synthesizing, and problem-solving, is lower, as discussed in the following paragraph. These results suggest that the educational curriculum maintains students' motivation regarding basic academic competencies but needs to further support their self-efficacy in the face of higher-level cognitive challenges (14, 15).

Woolcock et al. (2016) (7) noted that although students' confidence in theoretical knowledge is high in physiology courses, their self-efficacy in problem-solving and application skills is lower. Similarly, Hong et al. (2021) (16) emphasized the importance of active learning methods, such as Problem-Based Learning (PBL) and case studies, to increase students' self-efficacy in professional education. In alignment with this, the moderate level of students' overall self-efficacy aligns with their partially adequate perceptions of higher-order cognitive skills, such as explaining complex physiological processes (53.9%) and feeling competent in problem-solving tasks related to physiology (59.2%). This situation shows that, while students consider themselves competent in learning basic concepts, their self-efficacy is significantly lower in topics that require analysis, synthesis, and clinical reasoning. The abstract and interdisciplinary nature of physiology course content may be one of the main reasons for this difference.

Yılmaz et al. (2023) (17) reported that self-efficacy in anatomy courses positively affects professional competence. Jia et al. (2023) (14) revealed that low academic self-efficacy increases test anxiety and may negatively affect students' help-seeking behaviors, and similarly, Seçer et al. (2022) (18) indicated that deficiencies in problem-solving skills among health students may be linked to low self-efficacy. Consistent with the literature highlighting the importance of professional application and support-seeking, the study found that 69.0% of students believed they could transfer what they learned in physiology classes to clinical practice. This finding reflects a strong belief in integrating basic science knowledge into professional practice. However, it is noteworthy that 64.1% of students would not seek additional support to improve their course performance. This situation may be related to avoidance of perceived failure or social comparison anxiety. In this context, it can be said that teaching strategies aimed at developing students' support-seeking, resource utilization, and application skills are important, not just the transfer of theoretical knowledge. Such approaches can help students become more active and self-regulated learners.

This study also found that students who believed they could learn the important concepts of the physiology course. explain complex physiological processes. and correct the situation by retrying in case of failure

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had higher self-efficacy scores. This suggests that students' ability to manage their own learning processes strengthens their perception of self-efficacy. Hayat and colleagues (2020) (13) similarly stated that medical students with high academic self-efficacy have positive feelings towards learning and use cognitive strategies more effectively. When these findings are evaluated together. in introductory science courses such as physiology. students' self-efficacy affects the learning process not only at the cognitive level but also at the affective and motivational levels.

CONCLUSION

In conclusion, the academic self-efficacy beliefs of Vocational School of Health Services (VSHS) students in physiology courses are generally positive, but they are closely related to modifiable factors, Such as active student participation and study strategies. The study findings indicate that educators should integrate case-based teaching approaches into their courses, notably to support analytical skills in complex physiological processes. They should also guide students on seeking support when needed and effectively utilizing resources. These measures will strengthen not only what students learn but also their belief in their learning abilities.

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CASE REPORT

17 β-Hydroxysteroid Dehydrogenase Deficiency in an Infant: Clinical, Hormonal, Genetic Features and Management

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Abstract

17 β-hydroxysteroid dehydrogenase deficiency (17β-HSD3 deficiency) is a rare congenital disorder affecting male sexual differentiation. It results from mutations in the HSD17B3 gene, leading to impaired conversion of androstenedione to testosterone. This enzyme deficiency causes ambiguous genitalia at birth, with variable clinical presentations ranging from mild to severe forms. The condition follows an autosomal recessive inheritance pattern. A 3-day-old neonate with ambiguous genitalia and a family history of sexual development disorders was diagnosed with 17β-HSD3 deficiency. Diagnostic tests revealed low testosterone, elevated androstenedione, and increased dihydrotestosterone levels. Genetic testing confirmed mutations in the HSD17B3 gene, supporting the diagnosis. Pelvic ultrasound identified testicular tissue in the inguinal canal, and the absence of Müllerian structures confirmed the male phenotype. Testosterone replacement therapy was initiated, and surgical intervention for hypospadias repair and orchiopexy was planned. Early diagnosis and treatment are essential for optimal sexual differentiation and psychosocial development.

Keywords: 17β-HSD3 deficiency; Sexual differentiation; Testosterone replacement therapy.

INTRODUCTION

17 β-hydroxysteroid dehydrogenase deficiency (17β-HSD3 deficiency) is a rare congenital disorder that disrupts the normal synthesis of testosterone due to a deficiency in the 17β-hydroxysteroid dehydrogenase type 3 (17β-HSD3) enzyme. This enzyme plays a crucial role in the conversion of androstenedione to testosterone within the testes. As a result of this deficiency, individuals affected by this condition typically present with ambiguous genitalia at birth, as well as disorders of sexual differentiation (1). The severity of clinical features can vary depending on the extent of enzyme deficiency, ranging from mild forms with normal male sexual differentiation to more severe forms where ambiguous genitalia is prominent (2).

This disorder follows an autosomal recessive inheritance pattern, and genetic mutations in the HSD17B3 gene located on chromosome 9 lead to the dysfunction of the enzyme (3). The clinical manifestation primarily affects male sexual differentiation, with individuals often presenting with a small phallus, hypospadias, and cryptorchidism. These features, combined with the presence of normal or elevated levels of estrone, are indicative of the condition and require careful diagnostic evaluation and management (4).

The diagnosis of 17β-HSD3 deficiency is typically confirmed through a combination of hormonal testing, which shows low testosterone levels, high androstenedione, and genetic testing to identify mutations in the HSD17B3 gene (5). The treatment approach often involves testosterone replacement therapy to support masculinization, and in some cases, surgical intervention such as hypospadias repair and orchiopexy is required (6).

This case report presents an infant diagnosed with 17β-HSD3 deficiency, illustrating the clinical, hormonal,

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and genetic features of the condition, as well as the treatment plan and follow-up care. Early diagnosis and appropriate management are critical for optimizing the outcomes and ensuring normal sexual differentiation and psychosocial development in affected individuals.

CASE PRESENTATION

A 3-day-old neonate was referred to the clinic with ambiguous genitalia. The infant's family history revealed consanguinity (parents being first-degree cousins), with a known history of sexual development disorders in the family. This raised suspicion for a genetic disorder related to sexual differentiation. The infant presented with a 1 cm phallus, a single urogenital opening at the base of the phallus, and bilateral gonads palpable in the labioscrotal folds. In Figure 1, a single urogenital sinus, bifid scrotalization, a 1 cm phallic structure, and the appearance of Prader stage 3 are observed.

Upon physical examination, the findings included:

- 1 cm phallus
- Single urogenital opening at the base of the phallus
- Bilateral gonads palpable in the labioscrotal folds

Figure 1. Appearance of the Genital Organs

These clinical features were indicative of ambiguous genitalia, suggesting a possible 17β-HSD3) deficiency, a disorder affecting the conversion of androstenedione to testosterone, crucial for male sexual differentiation. Given the clinical features and family history, the suspicion of 17β-HSD3 deficiency was high.

Diagnostic Workup:

The following diagnostic tests were conducted to assess the hormonal and genetic status of the patient:

Hormonal levels (measured on 30/07/2024 and 06/08/2024) revealed:

- Glucose: 87 mg/dL
- Sodium: 138 mmol/L (normal range: 135-145 mmol/L)
- Potassium: 4.84 mmol/L (normal range: 3.5-5.0 mmol/L)
- Calcium: 9.9 mg/dL (normal range: 8.5-10.5 mg/dL)
- Phosphorus: 6.2 mg/dL (normal range: 2.5-4.5 mg/ dL)
- Magnesium: 2.10 mg/dL (normal range: 1.8-2.4 mg/ dL)
- Cortisol: 2.5 µg/dL (normal range: 6-23 µg/dL in the morning)
- ACTH: 37.8 pg/mL (normal range: 7.2–63.3 pg/mL)
- Testosterone: 0.56 ng/mL (normal male range: 2.5–9.0 ng/mL)
- Dihydrotestosterone (DHT): 262.34 pg/mL (normal prepubertal range: <30 pg/mL)
- 17-hydroxyprogesterone: 0.657 ng/mL (normal range: <1.0 ng/mL)
- Dehydroepiandrosterone (DHEA): 946 µg/dL (normal range: 70-500 µg/dL)
- Estradiol: 21.1 pg/mL (normal range: 15–50 pg/mL)
- Androstenedione: 1.5 ng/mL (normal range: 0.6–3.2 ng/mL)

Pelvic Ultrasound (USG) on 18/11/2024:

- Bladder wall thickness: Normal
- Bladder lumen: No pathological echogenicity
- Prostatic tissue: Nodular structure at the bladder base, thought to be prostatic in origin.
- Bilateral gonads: Testicular tissue visualized in the scrotum.
- Müllerian structures (uterus and ovaries): Not visualized, supporting male phenotype.

olnguinal canal: In the right inguinal canal, a homogeneous structure was observed with dimensions of 16x7 mm, which is consistent with testicular tissue, and in the left inguinal canal, a homogeneous structure with dimensions of 12x6 mm, consistent with testicular tissue, was observed in the proximal-middle segment.

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Genetic Testing: Chromosomal analysis and 17β-HSD3 gene sequencing were performed, confirming the diagnosis of 17β-HSD3 deficiency. Chromosomal analysis revealed 46 XY karyotype.

Differential Diagnosis:

- 17-20 lyase deficiency
- 3 β-hydroxysteroid dehydrogenase deficiency
- 5 alpha-reductase deficiency
- Androgen Insensitivity Syndrome

Management and Follow-up:

18/11/2024:The infant presented for follow-up. Testosterone therapy was ongoing, and the genital examination revealed a 1 cm phallus, with bilateral gonads palpable in the scrotum.

08/01/2025:The patient's parents gave informed consent for the gender assignment as male, and the infant was scheduled for further surgical procedures.

14/01/2025:Testosterone enanthate was planned, and the family was informed about the long-term management plan.

25/02/2025: The family found DHT, which was started as per the prescribed dose. The family was instructed to use the DHT and follow up in one month.

Surgical Plan:

- Hypospadias repair and orchiopexy for left inguinal testis were planned.
- Follow-up ultrasound showed bilateral gonads in the scrotum, with the right testis in the scrotum and left testis in the inguinal canal. The left testis orchiopexy is planned for 2 months later.
- Postoperative follow-up: The infant was monitored post-surgery, and the gender confirmation surgery is expected to be completed as per the management plan.

In Figure 2, pelvic ultrasonography reveals the right testis (arrow) measuring 16x7 mm in size, located in the mid-distal segment of the right inguinal canal. In Figure 3, pelvic ultrasonography demonstrates an image (arrow) of the left testis, measuring 12x6 mm in size, located in the proximal-middle segment of the left inguinal canal. In Figure 4, pelvic ultrasonography reveals no image indicative of the uterus posterior to the bladder.

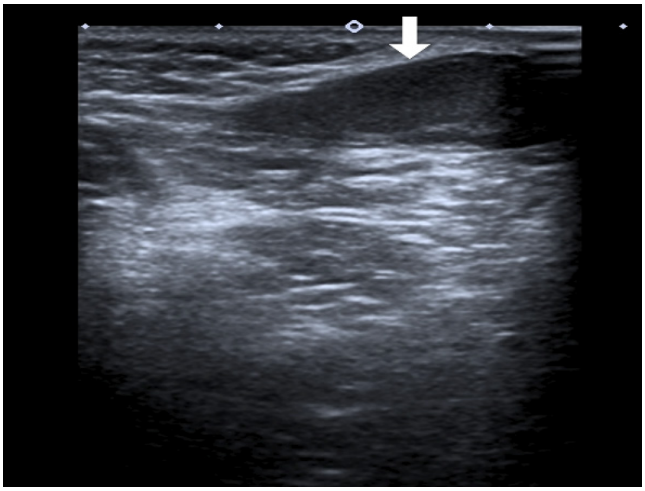

Figure 2. Ultrasonography 1

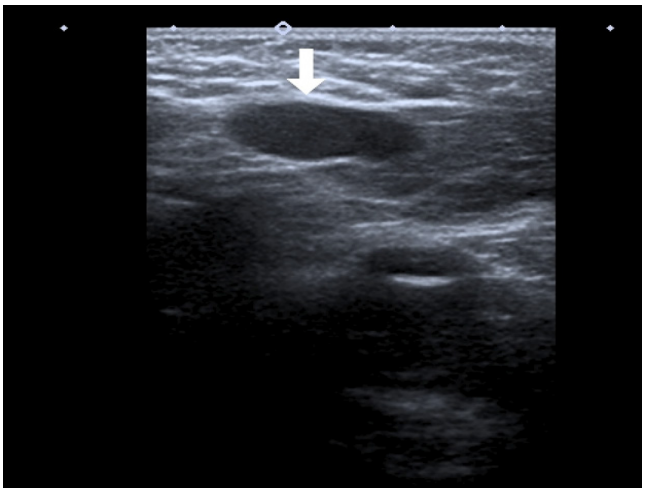

Figure 3. Ultrasonography 2

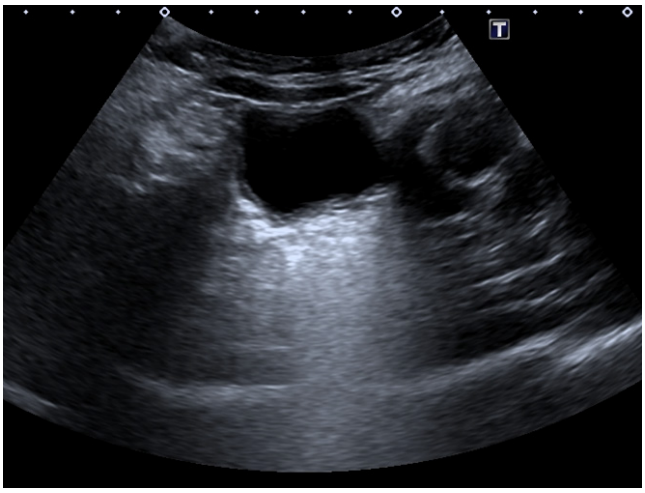

Figure 4. Ultrasonography 3

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DISCUSSION

17β-HSD3 deficiency is a rare congenital disorder that disrupts the synthesis of testosterone, leading to disorders of sexual differentiation in male infants. The 17β-HSD3 enzyme is responsible for converting androstenedione to testosterone, a crucial step in the development of male sexual characteristics (7).

In the case presented, the infant exhibited ambiguous genitalia with a 1 cm phallus, bilateral gonads palpable in the labioscrotal folds, and a single urogenital opening, all of which are characteristic findings of 17β-HSD3 deficiency. The diagnosis was further confirmed through genetic testing, which identified mutations in the HSD17B3 gene, resulting in the inability to convert androstenedione to testosterone. Hormonal analysis revealed low testosterone levels, high androstenedione, and elevated DHT levels, supporting the biochemical evidence of the disorder.

The clinical presentation of 17β-HSD3 deficiency can vary widely, depending on the severity of the enzyme defect (8). In this case, the infant demonstrated complete androgen insensitivity, resulting in a small phallus and ambiguous genitalia despite having a 46 XY karyotype, which is typically associated with male sexual differentiation. These findings emphasize the importance of early genetic testing and hormonal analysis in diagnosing disorders of sexual differentiation. The absence of Müllerian structures and the presence of testicular tissue, both visualized via ultrasound, confirmed the male phenotype. However, the degree of masculinization remains incomplete due to the enzyme deficiency, necessitating long-term management strategies including hormonal therapy and surgical correction.

Testosterone replacement therapy is the cornerstone of managing 17β-HSD3 deficiency, as it aids in promoting the development of male secondary sexual characteristics and normalizing genital morphology (9). In this case, the infant was started on testosterone enanthate (25 mg), a long-acting form of testosterone, followed by a switch to DHT, a topical testosterone preparation. Testosterone therapy helps address both physical and psychosocial aspects of sexual development. Early initiation of testosterone not only supports the physical masculinization process, including the growth of the phallus and scrotum, but also contributes to gender identity development, ensuring the child is raised with the correct gender identity in mind. Continued hormonal support is essential for fostering proper sexual differentiation throughout childhood and adolescence (10).

Surgical interventions are often required to address the anatomical abnormalities associated with 17β-HSD3 deficiency, including hypospadias and cryptorchidism (11). In this case, the infant was diagnosed with a left inguinal testis that was palpable during physical examination. A surgical plan was developed for orchiopexy to bring the testis into the scrotum, and hypospadias repair to correct the urogenital opening. These procedures are critical not only for improving the functional appearance of the genitalia but also for preserving fertility and ensuring normal sexual function in adulthood. Surgical intervention must be carefully planned and performed once hormonal therapy has had an adequate effect on masculinization, allowing for better surgical outcomes.

CONCLUSION

Genetic counseling plays an essential role in the management of 17β-HSD3 deficiency. Given the autosomal recessive inheritance of this disorder, both parents of the affected infant are carriers of the defective gene. Family members are at risk of having additional affected children, and genetic testing is crucial for assessing the carrier status of other siblings or family members. Furthermore, understanding the inheritance pattern can help parents make informed decisions regarding future pregnancies. In addition to genetic counseling, ongoing multidisciplinary care is required, including regular hormonal monitoring and psychosocial support. Regular follow-up visits will ensure proper adjustment of testosterone therapy and assess the progress of genital development and gender identity. With early intervention, proper management, and support, individuals with 17β-HSD3 deficiency can lead fulfilling lives with normal sexual and reproductive health.

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Ethical Approval: There is no requirement of ethical approval since this is a case report.

Author Contributions: Idea/Concept: V.B., H.Z.T., O.B.K.; Design: V.B., H.Z.T., O.B.K.; Supervision: V.B., O.B.K.; Resources: H.Z.T., O.B.K.; Materials: V.B., H.Z.T., O.B.K.; Data Collection and/or Processing: V.B., H.Z.T., O.B.K.; Analysis and/or Interpretation: V.B., O.B.K.; Literature Review: H.Z.T., O.B.K.; Written by: H.Z.T., O.B.K.; Critical Review: V.B., H.Z.T., O.B.K.

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REVIEW

Positional Plagiocephaly: Definition, Diagnosis and Treatment

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Abstract

Positional plagiocephaly (PP) is a non-synostotic cranial asymmetry that has risen in prevalence in the supine-sleep era. This review synthesizes current evidence on definition, differential diagnosis, assessment, and treatment, emphasizing practical steps for frontline clinicians. PP should be differentiated from craniosynostosis by careful history, examination of sutures and ridging, ear position, and the pattern of frontal/parietal bossing; targeted imaging is reserved for equivocal cases. Major risk factors include limited supervised prone time, preferential head positioning, congenital muscular torticollis, prematurity, multiple gestation, and prolonged device use. Severity should be documented with standardized grading (e.g., Argenta) and quantitative indices such as the cranial vault asymmetry index. First-line management is conservative—parental education on repositioning, generous daily "tummy time," and prompt physiotherapy when torticollis is present. For moderate–severe or persistent asymmetry despite these measures, cranial orthosis is most effective when initiated between 4 and 6 months and seldom indicated beyond 12 months. Prognosis is generally excellent, with earlier intervention yielding faster and greater correction. Clinically, PP is best addressed proactively in primary care through routine head-shape and neck range-of-motion screening at all well-baby visits in the first year, early identification of torticollis, structured counseling that preserves supine sleep for SIDS prevention while increasing daytime prone positioning, and timely reassessment within 4–6 weeks. Multidisciplinary pathways linking pediatricians, physiotherapists, orthotists, and craniofacial teams by 4–6 months for non-responders optimize outcomes and minimize overtreatment.

Keywords: Cranial deformities, positional plagiocephaly, helmet therapy.

INTRODUCTION

Positional plagiocephaly (PP), also referred to as deformational plagiocephaly or "flat-head syndrome," is characterized by non-synostotic asymmetrical occipital flattening, ipsilateral ear displacement, and contralateral frontal bossing, resulting from sustained external pressure on the malleable infant skull (1). Unlike craniosynostosis, cranial sutures remain patent, and the deformity arises from mechanical forces rather than premature suture fusion (2). The dramatic rise in PP incidence since the early 1990s closely parallels the success of the American Academy of Pediatrics' "Back to Sleep" campaign, which reduced sudden infant death syndrome (SIDS) by promoting supine sleep. Pre-campaign prevalence estimates placed PP at approximately 1–2% of infants; post-campaign data show rates as high as 20–46% by six to seven months of age, with one large prospective Dutch cohort reporting a 22.1% point prevalence at just seven weeks (3) and U.S. studies noting up to 51% among exclusively supine-sleeping infants (1).

Mechanical etiologies dominate PP pathogenesis. Congenital muscular torticollis (CMT) present in up to 60% of PP cases and constrains cervical rotation, perpetuating lateral occipital pressure on the side of the shortened sternocleidomastoid muscle (4). Intrauterine constraint factors (e.g., oligohydramnios, multiple gestation), prematurity with prolonged neonatal intensive care unit stays, and instrument-assisted or protracted labor further predispose infants to asymmetrical cranial molding (5,6). Surveys of affected infants routinely identify additional risk factors such as male sex, firstborn status, low birth weight, and limited fetal movement (7).

The infant skull's growth follows cephalocaudal and proximodistal gradients, with the occipital region particularly vulnerable in early months when head control is limited (8). Persistent supine positioning without sufficient variation reinforces localized deformation. Conversely, supervised prone "tummy time" stimulates

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cervical and truncal musculature, redistributing pressure and promoting symmetrical vault expansion (9). However, environmental contributors such as excessive time spent in car seats, swings, or carriers, as well as nutritional deficits affecting bone matrix quality, may modulate individual susceptibility (10,11).

Parental awareness and early recognition of head-shape asymmetry are critical. Clinical diagnosis hinges on physical measurements with diagonal cranial asymmetry (>3–4 mm) or cranial vault asymmetry index (CVAI >3.5%)—and standardized anthropometric or photographic protocols (12). While benign in most cases, untreated moderate-to-severe PP can lead to facial asymmetry, mandibular misalignment, and potential psychosocial sequelae. Accordingly, professional guidelines emphasize a stepped approach: repositioning strategies and physical therapy for torticollis as first-line interventions, followed by cranial orthoses for persistent deformities by four to six months of age (13).

This review underscores PP's transforming epidemiology, delineates its multifactorial mechanical and perinatal risk factors, and highlights the delicate balance between safe-sleep practices and cranial molding dynamics. Subsequent sections will examine standardized diagnostic criteria, evidence-based conservative therapies, orthotic helmet efficacy, and long-term developmental and psychosocial outcomes.

Incidence and Etiopathogenesis

Since the advent of the "Back to Sleep" campaign, which successfully reduced sudden infant death syndrome by recommending supine sleep, numerous epidemiological studies have documented a parallel and dramatic rise in PP. In the United States, PP prevalence increased from roughly 5% before 1992 to an astonishing 46% by seven months of age in exclusively supine-sleeping cohorts (14). A large, prospective cohort study of 440 infants reported a 46.6% incidence of PP at 7–12 weeks, with 63.2% of cases affecting the right occiput and 78.3% classified as mild (15).

Similar trends have been observed in Europe. In the Netherlands, routine well-baby clinic screenings revealed that, of 991 infants under one year, 69.5% exhibited occipital plagiocephaly, 18.4% brachycephaly, and 12.1% a mixed pattern (4). A national cohort of over 7,000 newborns found positional head-shape preference in 8.2% at six weeks and noted that up to 2.0% of adolescents (12–17 years) still had residual cranial asymmetry, illustrating the condition's persistence without intervention (16).

In a 2014 Finnish cross-sectional study of 155 healthy newborns, standardized digital cephalometric analysis and goniometric measurement of cervical range of motion demonstrated a 7.7% prevalence of PP, 3.9% prevalence of torticollis, and 46.4% prevalence of cervical mobility imbalances (8). Logistic regression identified associations between PP and factors such as vacuum-assisted delivery (adjusted OR 6.8) and gestational diabetes (adjusted OR 5.6), underscoring multifactorial perinatal contributions.

Mechanical etiologies predominate PP's pathogenesis. Congenital muscular torticollis seen in up to 60% of affected infants and restricts head rotation and channels supine pressure to a focal occipital region (17). Intrauterine constraints (e.g., oligohydramnios, multiple gestation), prematurity requiring prolonged neonatal intensive care recumbency, and instrument-assisted or protracted labor further exacerbate skull deformation. Male sex, firstborn status, low birth weight, and a family history of head-shape asymmetry have also been repeatedly identified as independent risk factors in multicenter surveys (18).

Together, these large-scale, studies reveal how safe-sleep initiatives, perinatal events, and individual mechanical susceptibilities converge to produce a strikingly high and rising global incidence of PP. Early recognition of these etiopathogenic factors is essential to implement timely preventive and corrective measures.

Diagnosis

Diagnosis of PP integrates a focused history, standardized anthropometry, and selective imaging to distinguish deformational from synostotic etiologies. Clinically, PP most often becomes evident between 4 and 8 weeks of age, when sustained supine positioning leads to unilateral occipital flattening, anterior displacement of the ipsilateral ear, and contralateral frontal bossing and producing the characteristic parallelogram-shaped cranial vault (19) (see Figure 1). A detailed perinatal and sleep history should document head-turning preference, evidence of congenital muscular torticollis (noted in up to 60% of PP cases) limiting cervical rotation (5), and prolonged infant carriage or car-seat use.

Objective assessment begins with diagonal caliper measurements: a difference of ≥ 5 mm between the two

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oblique diagonals—measured 30–40° from the midline—confirms clinically significant flattening (20). The CVAI provides a normalized severity scale (21):

$$\text{CVAI} = \frac{\text{long diagonal - short diagonal}}{\text{short diagonal}} \times 100$$

A CVAI > 3.5% is used to define moderate asymmetry, while values ≥ 10% or oblique differences ≥ 10 mm often indicate severe deformity and candidacy for orthotic intervention (22).

Photographic documentation—standardized vertex and lateral images taken monthly—allows for visual tracking of cranial shape against baseline newborn photographs and can alert clinicians to progressive asymmetry when repositioning has been inadequate (1). In ambiguous cases or when synostosis is suspected, high-resolution ultrasound of lambdoid sutures achieves near-perfect sensitivity (100%) and high specificity (89–95%) for patency assessment in infants under four months, offering a radiation-free screening tool (23). When ultrasound is inconclusive or if clinical suspicion persists, low-dose computed tomography with three-dimensional reconstruction remains the gold standard for visualizing suture fusion and planning potential surgical correction (24).

This figure 1 (25) shows a side-by-side profile comparison of a normal infant head (left) and positional plagiocephaly (right). In plagiocephaly, the affected occipital region is flattened, and there is compensatory bossing of the ipsilateral frontal/parietal area, which makes the forehead appear slightly more prominent on the same side. In clinical examination (best appreciated on vertex/posterior views), the ipsilateral ear is typically displaced anteriorly; sutures remain patent, indicating a non-synostotic deformity. The intent of the figure is to help clinicians and caregivers recognize the characteristic contour change of positional plagiocephaly and distinguish it from craniosynostosis-particularly lambdoid synostosis, where the ear is displaced posterior-inferiorly and contralateral parietal bossing is seen.

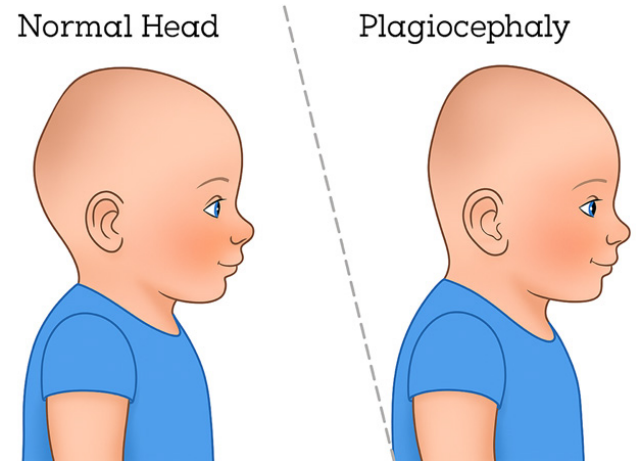

Figure 1. Normal Head and Positional Plagiocephaly (25)

Early identification and differentiation of PP from craniosynostosis are critical to prevent unnecessary surgery and to initiate timely conservative therapy. By combining history, precise anthropometric thresholds (≥ 5 mm diagonals, CVAI > 3.5%), parental-photographic monitoring, and judicious imaging, clinicians can confidently classify cranial deformities and tailor management strategies to optimize infant cranial symmetry and developmental outcomes (26).

Types of PP according to Argenta et al. (27) was shown in Figure 2.

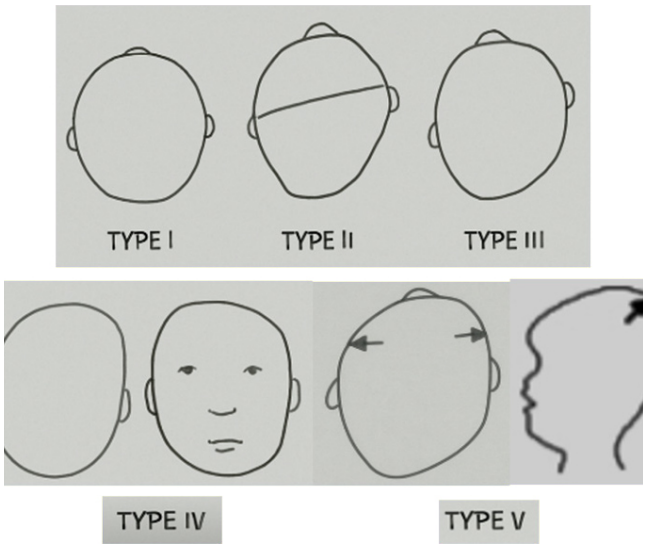

Figure 2. Argenta clinical classification of positional plagiocephaly. Type I: isolated posterior flattening; Type II: + ipsilateral anterior ear displacement; Type III: + ipsilateral frontal/temporal bossing; Type IV: + facial asymmetry; Type V: + vertical cranial asymmetry (increased skull height on the affected side). Each stage is cumulative and guides management severity and referral timing (11).

Classification of PP:

1. Type I PP (PPI) – The mildest presentation, featuring asymmetry confined to the rear of the skull with variable indentation. No ear misalignment, frontal bone irregularities, or facial elongation is observed.

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2. Type II PP (PPII) – A more pronounced form, involving posterior cranial flattening with skull base and temporal fossa alterations. The ear on the affected side shifts forward and/or downward (visible from a top-down view). The forehead remains symmetrical, with no facial asymmetry or vertical cranial compression.

3. Type III PP (PPIII) – Distinguished by a parallelogram-shaped skull. Posterior flattening is accompanied by ipsilateral ear displacement and frontal bone involvement (bulging on the same side as the flattening, observable from above). Facial symmetry is preserved.

4. Type IV PP (PPIV) – Combines posterior cranial distortion with facial asymmetry. The frontal bone and ear rotate toward the flattened side, occasionally with zygomatic process overgrowth or cheek tissue displacement, leading to facial imbalance.

5. Type V PP (PPV) – The most severe form, exhibiting posterior cranial flattening with facial asymmetry, frontal/ear displacement, and abnormal vertical skull growth. A temporal bulge and occipitoparietal deformation are also present (13).

Treatment

Helmet therapy is one treatment option for PP. Its effectiveness has been shown to be associated with the age at initiation. Nonetheless, the optimal duration of treatment remains debated. For example, studies have reported that approximately 83% of late-diagnosed patients experienced effective outcomes with helmet therapy (28).

Posterior deformities tend to worsen during the first six months of life; in such cases, positional changes and typically a three-month course of helmet therapy are recommended (29).

In a study involving 181 children with non-synostotic cranial deformities, 3D photographic measurements taken before and after helmet orthotic treatment revealed the following:

- In plagiocephaly, the cranial asymmetry index improved by 7.16% and asymmetry decreased by 0.86 cm.
- In brachycephaly, the cranial index decreased by 7.32%.
- In children with combined plagiocephaly and brachycephaly, cranial asymmetry improved by 5.77%, asymmetry decreased by 0.71 cm, and the cranial index improved by 5.48% (30).

Another study involving 175 infants with PP treated over six months used 3D surface scanning laser and objective asymmetry measurements, and demonstrated significant improvement in patients who adhered to helmet therapy (31).

A study involving 75 patients aimed to evaluate the effectiveness of a newly developed pneumatic orthotic cranial molding helmet in correcting PP. The study analyzed longitudinal changes in oblique diameter ratios by patient age and head circumference. It reported significant improvement and normalization of cranial ratios compared with pre-treatment measurements (32).

A three-month prospective study in Lausanne (1995–2001) evaluated 260 children treated with dynamic orthotic cranial remodeling for posterior PP. It demonstrated effectiveness in infants whose cranial deformities did not improve with physiotherapy alone (33).

Although the risk of SIDS previously led to the promotion of supine sleeping, long-term gravitational effects may contribute to skull deformities. As a solution, publications recommend encouraging tummy time, allowing infants to spend supervised time in the prone position (34).

In the Netherlands, among a cohort of 400 consecutively born infants, 65 had a positional preference identified at 7 weeks of age. They were then divided into a physiotherapy group and a control group. Studies indicated that the incidence of plagiocephaly was significantly higher in the control group (35).

Current guidance is broadly aligned in prioritizing conservative measures and reserving helmets for selected cases. The American Academy of Pediatrics emphasizes early repositioning and physical therapy, discouraging helmet use in mild–moderate cases and considering cranial orthosis for persistent, moderate–severe asymmetry—ideally when initiated in the 4–6-month window (36).

The 2016 Congress of Neurological Surgeons evidence-based guideline recommends helmet therapy for infants with persistent moderate–severe deformity after a course of repositioning and/or physical

therapy, or for those presenting at a more advanced age; physical therapy is favored over repositioning devices, and improvement is generally faster and greater with helmets in appropriately selected patients (37).

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European radiology consensus statements (ESPR/ESNR/UEMS) focus on diagnosis rather than treatment, advising that imaging is typically unnecessary in straightforward positional cases and should be reserved for equivocal examinations—an approach consistent with neurosurgical guidance to rely primarily on clinical assessment (38).

Complications

Although PP itself is not life-threatening, both the condition and its treatment can be associated with specific complications:

1 Skin Irritation and Pressure Sores

- Helmet Therapy: Cranial orthoses may exert focal pressure on the infant's scalp. A recent study reported that current helmet designs can fail to adapt to rapid head growth, leading to excessive pressure, skin redness, and, in some cases, pressure ulcers (39).

- Prevalence: Minor skin irritation occurs in up to 30–40% of helmeted infants; pressure sores are rare (< 5%) if helmets are properly adjusted (39).

2 Discomfort and Compliance Issues

- Infants may experience discomfort, fussiness, or difficulty tolerating the helmet for the recommended 23 hours per day. Suboptimal daily wear time (< 15–18 h) has been linked to reduced correction rates and prolonged treatment duration (40).

- Parental stress and social stigma (e.g., public visibility of the helmet) can also impact adherence (40).

3 Risk of Overcorrection or Asymmetrical Growth

- Inadequate adjustments or poorly fitting orthoses may concentrate growth in unintended regions, potentially causing vault asymmetries elsewhere. Regular follow-up (every 2–4 weeks) is essential to remodel helmet fit and minimize this risk (41).

4 Residual or Recurrent Deformity

- Mild PP managed conservatively can sometimes recur if repositioning guidelines are not maintained throughout the infant's first year.

- In a large follow-up study, untreated moderate-to-severe PP persisted in 1–2% of adolescents, underscoring the importance of early and consistent intervention (42).

5 No Long-Term Neurodevelopmental Sequelae

- Long-term outcome studies have not demonstrated persistent developmental or neurological deficits attributable to PP or its treatment. In follow-up of over 100 helmeted and non-helmeted children, no delayed complications—neurological or cognitive— were observed at school age (43).

Clinical Implications

Early identification of potential complications particularly skin issues and compliance challenges allows clinicians to tailor follow-up schedules, provide parental support, and optimize orthosis design. With vigilant monitoring and multidisciplinary care (including orthotists, pediatricians, and physical therapists), the vast majority of infants achieve symmetric cranial vaults without lasting adverse effects.

CONCLUSION

PP has become a prevalent cranial molding deformity in infancy, largely driven by well-intentioned safe-sleep practices and various perinatal mechanical factors. Early recognition through routine head-shape surveillance during well-child visits and parental education on positional preference, remains the cornerstone of effective management. When detected before four months of age, simple, noninvasive measures such as repositioning strategies, structured "tummy time," and targeted stretching exercises for coexisting torticollis frequently suffice to redirect cranial growth along natural cephalocaudal and proximodistal gradients. These conservative interventions not only reduce the severity of skull asymmetry but also empower families to participate actively in their infant's care, minimizing the psychosocial and financial burden of more intensive treatments.

For moderate-to-severe deformities characterized by a CVAI above 8–10% or persistent diagonal differences exceeding 5 mm past six months; cranial orthotic therapy offers a highly effective second-line approach, with most infants achieving over 80–90% correction in symmetry within three to four months of consistent helmet wear. The risk of complications is low and typically limited to mild skin irritation. Importantly, current evidence indicates that neither conservative nor orthotic interventions adversely affect long-term

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neurodevelopmental outcomes, and improvements in cranial shape can contribute positively to later psychosocial well-being.

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REVIEW

Respiratory Mechanics and Diaphragm Function in Patients with Epilepsy: A Current Review from a Neurological and Physiological Perspective

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Abstract

Beyond its hallmark seizures, epilepsy can profoundly impact the respiratory system. Recent investigations have uncovered marked impairments in respiratory mechanics, with particular deterioration in diaphragmatic function among affected individuals. Peri-ictal and postictal events such as apnea, hypoventilation, and irregular breathing patterns constitute primary contributors to the heightened risk of sudden unexpected death in epilepsy (SUDEP). Neuromodulatory influences originating in regions like the brainstem and amygdala can induce transient or sustained suppression of respiratory centers. Diminished diaphragmatic performance, in turn, predisposes patients to serious complications including hypoxia and hypercarbia. Furthermore, certain antiseizure medications are recognized for their potential respiratory depressant properties. Assessment of respiratory status employs techniques including pulmonary function testing, diaphragmatic ultrasonography, and polysomnography. In respiratory rehabilitation, exercises aimed at strengthening the diaphragm and improving breath control are vital for complication prevention. Epilepsy management should embrace a multidisciplinary framework, ensuring early identification and intervention for respiratory dysfunction. Continued research in this field remains essential for reducing SUDEP risk and advancing the quality of patient care.

Keywords: Epilepsy, Respiratory Mechanics, Diaphragm Function, SUDEP, Respiratory Rehabilitation

INTRODUCTION

Epilepsy is a persistent neurological condition marked by repetitive and unprovoked seizures, with a global prevalence impacting around 50 million individuals (1). The consequences of the disorder extend beyond seizure activity, often resulting in substantial dysfunction of autonomic processes, including those governing cardiovascular and respiratory operations (2). Notably, respiratory function compromise has been identified as a pivotal factor in the mechanisms underlying sudden unexpected death in epilepsy (SUDEP) and in the development of postictal complications (3,4).

Breathing is an essential physiological process governed by intricate control mechanisms within the central nervous system (5). Within this regulatory framework, the diaphragm serves as a fundamental component, holding a pivotal position in sustaining adequate ventilation (5,6). The influence of epileptic seizures on respiratory control centers can induce transient or enduring dysfunction in diaphragmatic performance (7,8).

The present review will elaborate on the pathophysiological aspects of respiratory mechanics and diaphragmatic operation in individuals with epilepsy, examining both immediate and prolonged respiratory consequences of seizures. It will also address the potential influence of antiseizure medications on respiratory function. Drawing upon contemporary evidence, the discussion will extend to revised guidance concerning clinical surveillance, rehabilitative strategies, and therapeutic management.

Epilepsy and Respiratory Mechanics

Epileptic seizures have the potential to disrupt multiple aspects of respiratory regulation. The propagation of ictal activity to brainstem respiratory nuclei can induce functional disturbances, manifesting clinically as episodes of apnea, hypoventilation, and blunted ventilatory drive (3,4,9). A marked interruption of breathing or pronounced irregularities in respiratory

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rhythm are especially evident during the tonic and clonic stages of a seizure (4).

This phenomenon is attributed to the suppression of brainstem respiratory nuclei, coupled with the involvement of limbic regions like the amygdala. Research indicates that amygdala activation can induce transient apnea and elevate the likelihood of abrupt respiratory cessation (10,11). Such a pathway is considered integral to the pathological sequence leading to SUDEP (4,12).

Respiratory dysfunction in epilepsy is not confined to the ictal phase but may persist interictally. In patients with chronic epilepsy, enduring alterations can arise within ventilatory control pathways, leading to persistent hypoventilation and attenuated chemoreceptor sensitivity to CO_2 (9,13,14). As a result, these individuals often exhibit an insufficient compensatory increase in ventilation in response to elevated carbon dioxide levels (14).

The nature and intensity of seizures directly influence the extent of respiratory compromise. Ictal propagation to brainstem respiratory nuclei occurs more frequently in focal epilepsies, including those of temporal lobe origin, whereas generalized seizure types are associated with a greater propensity for complete respiratory arrest (15,16). Furthermore, the chronicity of the epilepsy condition and the patient's age represent significant variables that modulate respiratory performance (17).

In summary, epileptic activity can induce critical disruptions within the respiratory system, with considerable implications for both mortality risk and quality of life. Consequently, vigilant and regular assessment of respiratory parameters constitutes an indispensable component of comprehensive epilepsy care (13,17).

Diaphragm Function and the Effects of Seizures

Acting as the principal effector muscle for breathing, the diaphragm is fundamental to maintaining ventilation and contributes to the modulation of both volitional and automatic respiration (5,15). Among individuals with epilepsy, notable alterations in diaphragmatic muscle activity are frequently documented both during seizure events and throughout the subsequent postictal phase (7,8).

Seizure-related impact on the diaphragm stems from the propagation of aberrant neuronal discharges to the neural circuits governing respiratory muscles. This can inhibit diaphragmatic contraction, resulting in a transient halt of ventilation (4,7). Furthermore, inhibitory signaling originating in the amygdala has been demonstrated to diminish the diaphragmatic motor command (11).

During the postictal phase, diminished diaphragmatic activity elevates the likelihood of hypoventilation, thereby predisposing the individual to hypoxia and hypercarbia (9,14). This pathophysiological state represents a significant contributor to elevated SUDEP risk (4,5). Consequently, diaphragmatic functional impairment serves as a crucial clinical indicator for impending respiratory compromise and ventilatory failure (18).

Assessment of diaphragmatic performance in epilepsy utilizes modalities including ultrasonography and electromyography. These techniques yield dependable data on diaphragmatic thickness, contractile activity, and range of motion (19). Clinically, ultrasonography is favored for its non-invasive nature, bedside feasibility, and absence of ionizing radiation. In contrast, electromyography provides the distinct advantage of directly quantifying the muscle's electrophysiological function (19). Surveillance of diaphragmatic functional capacity is therefore vital for the preemptive management of respiratory complications in epilepsy (7,18).

To conclude, seizure-induced compromise of diaphragmatic operation diminishes respiratory efficacy, adversely impacts patient well-being, and augments the likelihood of pulmonary sequelae. Hence, routine evaluation and, where indicated, therapeutic support of diaphragmatic function are advised in the care of individuals with epilepsy (7,9).

Respiratory Disorders and Clinical Outcomes

Respiratory disturbances are highly prevalent in the epilepsy population, presenting with a spectrum of clinical features. Ictally occurring apnea, hypoventilation, and dysrhythmic breathing patterns can precipitate episodes of acute respiratory insufficiency (4,9). Notably, these specific respiratory events rank among the principal determinants that elevate the risk for SUDEP (3,4).

Sleep-disordered breathing represents a significant comorbid condition in epilepsy. Obstructive sleep apnea syndrome (OSAS), marked by repetitive nocturnal breathing interruptions, is associated with exacerbated

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epilepsy severity and heightened seizure recurrence (20,21). This comorbidity not only complicates seizure management but also contributes to a decline in overall quality of life (21).

Compromised respiratory function may result in diminished sensitivity to carbon dioxide (CO_2). This attenuation of chemoreceptor drive impairs the compensatory ventilatory response, thereby elevating the susceptibility to persistent hypercapnia (9,13,14). Prolonged exposure to elevated CO_2 and concomitant hypoxia possesses the capacity to inflict neuronal injury and may adversely influence the progression of the epileptic disorder (9,14).

Pulmonary complications constitute a major cause for healthcare encounters and recurrent hospitalizations among individuals with epilepsy. Morbidity is frequently heightened by issues including respiratory tract infections, aspiration pneumonia, and ventilatory compromise (22). Moreover, the sustained cardiorespiratory strain imposed by chronic respiratory dysfunction contributes to an increased long-term mortality risk (8,22).

Consequently, systematic surveillance of respiratory parameters in epilepsy is crucial for the timely identification and management of pulmonary disorders. Clinical guidelines advocate for routine screening for sleep apnea, particularly in individuals presenting with pharmacoresistant epilepsy, obesity, or reported snoring (20). The detection and appropriate management of such comorbid conditions, including obstructive sleep apnea, can yield a favorable impact on overall seizure management (20).

Effects of Antiepileptic Drugs on Respiration

While antiseizure medications (ASMs) constitute the cornerstone of epilepsy management, certain agents within this class may induce unfavorable effects on respiration (23). Notably, benzodiazepines and barbiturates are pharmacological categories associated with a potential for respiratory suppression (24,25).

The central nervous system depressant properties of benzodiazepines can result in inhibition of brainstem respiratory nuclei. This effect may precipitate hypoventilation or even respiratory arrest, particularly with high-dose administration or concomitant use of other sedating agents (25). Additionally, prolonged benzodiazepine therapy has been linked to weakness of the respiratory musculature (24).

Barbiturates, conversely, are recognized for their potent inhibitory action on respiratory drive centers, thereby elevating the risk of acute ventilatory depression (26). Vigilant monitoring of respiratory status is therefore imperative during treatment with these medications (26).

The respiratory impact of other antiseizure drugs is generally more modest. However, isolated cases of allergic responses or bronchospasm have been documented as infrequent adverse events (23). Investigation into the potential respiratory influences of newer-generation ASMs remains an active area of research (27).

Pharmacovigilance reports indicate associations between antiseizure medication use and serious adverse events, including respiratory aspiration and failure. Consequently, therapeutic agent selection and dosage titration must be guided by careful consideration of the patient's baseline respiratory status (28).

In summary, cognizance of the potential respiratory sequelae of antiseizure pharmacotherapy is essential for optimal treatment strategy formulation. For patients with pre-existing respiratory vulnerabilities— such as obesity, chronic obstructive pulmonary disease (COPD), or sleep apnea—medication choices require heightened prudence, accompanied by systematic evaluation of pulmonary function (23,25).

Assessment of Respiratory Functions in Epilepsy

Systematic and objective monitoring of respiratory status is a cornerstone of effective epilepsy management, directly impacting long-term outcomes and complication rates (29). An ideal evaluation framework integrates three core components: the mechanical capacity for ventilation, the efficacy of alveolar gas exchange, and the functional integrity of the muscles responsible for breathing.

In clinical practice, the detection of compromised breathing patterns—specifically inadequate ventilation (hypoventilation) and broader respiratory insufficiency—relies on established techniques. These include comprehensive pulmonary function tests (PFTs), spirometric measurements of airflow, and assessments of arterial blood gases or transcutaneous gas monitoring (30, 31). The data derived from these investigations are crucial for pinpointing the exact nature and extent of dysfunction within the respiratory system (32).

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The functional evaluation of the diaphragm employs several imaging and neurophysiological modalities, including ultrasonography, electromyography (EMG), and magnetic resonance imaging (MRI) (18). Among these, ultrasonography provides a practical, bedside-capable method for quantifying diaphragmatic thickness and excursion without invasiveness (18). EMG, in contrast, delivers a direct measurement of muscular electrical activity, offering unique insights into seizure-related alterations in diaphragmatic neurophysiology (33). Utilizing these techniques in a complementary fashion enables a tailored and holistic assessment aligned with specific clinical presentations and investigative goals.

Beyond structural and electrical evaluation, the functional integrity of central respiratory chemoreception can be probed through tests measuring ventilatory sensitivity to carbon dioxide (CO_2) and oxygen (O_2) (13, 14). Such assessments are particularly valuable for unmasking blunted or abnormal ventilatory drives in the postictal period, a common vulnerability in individuals with epilepsy (14).

For the definitive identification of sleep-disordered breathing, polysomnography (PSG) is universally regarded as the reference diagnostic standard (20). The co-occurrence of disorders like obstructive sleep apnea with epilepsy exerts a considerable influence, often undermining seizure management strategies and detrimentally affecting the patient's overall health status (20).

The consistent integration of these diverse assessment tools into clinical practice is instrumental. It promotes the timely recognition and intervention for respiratory issues in the epilepsy population, thereby playing a direct role in enhancing long-term quality of life outcomes (29, 30).

Rehabilitation of Respiratory Functions and Clinical Approaches in Epilepsy

Therapeutic interventions aimed at correcting respiratory dysfunction are a vital component of comprehensive epilepsy care, serving to optimize patient well-being and avert pulmonary sequelae (34). Key rehabilitative objectives encompass augmenting the strength of inspiratory and expiratory muscles, enhancing maximal ventilatory capacity, and normalizing disordered breathing patterns (35).

Standard rehabilitative protocols often incorporate modalities such as targeted inspiratory muscle training, instruction in diaphragmatic breathing patterns, and exercises designed to improve voluntary breath control (36). Implementation of these techniques promotes diaphragmatic fortification, which in turn mitigates the propensity for hypoventilation and augments overall pulmonary mechanics (18, 36).

A synergistic approach that integrates structured respiratory rehabilitation with effective pharmacologic seizure management holds promise for diminishing the incidence of breathing-related complications and elevating the patient's holistic health profile (23, 37). To maximize efficacy, such rehabilitative regimens must be customized, with programming adaptations reflecting the individual's specific seizure semiology, baseline pulmonary function metrics, and functional physical reserves (34).

Addressing concurrent pulmonary conditions, notably sleep-disordered breathing, represents a critical facet of holistic epilepsy care. The application of positive airway pressure therapy, exemplified by continuous positive airway pressure (CPAP), has demonstrated efficacy in diminishing seizure occurrence among individuals diagnosed with comorbid obstructive sleep apnea (20, 38).

Within the clinical care team, physiotherapists serve as essential contributors to the execution of pulmonary rehabilitative strategies. Empirical evidence corroborates the utility of regimented interventions, including inspiratory muscle strengthening facilitated by isokinetic instrumentation (39). Instituting such rehabilitative measures promptly after identification of need and ensuring their consistent application are proven strategies for attenuating the burden of respiratory morbidity and elevating overall patient well-being.

CONCLUSION

The pathophysiological impact of epileptic seizures frequently extends to the respiratory apparatus, manifesting as considerable dysfunction in both pulmonary mechanics and diaphragmatic operation. Such deficits precipitate severe clinical outcomes, including postictal hypoventilation, apneic episodes, and an elevated propensity for sudden unexpected death in epilepsy (SUDEP). Consequently, vigilant evaluation and continuous surveillance of pulmonary parameters constitute an indispensable element of comprehensive epilepsy care.

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Therapeutic decision-making must also account for the possible respiratory depressant effects associated with various antiseizure medications, with treatment regimens being tailored to mitigate this risk. Concurrently, proactive measures aimed at augmenting and restoring respiratory capacity demonstrate significant efficacy in enhancing patient well-being and forestalling complications of pulmonary origin.

Optimal management necessitates a collaborative, multidisciplinary framework wherein regular surveillance of respiratory status is standard, and concomitant sleep-disordered breathing is proactively diagnosed and managed. Within this team-based model, physiotherapists provide indispensable expertise in pulmonary rehabilitation, directly facilitating enhancements in ventilatory efficiency for individuals with epilepsy.

Ultimately, a clear imperative exists for expanded research efforts focused on elucidating the intricacies of respiratory mechanics and diaphragmatic pathophysiology in the context of epilepsy. Augmenting the foundational understanding in this domain is paramount for developing more effective strategies to curtail SUDEP incidence and refine overall clinical care paradigms.

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REVIEW

Evaluation of Hyoid Bone Fusion Deficiency as a Fracture: A Review

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Abstract

The aim of this review is to raise awareness that delayed fusion between the body of the hyoid bone and the greater horns should not be misinterpreted as a fracture. The hyoid bone is the only bone in the human body that does not articulate with any other bone and, due to its multidirectional mobility, possesses a certain protective capacity against traumatic forces. The junction between the body of the hyoid bone and the greater horns may present as non-fused, partially fused, or completely fused. However, the number of studies directly addressing the fusion process of the hyoid bone remains limited. Previous literature has reported the mean ages of unilateral and bilateral fusion as 38.25 and 53.16 years in males, and 38.00 and 48.50 years in females, respectively. Another study noted that fusion of the greater horns with the body of the hyoid bone rarely occurs before the age of 35-45 years. Such age-related delays in fusion increase the risk that non-fused regions may be misinterpreted as fracture lines or dislocations, particularly in younger individuals. Therefore, especially in individuals under 35 years of age, the wide spectrum of non-fusion and partial fusion should be carefully considered. Given the limited diagnostic value of conventional radiography, evaluation of suspicious cases should be supported by computed tomography, and advanced imaging modalities should be preferred to achieve an accurate diagnosis. This approach significantly improves diagnostic accuracy in distinguishing true hyoid bone fractures from fusion variants.

Keywords: Hyoid bone, Fusion deficiency, Fusion delay, Hyoid bone fusion, Misinterpreted

INTRODUCTION

This review was designed as a narrative literature review. The literature search was conducted using PubMed, Google Scholar, and the National Thesis Center of the Council of Higher Education (YÖK) databases. Studies published between 1908 and 2025 were included.

The following keywords were used individually and in combination during the search process: “hyoid bone”, “os hyoideum”, “hyoid fusion”, “greater horn fusion”, “hyoid bone fracture”, “fusion deficiency”, and “partial fusion”.

The retrieved studies were evaluated according to their content with respect to:

- fusion status between the body and greater horns of the hyoid bone,
- age- and sex-related fusion variations,
- radiological evaluation methods, and
- the risk of misinterpreting fusion variants as fractures.

Studies not directly related to the topic, lacking case-based evidence, or consisting of repetitive data were excluded. The review primarily focused on frequently cited core studies in the anatomical, radiological, and forensic medicine literature.

The hyoid bone is located in the anterior region of the neck, superior to the larynx, has a U-shaped configuration, and measures approximately 3-5 cm in size. It consists of a central body and paired projections on each side known as the greater and lesser horns.

The hyoid bone is suspended by muscles and ligaments connecting it to the mandible, the styloid process of the temporal bone, the thyroid cartilage, the sternum, and the scapula, allowing considerable mobility. Serving as a primary attachment site for the suprahyoid and infrahyoid muscle groups, the hyoid bone plays a dynamic role between the mandible, tongue, larynx, and sternum. The suprahyoid muscles (digastric, mylohyoid, geniohyoid, and stylohyoid muscles) elevate and

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advance the hyoid bone during swallowing and speech, whereas the infrahyoid muscles (sternohyoid, omohyoid, sternothyroid, and thyrohyoid muscles) contribute to laryngeal stabilization and respiratory mechanics. The hyoid bone is unique in that it does not articulate with any other bone in the human body. This anatomical characteristic provides multidirectional mobility and contributes to protection against traumatic injury, which is considered one of the primary reasons for the relative rarity of hyoid bone fractures (1-4).

Bone development occurs through mesenchymal and cartilaginous connective tissues. The hyoid bone ossifies from six centers: two for the body and four for the greater and lesser horns. Ossification begins in the greater horns toward the end of intrauterine life, followed shortly by the body of the hyoid bone, while ossification of the lesser horns typically begins at 1-2 years of age. Although complete ossification is expected with advancing age, this process may not always occur (1,2,5). As a result of these developmental variations, naturally occurring anatomical variants of the hyoid bone may be observed, including non-fused, partially fused, and completely fused forms (6,7).

In a study demonstrating the heterogeneity of the partial fusion group, fusion types between the body of the hyoid bone and the greater horns were classified as follows: absence of contact between the body and horns was defined as "non-fusion," bilateral complete fusion lines were defined as "complete fusion," and intermediate forms between these two extremes were defined as "partial fusion" (Figure 1) (8). Due to its wide range of morphological variation and marked interindividual structural variability, the hyoid bone is considered one of the most polymorphic elements of the human skeletal system (9).

The number of studies directly addressing the fusion process of the hyoid bone is limited. Nevertheless, existing literature indicates that fusion between the body and greater horns shows considerable variation depending on age and sex (6,7,10). In males, the mean ages of unilateral and bilateral fusion have been reported as 38.25 and 53.16 years, respectively, while in females these values are 38.00 and 48.50 years (10). Other studies have suggested that fusion between the body and greater horns typically occurs on one side earlier than the other, with unilateral fusion appearing as early as the second decade, whereas bilateral fusion remains rare until the fifth decade. It has also been reported that the greater horns may rarely fuse with the body of the hyoid bone before 35-45 years of age and, in some individuals, may never fuse throughout life. These findings indicate that fusion deficiency may represent a physiological variation rather than a pathological condition (5,11).

Although the anatomy of the hyoid bone is well established, the timing and characteristics of its developmental fusion process have not been fully elucidated. A better understanding of this process has been suggested to provide significant contributions to researchers (6). Fusion of the anatomical components of the hyoid bone may be observed with increasing age; however, fusion is generally absent before 20 years of age and cannot be considered inevitable even after 60 years. Although a statistically significant relationship between increasing age and the likelihood of fusion has been reported, the high degree of individual variability limits its reliability as a sole marker for age estimation (6,12). Another study reported that bilateral fusion was not observed before the age of 30–35 years, whereas complete fusion was present in all individuals over 60 years of age (10).

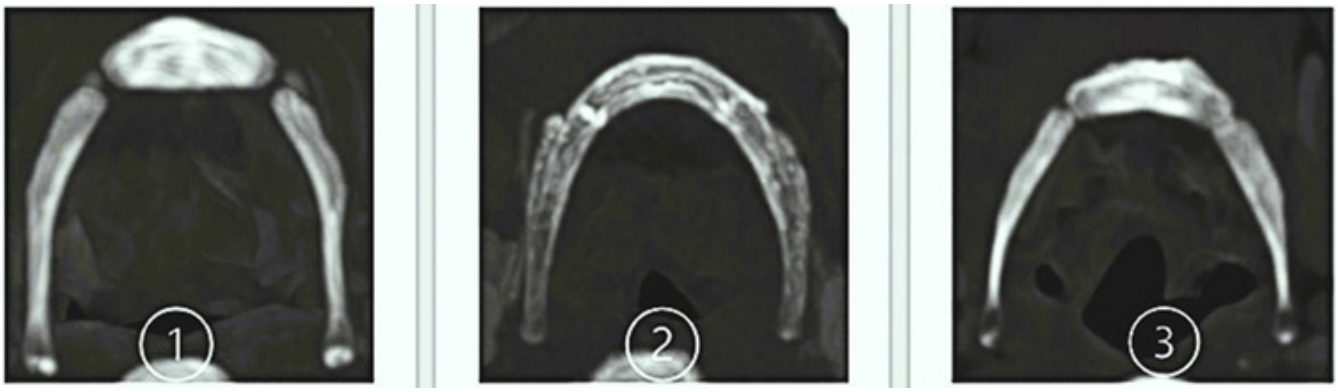

Figure 1. Fusion types of the hyoid bone: 1. Non-fusion, 2. Complete fusion, 3. Partial fusion.

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In some hyoid bones, a synovial-like space resembling a diarthrodial joint may be present between the body and greater horns. The reduction of this space with advancing age suggests that it may initially be present and subsequently undergo fusion over time (13). Studies investigating the relationship between sex and hyoid bone fusion have yielded conflicting results. While some studies reported no significant sex-related differences, others described delayed and irregular fusion patterns in males (6,10,14-16). Findings regarding right–left distribution of fusion are also inconsistent, which is thought to be due to the absence of universally accepted criteria for evaluating hyoid bone fusion (5-7,10,15,16). Consequently, several authors have proposed classification and grading systems for fusion degree (6,7).

In the forensic medicine literature, fractures at the junction between the body and greater horns of the hyoid bone are reported to be rare, and the body of the hyoid bone is generally preserved (17,18).

Baier et al. demonstrated, using micro-computed tomography, that fusion or non-fusion between the body of the hyoid bone and the greater horns can be easily misinterpreted. The authors emphasized that, depending on the observer's level of experience, a natural non-fusion pattern may be confused with a traumatic fracture, and that a narrow gap or incomplete fusion observed radiologically between the body and greater horns may mimic a fracture line (19). In addition, the sensitivity of radiography and palpation in detecting hyoid bone fractures has been reported to be limited (33-60%), and these methods may be misleading. Therefore, they should be considered as preliminary and guiding tools in forensic evaluation rather than definitive diagnostic methods (17,18).

In clinical practice, whole-body computed tomography performed in patients with blunt trauma has been reported to provide a sensitivity of 84.6% and a specificity of 98.9% for head and neck injuries (20). Diagnosis of hyoid bone fractures may be challenging, and in the presence of clinical suspicion, diagnosis may be established using radiography, computed tomography, direct laryngoscopy, nasal endoscopy, or surgical exploration (21,22).

CONCLUSION

Fusion deficiency between the greater horns and the body of the hyoid bone represents a significant anatomical variation that can closely mimic a fracture line or bone dislocation. This issue is of particular diagnostic importance in individuals under 35 years of age, in whom fusion deficiency is a common physiological finding. Recognition of this variation is critical for preventing misdiagnosis of hyoid bone fractures. Considering the limited diagnostic value of conventional radiography, evaluation of all suspicious cases should be supported by computed tomography, and the use of advanced imaging modalities, when necessary, will significantly improve diagnostic accuracy.

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LETTER TO THE EDITOR

Alterations in Pupil Diameter Including Photopic, Mesopic, and Scotopic Vision When Not Under the Influence of Alcohol in Alcohol Use Disorder

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INTRODUCTION

It is usually assumed that alcohol use causes pupil dilatation (1), yet other limited number of studies report that alcohol use has no effect on iris recognition (2). On the other hand, literature demonstrates that the pupil dilates until a certain amount of alcohol use, after which it begins to constrict (3). The changes in pupil diameter under various lighting conditions in individuals diagnosed with alcohol use disorder (AUD) but not under the influence of alcohol have not yet been investigated. This study aims to compare the photopic, mesopic, and scotopic vision of individuals diagnosed with AUD with healthy controls (HCs).

In this retrospective study, individuals who had pupil measurements performed for any reason and who did not have any ocular pathology were evaluated for eligibility for the study, taking into account their e-nabiz (comprehensive patient registration system) records. The AUD group was composed of individuals who were diagnosed with AUD according to DSM-5- TR in the alcohol/substance treatment unit and who had a negative ethyl alcohol result on the day the pupil measurement was performed. Individuals with organic disease or those with the potential to affect the measured parameters (e.g., medication use, diabetes mellitus, hypertension, rheumatologic diseases, and coronary artery disease) were excluded. Individuals with normal eye findings were included. HC group did not have any active disease and medication use. The measurements (mm) had been performed in light, soft light, and dark environments using Sirius 3D Rotating Scheimpflug Camera & Topography System. Pupil diameter measured in light is called as photopic (50 lux), called as mesopic in soft light (4 lux), and called as scotopic in dark (0.04 lux). We considered one alcohol unit equal to 10 ml or 8 g of pure alcohol. The entire AUD group had answered 'yes' to all four items of the CAGE (an acronym for cut down, annoy, guilty, and eye opener) alcohol questionnaire. The Brief Psychiatric Rating Scale (BPRS) had been administered to all individuals. Statistical analyses were performed using SPSS 26.0 package program (IBM Corp., Armonk, NY, USA). Local ethics committee approval was obtained (Adıyaman University, Date: April 16, 2024; Number: 2024/4-32).

While there was no difference in age (p=0.742) and cigarette package/year (p=0.157) between the AUD (n=33 males) and HC (n=33 males) groups, there were differences in BPRS (p<0.001), gamma-glutamyl transferase (GGT) (p<0.001), mean corpuscular volume (MCV) (p<0.001), aspartate aminotransferase to platelet ratio index (APRI) (p<0.001). The proportion of divorced and single individuals (p=0.003), those without a regular job (p=0.003), those with a history of psychiatric admission (p<0.001), and those with a family history of AUD (p<0.001) was higher in the AUD group compared to the HC group. Right scotopic (p=0.005), right mesopic (p=0.033), right photopic (p<0.001), left scotopic (p<0.001), left mesopic (p<0.001), and left photopic (p=0.001) visions were higher in the AUD

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group than in the HC group. In the correlation analysis performed by controlling the effect of age in the AUD group, a significant positive relationship was found between alcohol unit/year and MCV, GGT, APRI ($p<0.05$); a negative relationship between alcohol unit/year and BPRS; a negative relationship between BPRS and MCV, GGT, APRI ($p<0.05$). No significant correlation was found between alcohol unit/year and pupil diameters ($p>0.05$). The area under the ROC curve of right photopic was 0.804 ($p<0.001$; 95%CI [0.693–0.916]).

This study is noteworthy in that it shows that individuals who were not under the influence of alcohol but had an existing diagnosis of AUD had higher pupil diameters, including photopic, mesopic, and scotopic vision, than HCs. Literature shows that pupil diameter decreases more during miosis and increases more during mydriasis in individuals under the influence of alcohol compared to those not under the influence of alcohol. In other words, alcohol has effects that result in an increase in the lower/ upper limits of the pupil diameter. Due to alcohol consumption, the pupil dilates/constricts more than normal which may causes deformation in iris pattern, possibly affecting iris recognition performance (3). Additionally, the sympathetic-parasympathetic hierarchy may be disrupted due to alcohol use (4,5). This retrospective, single-center study enrolled only male participants and relied on electronic records plus a same-day negative ethanol test to verify non-intoxication, introducing potential selection and misclassification biases. Despite excluding major ocular/systemic conditions and medication use, residual confounding (e.g., autonomic changes related to liver status or psychiatric burden) may persist. Pupil size was captured as static diameters under three illumination levels with a single device, without dynamic pupillary reflex metrics, repeated-day measurements, or time-of-day control, which may affect precision. The modest sample size also limits statistical power and generalizability, and the cross-sectional design precludes causal inference. Retrospective nature and inability to verify e-nabiz records are important limitations. Further studies are needed to reduce these limitations.

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