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A morphometric analysis of the ventricular system in scaphocephaly within a select KwaZulu-Natal population: a comparative computed tomographic study

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SUMMARY

Scaphocephaly is a congenital skull deformity that occurs due to the premature closure of the sagittal suture. The resultant skull dysmorphia can cause increased intracranial pressure, leading to ventriculomegaly or hydrocephalus. Previous research focuses on the cranium, with only few studies having analyzed the ventricular system in scaphocephaly. This study aimed to evaluate the morphometry of the ventricular system in patients with scaphocephaly, compared with normal individuals. Computerized tomography scans of 20 patients diagnosed with scaphocephaly and those of 20 control patients were utilized. The following linear dimensions were measured: right and left frontal horn length, third ventricle width, and fourth ventricle length and width. The following linear indices were calculated: Evans index, Bifrontal index, Bicaudate index, Bicaudate frontal index, Bicaudate temporal index, and the Huckman number.

The right and left frontal horn length and the third ventricle width were significantly larger in scaphocephaly. The Evans index ($p<0.001$), bifrontal index ($p=0.002$), bicaudate index ($p=0.003$), and bicaudate temporal index ($p<0.001$) were significantly increased in scaphocephaly compared to the control group. The linear indices were larger in females when compared to males, while the linear dimensions were larger in males than in females in both study groups. The parameters increased with advancing age. The Evans, Bifrontal, Bicaudate Frontal, and Bicaudate temporal indices were significantly larger in the severe scaphocephaly group as opposed to the control group. The ventricles are enlarged in scaphocephaly, mainly observed in the anterior aspect, and ventricular constriction in the posterior aspect of the

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brain. The ventricular morphometry is also affected by age, sex, and severity of deformity.

Key words: Hydrocephaly – Linear dimensions – Linear indices – Scaphocephaly – Ventricles – Ventriculomegaly

INTRODUCTION

Isolated sagittal synostosis, also known as scaphocephaly, refers to the premature closure of the sagittal suture, resulting in an abnormal head shape. The dysmorphism includes an antero-posteriorly expanded neurocranium, larger head circumference, bony ridging over the sagittal suture, biparietal and bitemporal narrowing, and increased prominence of the forehead and occiput (Aldrigde et al., 2005; Mercan et al., 2019; Calandrelli et al., 2020). Sagittal suture craniosynostosis is the most common type of isolated craniosynostosis, with a prevalence of 1:5000 of all isolated craniosynostosis cases reported, with males being more affected than females with a ratio of 4:1 (Heuze et al., 2010; Van Veelen-Vincent et al., 2010; Mercan et al., 2019; Calandrelli et al., 2020). The etiology remains unknown, but may be attributed to environmental and genetic risk factors (Heuze et al., 2010; Van Veelen-Vincent et al., 2010). Scaphocephaly is diagnosed upon physical examination of the skull, which is characterized by a narrow and elongated boat-shape skull and, sometimes, the presence of a sagittal ridge. A reduction in the cephalic index also supports the diagnosis (Massimi et al., 2012). The clinical diagnosis can further be confirmed by radiographic evidence of a non-patent sagittal suture between the two parietal bones (Aldridge et al., 2005; Heuze et al., 2010; Calandrelli et al., 2020). Morphology and morphometry of the cranium or skull in scaphocephaly has long been the focal point for researchers globally (Aldridge et al., 2005; Heuze et al., 2010; Bisetty et al., 2021).

It has been reported that the morphology of the brain structures, including the ventricular system, mirrors the skeletal changes in craniosynostosis. In scaphocephaly, the mirrored organization is observed in the abnormal anteroposterior (A-P) expansion of the brain (Aldridge et al., 2002; 2005). The ventricular system is a network of interconnected cavities within the brain, which contains cerebrospinal fluid. The system consists of two lateral ventricles found in each cerebral hemisphere, a midline third ventricle in the diencephalon between the two thalami, and a fourth ventricle between the cerebellum and the pons, connected by the interventricular foramen and cerebral aqueduct, respectively (Gameraddin et al., 2015; Kolsur et al. 2018; Baruah et al., 2020). The morphology and morphometry of the ventricular system are affected by various factors, including age, sex, and pathology; thus, the cerebral ventricles function as a vital neurodevelopmental and pathological marker (Wilk et al., 2011; Baruah et al., 2020). According to the literature, changes in ventricular anatomy are more common in complex or syndromic craniosynostoses compared to single-suture non-syndromic synostoses, like scaphocephaly (Lui et al., 2024). However, there are studies, albeit a few, that have reported significant morphological and morphometric changes in the ventricular system in scaphocephaly (Usami et al., 2016; Aldridge et al., 2017; Di Rocco et al., 2019; Lui et al., 2024). Ventricular dilation above its normal variations is described inconsistently in literature for isolated sagittal suture, with estimated occurrence equivalent to normal patients. However, the enlargement of the cerebral ventricles is not always associated with severe hydrocephalus, but it may indicate primary cerebral maldevelopment; as a result, all ventricular enlargement requires attention (Usami et al., 2016).

Some scaphocephalic cases require monitoring of intracranial pressure. In such cases, ventricular shunt replacement surgery is recommended, with a monitor placed in the cerebral ventricles. The cranial morphology of affected individuals significantly differs from unaffected individuals, resulting in the traditional ventricular access points being considered unreliable in scaphocephaly (Bisetty et al., 2021). Ventricular access points are used in ventricular shunt therapy, whereby a catheter is placed in the ventricular system to stabilize ventricular dilation (Bisetty et al., 2021). Precise measurements of the ventricles provide a practical and reliable method to assist in the identification of certain neurological conditions, like early detection of hydrocephalus. It also provides essential data for monitoring ventricular enlargement after ventricular shunt therapy. Neuroradiologists frequently encounter challenges in determining whether the cerebral ventricles are within normal limits or enlarged with the age of the affected individual (Baruah et al., 2020). Posterior cranial fossa reconstructive surgery is commonly performed in patients with syndromic craniosynostosis to release intracranial pressure which stabilizes the ventricular dilation (Liu et al., 2024). However, in scaphocephaly, the recommended surgical intervention is mainly performed in order to return the skull to a more normative head shape (Aldridge et al., 2005). The ideal time for surgery in non-syndromic craniosynostosis remains unknown, and whether it is of clinical significance or for cosmetic reasons (Aldridge et al., 2005; Liu et al., 2024). Few studies report on the morphometry of the ventricular system using the linear indices (Evans index), with no study having explored the ventricular anatomy using the linear dimensions in patients with scaphocephaly.

Therefore, this study aimed to provide a detailed morphometric analysis of the ventricular system using linear dimensions and indices in patients with scaphocephaly, compared to individuals without any skull deformity, in relation to age, sex and degree of severity.

MATERIALS AND METHODS

Patients

For this retrospective study, 20 preoperative computerized tomography (CT) scans of pediatric patients diagnosed with scaphocephaly were obtained from the database at a quaternary hospital in Durban, South Africa. These scans were of patients who visited the Craniofacial Unit between January 2014 and June 2020. A total of 20 control CT scans were also obtained from a private radiological database. These scans were of patients whose heads' CT scans showed no cranial or intracranial pathology. Only CT scans that met the inclusion criteria were used for the analysis.

Inclusion criteria- Scaphocephaly patients

- Patients diagnosed with scaphocephaly and confirmed by radiological imaging
- Patients aged between 0 to 10 years
- Patients with CT scans of clear and good quality imaging
- CT scan slice thickness of 0.5 mm to 5 mm

Exclusion criteria - Scaphocephaly patients

- Patients with multi-sutural or syndromic craniosynostosis
- Patients aged above 10 years
- CT scans that are of poor quality and unclear ventricular anatomy
- CT scans slice thickness <0.5 mm and > 5mm

Inclusion criteria- control patients

- Patients not affected by craniosynostosis or any craniofacial deformity
- Patients with unaffected intracranial structures
- Patients aged between 0 to 10 years
- CT scans of good quality and clearly visible ventricles
- CT scans slice thickness between 0.5 mm and 5 mm

Exclusion criteria- control patients

- Patients affected by craniosynostosis or with any other craniofacial deformity
- Patients with affected intracranial structures (tumors, intracranial hemorrhage, et c.)
- Patients above 10 years old
- CT scans with poor imaging quality and unclear anatomy
- CT slice thickness <0.5 mm and >5 mm

CT scan acquisition and analysis

Axial CT scans were acquired from the Picture Archiving and Communication System (PACS) and saved onto a hard drive in DICOM (Digital Imaging and Communication in Medicine) format. CT scans were acquired as part of regular clinical procedures with a 128-slice SOMATOM Definition AS scanner or a SOMATOM Definition Flash CT Scanner (Siemens Healthineers, Forcheim, Germany). The slice thickness for the identified CT scans ranged from 0.5 mm to 5 mm. The Horos Project software was used to view and standardize all CT images to a 1 cm reference scale. The standardization was confirmed manually using the orbitomeatal plane (a line passing through the outer canthus of the eye and the midpoint of the external acoustic meatus). All measurements were taken using the length tool on the Horos Project software program. Measurements were taken three times by the first author to ensure reliability and accuracy; a further 50% (20 CT scans) of the sample size was analyzed by a second observer to ensure reproducibility.

Morphometry of the ventricular system (linear dimensions)

The length of the lateral ventricle (left and right), the width of the third ventricle, as well as the length and width of the fourth ventricle, were measured in millimeters on an axial slice. In the brain setting, the lateral ventricles were identified as two band-shaped structures on the left and right hemispheres of the brain, where the frontal horn is anteriorly bounded by the body of the corpus callosum and laterally by the caudate nucleus (Fig. 1). The third ventricle was identified as the midline space between the left and right thalamus (Fig. 2). The fourth ventricle was identified as a cavity located in the posterior cranial fossa between the cerebellum and the pons of the brainstem (Fig. 3). The measurements were taken as follows:

(i) Length of the frontal horns: the distance from the anterior-most point of the frontal horn (left and right) to the interventricular foramen was measured at the level of the interventricular foramen (Fig 1).

(ii) Width of the third ventricle: the maximum distance between the medial wall of the left and right thalamus at the level of the interventricular foramen (Fig. 2).

(iii) Fourth ventricle length and width: the length was measured as the maximum distance from the fastigium or apex of the cavity to the floor of the fourth ventricle on the pons. The width was measured as the maximum transverse diameter between the medial walls of the fourth ventricle (Fig. 3).

Morphometry of the ventricular system (linear indices)

Linear measurements were taken on standardized axial CT scans at the level of the interventricular foramen using the length tool on the brain window setting according to Wilk et al. (2011). The following linear measurements were taken (Fig. 4): maximum distance between the anterior horns (AB), maximum internal skull distance of the frontal bone (CD), minimum bicaudate distance (EF), the internal diameter of the skull at the level of the caudate nucleus (GH), and the maximum internal skull diameter (IJ). Based on the measurement taken, the following linear indices were calculated:

(i) Evans index was calculated by dividing the maximum distance between anterior horns by the maximum internal skull diameter (AB/IJ) (Fig. 4).

(ii) Bifrontal index was calculated by dividing the maximum distance between anterior horns by the maximum internal diameter of the frontal bone (AB/CD) (Fig. 4).

(iii) Bicaudate frontal index was calculated by dividing the minimum bicaudate nuclei distance by the maximum distance between anterior horns (EF/AB) (Fig. 4).

(iv) Bicaudate index was calculated by dividing the minimum bicaudate nuclei distance internal skull diameter measured along the same line (EF/GH) (Fig. 4).

(v) Bicaudate temporal index was calculated by dividing the minimum bicaudate nuclei distance by the maximum internal skull diameter (EF/IJ) (Fig. 4).

(vi) The Huckman number was calculated by adding the maximum distance between anterior horns with the minimum bicaudate nuclei distance (AB+EF) (Fig. 4).

Fig. 1.- Length of frontal horns of lateral ventricle. AB- right horn, CD- left horn

Statistical analysis

The statistical data analysis was conducted in R Statistical computing software of the R Core Team, 2020, version 3.6.3. The results were presented in the form of descriptive and inferential statistics. Where applicable, the descriptive statistics of numerical measurements were summarized as the minimum, maximum, quartiles, interquartile range, means, standard deviation and the coefficient of variation. In addition, boxplots were used for the visual display of the descriptive patterns. On the other hand, the categorical variables were described as counts and percentage frequencies. Depending on the distribution of the numerical variables between two independent groups, mean or median differences were assessed using either t-test or Wilcoxon, respectively. In order to assess the mean difference of numerical variables across at least three levels of a categorical variable, the ANOVA test was used for normally distributed measurements and the Kruskal Wallis for assessing the median difference of the non-normally distributed measurements. In the case of significant mean difference, post-hoc tests were conducted using the Tukey's HSD (Honestly Significant Difference) single-step multiple comparison procedure, and similarly with the Dunn test for significant differences in the medians. In the case of pairwise comparison of the groups, the t-test was used for normally distributed data, or the Rank sum test was used where the numerical measurements were non-normally distributed. The results were also graphically displayed as barplots annotated with the statistical test results. The intraclass correlation coefficient (ICC) was used to assess the accuracy of repeat intra and inter observer measurements. All inferential statistical analysis tests were conducted at 5% levels

Fig. 2.- Width (AB) of third ventricle.

of significance.

RESULTS

Table 1 illustrates the demographic information of the scaphocephaly patients (n=20) and control group (n=20). Of the 20 scaphocephaly patients that were analyzed, 16 were male and 4 were female, with an age range of 0.20-7.70 years. There were 10 male and 10 female patients in the control group, with an age range of 0.60-10.00 years. Patients were categorized into four age groups, viz. <1 year (n=8), 1-2 years (n=9), 3-5 years (n=5), 6+years (n=18). Furthermore, scaphocephaly patients were categorized according to severity based on the cephalic index, viz. 3 were mild, 10 were moderate and 7 were severe.

The mean length of the left frontal horn was significantly larger in scaphocephaly compared to the control group (p=0.026). The right frontal horn length was found to be significantly greater in scaphocephaly (p=0.006). The mean width of the third ventricle was significantly greater in scaphocephaly compared to the control (p=0.004). Mean values for the fourth ventricle dimensions were comparable (Table 2).

There were no statistically significant differences between males and females in terms of linear dimensions in both study groups. However, mean values for the following parameters were generally larger in males with scaphocephaly compared to females, viz. left and right frontal horn length and fourth ventricle length and width (Table 3).

Frontal horn length was highest in the oldest age group, and increased in both study groups. The third ventricle width increased with advanc-

Table 1. Demographic data

Demographics	Scaphocephaly (n=20)	Control (n=20)	Overall (n=40)
Sex			
Male	16 (80.0%)	10 (50.0%)	26 (65.0%)
Female	4 (20.0%)	10 (50.0%)	14 (35.0%)
Age			
<1yr	7 (35.0%)	1 (5.0%)	8 (20.0%)
1-<3yrs	7 (35.0%)	2 (10.0%)	9 (22.5%)
3-<6yrs	3 (15.0%)	2 (10.0%)	5 (12.5%)
6+yrs	3 (15.0%)	15 (75.0%)	18 (45.0%)
n (Min-Max)	20 (0.200-7.70)	20 (0.600-10.0)	40 (0.200-10.0)
Severity			
Mild [CI>70]	3 (15.0%)	20 (100.0%)	23 (57.5%)
Moderate [CI: 65-70]	10 (50.0%)	0 (0.0%)	10 (25.0%)
Severe [CI<65]	7 (35.0%)	0 (0.0%)	7 (17.5%)

Table 2. Ventricular lengths and widths in scaphocephaly vs control patients

Linear dimensions	Scaphocephaly (n=20) (Mean±SD)	Control (n=20) (Mean±SD)	p-value
Left lateral frontal horn length	27.00±3.25	24.90±2.34	**0.026**
Right lateral frontal horn length	27.30±3.34	24.80±2.04	**0.006**
Third ventricle width	3.97±0.995	3.14±0.687	**0.004**
Fourth ventricle width	9.99 ^{m}	9.28 ^{m}	0.694
Fourth ventricle length	8.86 ^{m}	9.74 ^{m}	0.375

^{m}: median; Bold: statistical significant (p-value<0.05)

Table 3. Sex differences in ventricular lengths and widths in scaphocephaly vs. control patients

	Scaphocephaly (Mean±SD)			Control (Mean±SD)		
	Male	**Female**	**p-value**	**Male**	**Female**	**p-value**
Left lateral frontal horn length	27.6±2.24	25.4±2.14	0.854	25.4±2.57	24.5±2.13	0.406
Right lateral frontal horn length	27.6±3.54	26.3±2.52	0.517	25.7±2.15	23.9±1.59	0.057
Third ventricle width	3.77±0.896	4.77±1.09	0.071	3.13±0.689	3.15±0.723	0.953
Fourth ventricle width	10.2±1.24	9.56±2.37	0.429	9.34±2.12	9.28±0.54	0.791
Fourth ventricle length	9.20±1.42	8.33±1.54	0.349	9.31±2.26	10.6±1.34	0.146

Table 4. Mean ventricular lengths and widths in scaphocephaly vs control patients according to age

	Scaphocephaly (Mean±SD)				Control (Mean±SD)			
	<1yr (n=7)	**1-2yrs (n=7)**	**3-6yrs (n=3)**	**6+yrs (n=3)**	**<1yr (n=1)**	**1-<3yrs (n=2)**	**3-<6yrs (n=2)**	**6+yrs (n=15)**
Left lateral frontal horn length	24.7±3.04	28.1±2.97	26.5±1.46	29.5±3.30	24.00 ^{m}	24.40±0.84	24.8±1.54	25.4±2.26
Right lateral frontal horn length	25.5±3.40	27.9±2.77	30.2±4.49	27.6±1.64	25.20 ^{m}	22.9±1.65	23.3±1.43	25.7±1.56
Third ventricle width	3.75±0.94	4.22±1.17	3.53±1.18	4.36±0.59	3.78 ^{m}	3.64±1.46	3.18±3.46	2.96±1.23
Fourth ventricle width	10.1±1.22	9.99±2.09	10.2±1.66	10.3±0.52	7.93 ^{m}	9.07±0.86	9.26±2.32	10.0±0.46
Fourth ventricle length	8.94±1.83	8.61±0.97	10.6±3.32	11.0±2.78	8.88 ^{m}	11.5±0.96	9.40±3.02	9.72±1.76

^{m}: median

ing age in scaphocephaly and decreased with age progression in normal patients. An increase in the fourth ventricle width was observed among the consecutive age groups (Table 4).

The length of the right frontal horn and the third ventricle width was significantly larger in the severe group compared to the control group (Table 5) (Figs. 5 and 6).

The following ratios were found to be significantly larger in patients with scaphocephaly compared with control patients: the Evans index (<0.001), Bifrontal index (0.002), Bicaudate index (0.003), and the bicaudate temporal index (<0.001) (Table 6).

In terms of sex, no statistically significant differences were found between the two groups. However, a trend was observed where females were found to have larger values compared to males in both the scaphocephaly and control groups. The following ratios were found to be larger in females than in males with scaphocephaly: the Evans index, bifrontal index, bicaudate index, bicaudate temporal index, and the Huckman number. In the control group, the following ratios were higher in females than in males: the Evans index, bifrontal index, bicaudate frontal index, bicaudate index, and the bicaudate temporal index (Table 7).

Due to the limited sample size, the linear indices could not be compared by age. It may also be worth to note that all the linear indices decreased with advancing age in the control group, whilst in scaphocephaly the ratios were highest in the oldest age group (Table 8).

When the indices of the ventricles were compared according to the degree of severity of scaphocephaly (cephalic index), the bifrontal and the bicaudate indices were found to be significantly larger in the severe group compared to the control group (Table 9) (Figs. 8 and 9). The Evans index and the bicaudate temporal index were significantly larger in the severe and moderate groups compared to the control group (Table 9)

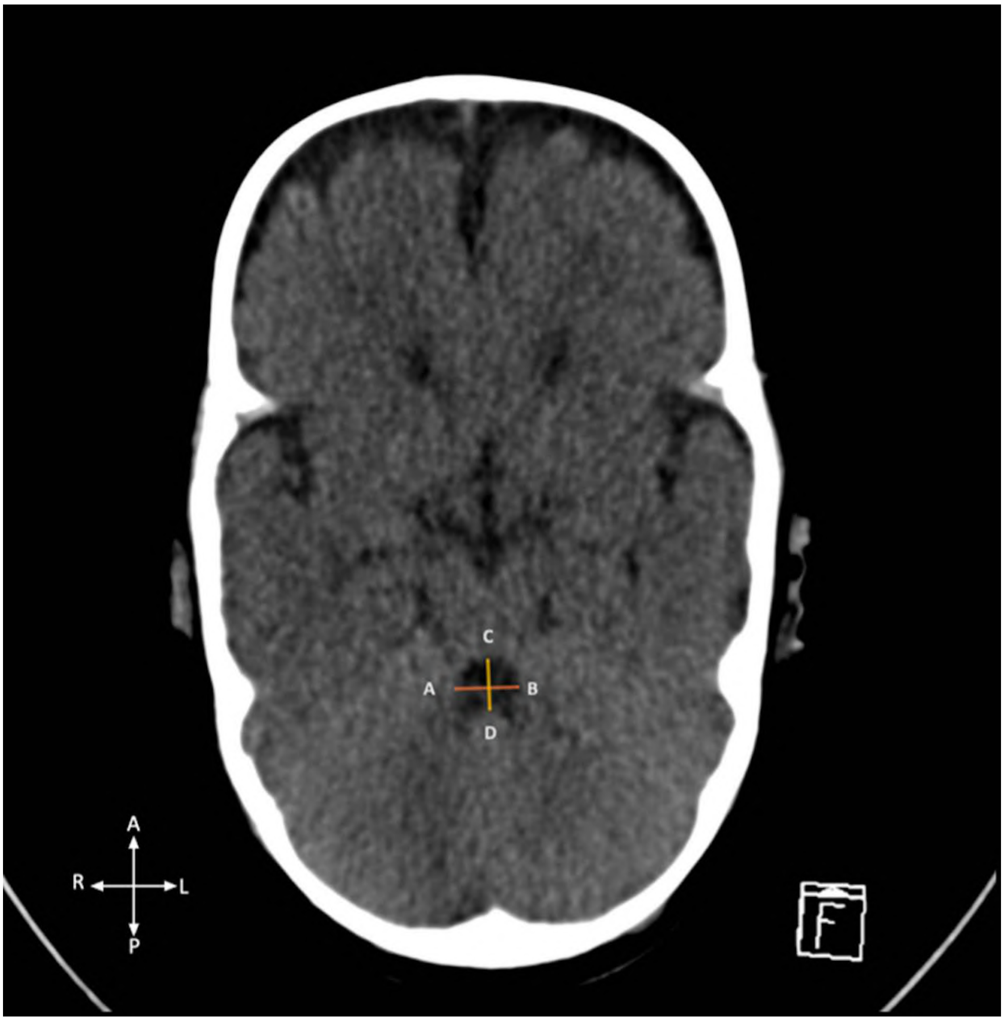

Fig. 3.- Width (AB) and length (CD) of fourth ventricle.

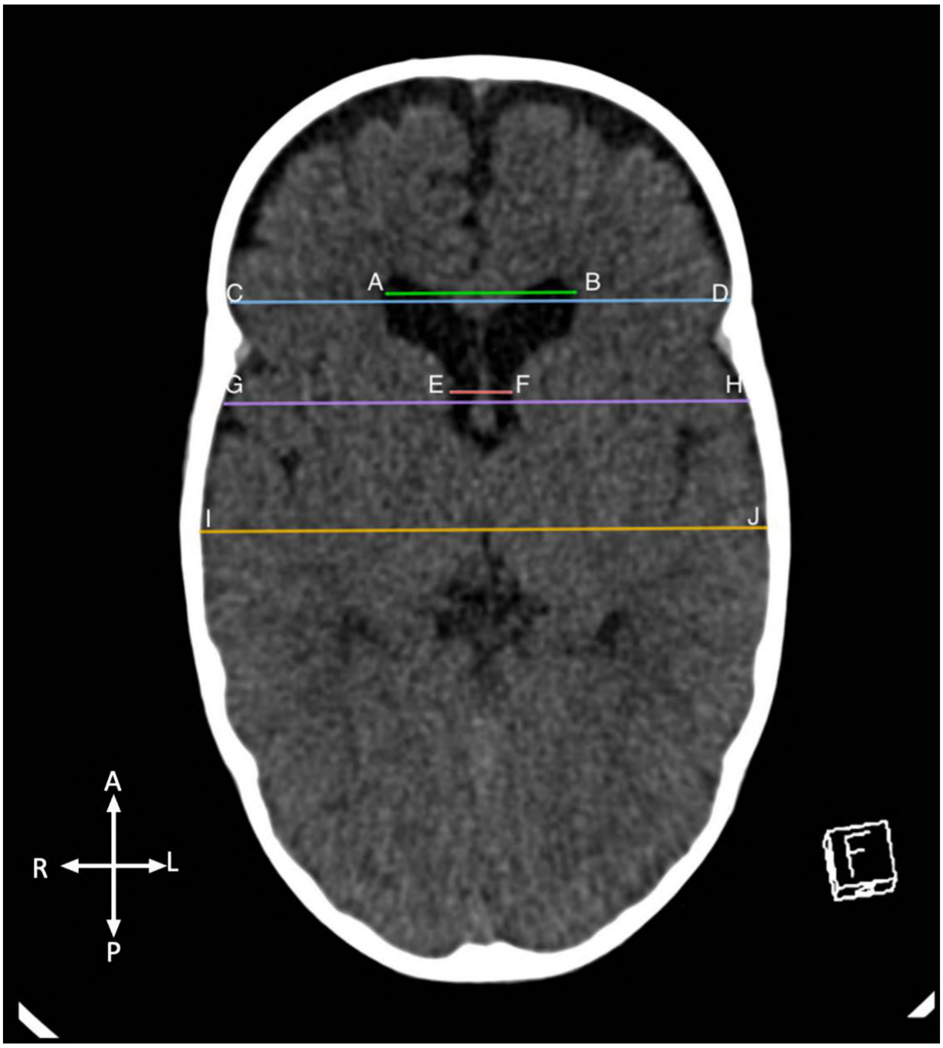

Fig. 4.- Axial view of lateral ventricles indicating linear dimensions. AB- maximum distance between the frontal horns, CD- maximum internal distance of frontal bone, EF- minimum bicaudate distance, GH- distance of inner skull tables at same level as minimum bicaudate distance, and IJ- maximum internal skull distance.

(Figs. 7 and 10).

Intra-observer reliability indices were as follows: Evans index (ICC= 0.96), Bifrontal index (ICC= 0.97), Bicaudate frontal index (ICC= 0.99), Bicaudate index (ICC= 0.80), Bicaudate temporal index (ICC= 0.80), Huckman number (ICC=1.00). Left frontal horn length (ICC=1), Right frontal horn length (ICC=1), Third ventricle width (ICC=1), Fourth ventricle width (ICC=1), Fourth ventricle length (ICC=1).

Inter-observer reliability indices were as follows: Evans index (ICC= 0.99), Bifrontal index (ICC= 0.98), Bicaudate frontal index (ICC=0.99), Bicaudate index (ICC= 0.97), Bicaudate temporal

Table 5. Linear dimensions in patients with scaphocephaly vs. control group according to severity

	Scaphocephaly (Mean±SD)				
Parameter	Mild n=3	Moderate n=10	Severe n=7	Control (Mean±SD) n=20	p-value
Left lateral frontal horn length	26.80±1.10	26.10±2.44	28.30±4.55	24.90±2.34	0.060
Right lateral frontal horn length	26.80±1.35	26.40±2.57	28.90±4.49	24.80±2.04	**0.012**
Third ventricle width	3.41±0.49	3.78±0.99	4.49±1.02	3.14±0.687	**0.006**
Fourth ventricle width	11.5 ^{m}	9.83 ^{m}	9.73 ^{m}	9.28 ^{m}	0.256
Fourth ventricle length	8.96 ^{m}	8.68 ^{m}	9.53 ^{m}	9.74 ^{m}	0.541

^{m}: median; Bold: statistical significant (p-value<0.05)

Table 6. Linear indices of the ventricular system in scaphocephaly vs. control patients

Linear indices	Scaphocephaly (n=20) (Mean±SD)	Control (n=20) (Mean±SD)	p-value
Evans index	0.30±0.03	0.25±0.02	<0.001
Bifrontal index	0.33±0.04	0.29±0.02	0.002
Bicaudate frontal index	0.27±0.08	0.24±0.04	0.097
Bicaudate index	0.09±0.03	0.07±0.01	0.003
Bicaudate temporal index	0.60 ^{m}	0.06 ^{m}	<0.001
Huckman number	3.86±0.58	3.79±0.38	0.670

^{m}: median; Bold: statistical significant (p-value<0.05)

Table 7. Sex differences in ventricular linear indices in scaphocephaly vs control patients

	Scaphocephaly (n=20) (Mean±SD)			Control (n=20) (Mean±SD)		
Indices	**Male**	**Female**	**p-value**	**Male**	**Female**	**p-value**
Evans index	0.28±0.03	0.30±0.03	0.221	0.25±0.02	0.25±0.02	0.920
Bifrontal index	0.31±0.03	0.36±0.03	0.069	0.30 m	0.30 m	0.927
Bicaudate frontal index	0.28±0.07	0.24±0.11	0.392	0.23±0.04	0.25±0.05	0.571
Bicaudate index	0.09±0.03	0.10±0.03	0.286	0.06±0.01	0.07±0.02	0.529
Bicaudate temporal index	0.50 ^{m}	0.85 ^{m}	0.344	0.05±0.01	0.06±0.01	0.587
Huckman number	3.80±0.58	4.08±0.56	0.414	3.85±0.40	3.74±0.366	0.527

^{m}: median

Table 8. Linear indices results of patients with scaphocephaly vs. control group in terms of age

	Scaphocephaly (n=20) (Mean±SD)				Control (n=20) (Mean±SD)			
	<1yr (n=7)	**1-2yrs (n=7)**	**3-6yrs (n=3)**	**6+yrs (n=3)**	**<1yrÇ (n=1)**	**1-2yrs (n=2)**	**3-5yrs (n=2)**	**6+yrs (n=15)**
Evans index	0.28±0.04	0.29±0.03	0.30±0.12	0.28±0.03	0.28 ^{m}	0.24±0.12	0.25±0.10	0.25±0.02
Bifrontal index	0.31±0.05	0.34±0.03	0.31±0.02	0.34±0.03	0.34 ^{m}	0.30±0.03	0.29±0.03	0.29±0.02
Bicaudate frontal index	0.30±0.07	0.25±0.10	0.30±0.03	0.30±0.03	0.29 ^{m}	0.28±0.03	0.26±0.01	0.23±0.04
Bicaudate index	0.09±0.03	0.09±0.03	0.07±0.02	0.10±0.01	0.09 ^{m}	0.08±0.031	0.08±0.02	0.07±0.03
Bicaudate temporal index	0.36±0.33	0.71±0.35	0.45±0.37	0.80±0.10	0.08 ^{m}	0.07±0.04	0.06±0.04	0.05±0.01
Huckman number	3.64±0.75	3.92±0.48	3.84±0.31	4.23±0.50	4.33 ^{m}	3.60±0.02	3.71±0.03	3.79±0.407

^{m}: median

Table 9. Linear indices of the ventricular system in scaphocephaly vs. control patients according to severity

	Scaphocephaly (n=20) (Mean±SD)				
	Mild n=3	**Moderate n=10**	**Severe n=7**	**Control (n=20) (Mean±SD)**	**p-value**
Evans index	0.27±0.03	0.28±0.03	0.30±0.06	0.25±0.02	<0.001
Bifrontal index	0.32±0.02	0.33±0.03	0.34±0.04	0.30±0.02	0.009
Bicaudate frontal index	0.25±0.04	0.26±0.09	0.31±0.07	0.24±0.04	0.125
Bicaudate index	0.08 ^{m}	0.09 ^{m}	0.09 ^{m}	0.07 ^{m}	0.003
Bicaudate temporal index	0.50 ^{m}	0.65 ^{m}	0.80 ^{m}	0.06 ^{m}	<0.001
Huckman number	4.09±0.56	3.62±0.44	4.10±0.68	3.79±0.38	0.170

^{m}: median; Bold: statistical significant (p-value<0.05)

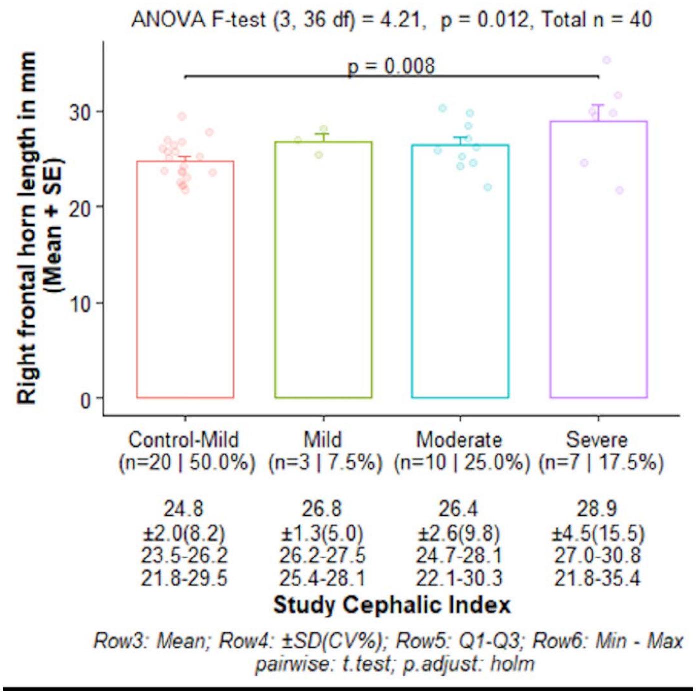

Fig. 5.- Post-hoc analysis of right frontal horn length in terms of the degree of severity in scaphocephaly compared to control patients.

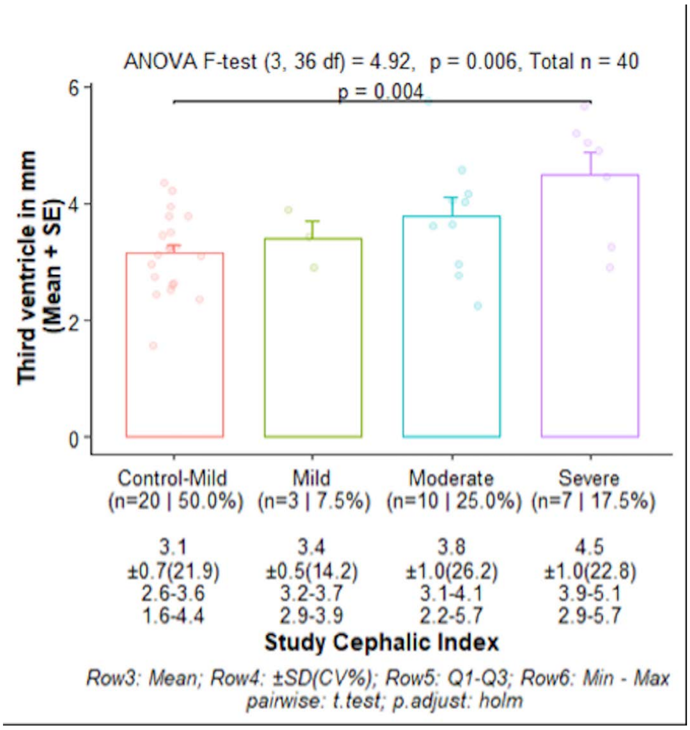

Fig. 6.- Post-hoc analysis of the third ventricle width in terms of the degree of severity in scaphocephaly compared to control patients.

index (ICC= 0.98), Huckman number (ICC=1.00). Left frontal horn length (ICC=1), Right frontal horn length (ICC=0.93), Third ventricle width (ICC=1), Fourth ventricle width (ICC=1), Fourth ventricle length (ICC=1).

DISCUSSION

The morphology and morphometry of the ventricular system can be affected by various factors such as age, sex, and pathologies; thus, the cerebral ventricles act as a neurodevelopmental and pathological marker (Sari et al., 2015). Quan-

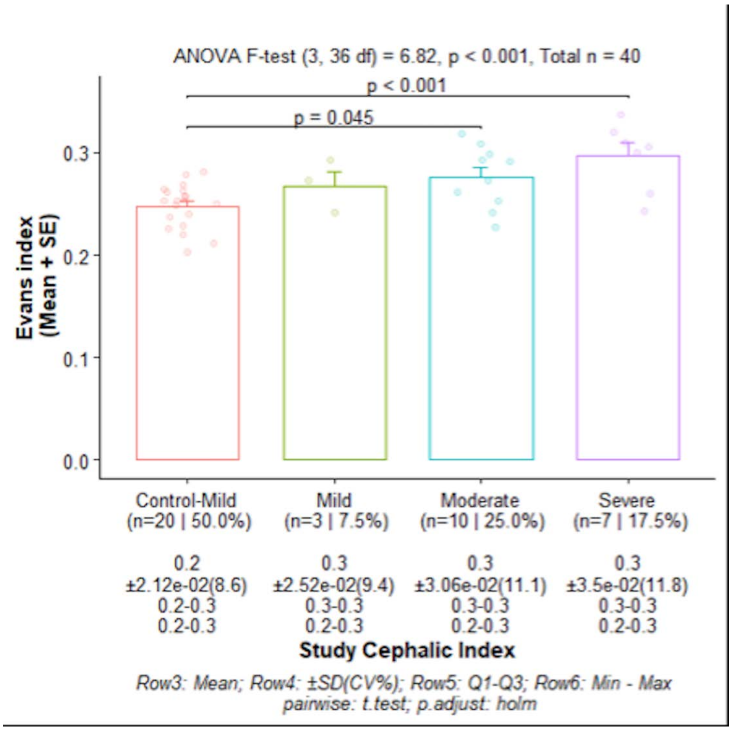

Fig. 7.- Post-hoc analysis of Evans index in terms of the degree of severity in scaphocephaly compared to control patients.

titative assessment of the ventricular volume is essential for early detection and diagnosis of ventriculomegaly, which can ultimately lead to hydrocephalus (Kolsur, 2018). Although hydrocephalus is usually associated with complex craniosynostosis, it can also occur in severe cases of simple craniosynostosis. Limited literature is available on the anatomy of the ventricular system in scaphocephaly.

Whilst ventricular volume serves as a gold standard for assessing ventricular size, its measurement is often impractical in clinical settings due to time constraints (Kolsur, 2018). Ragan et al. (2015) discovered a positive correlation between

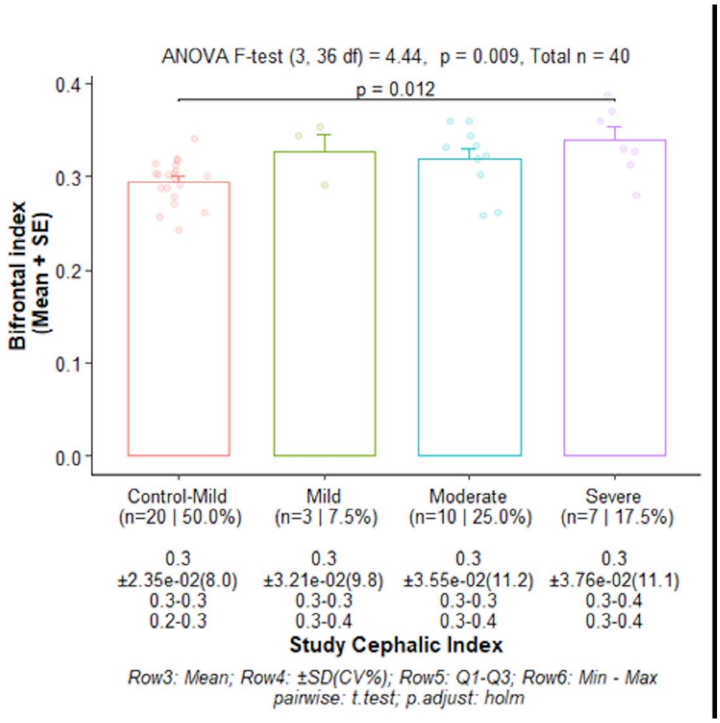

Fig. 8.- Post-hoc analysis of bifrontal index in terms of the degree of severity in scaphocephaly compared to the control patients.

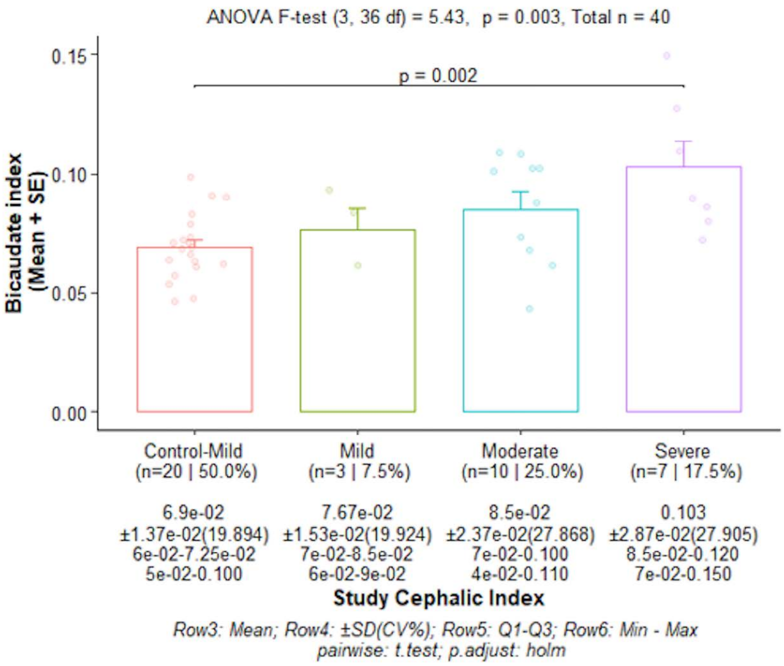

Fig. 9.- Post-hoc analysis of Evans index in terms of the degree of severity in scaphocephaly compared to control patients.

linear measurements and indices of the ventricles and ventricular volume in adults. In this study, linear dimensions of the lateral, third and fourth ventricles, and linear indices such as the Evans index, bifrontal index, bicaudate index, bicaudate frontal index, bicaudate temporal index, and the Huckman number were used to evaluate the ventricular size in patients affected by scaphocephaly.

The right and left frontal horn lengths were found to be significantly larger in scaphocephaly compared to the normal group; this may be the result of the A-P elongation and the frontal bossing in scaphocephaly, inducing elongation of the anterior horns of the lateral ventricles (Table 2). In relation to sex, the frontal horn lengths were higher in males than in females in both study groups. Males generally have larger lateral ventricles, which is largely observed in the anterior horns and the body of the lateral ventricles. This can be associated with facts that males have larger brain volumes. The right frontal horn was found to be significantly larger in the severe scaphocephaly group compared to the control group (Table 5) (Fig. 5). This may be due to the nature of the deformity in severe conditions, where biparietal growth is restricted and compensatory growth occurs in the frontal region, causing the cortical and subcortical structures of the brain to grow in the same direction.

The third ventricle width is an essential parameter for the detection of third ventriculomegaly. In this study, the ventricular width was significantly larger in scaphocephaly than in the control group (Table 2). It has been reported that males tend to have a larger third ventricle width than females (Gameraddin et al., 2015). However, in this study the value was found to be larger in females than in males. The third ventricular width has also been well correlated with age in the literature (Wilk et al., 2011; Gameraddin et al., 2015; Baruah et al., 2020). Aldridge et al. (2002) hypothesized that the progressive ventricular enlargement with age in scaphocephaly is due to the intrinsic growth of the brain structures, not the skull deformity. A study by Wilk et al. (2011) in healthy individuals reported that the width of the third ventricle is larger in infants compared to adolescents. The present study reported similar results, where the width of the third ventricle in the control group was largest in infants and decreased with age (Table 4). In contrast to this, the third ventricle width was largest in patients within the oldest age group of scaphocephaly, possibly implying that

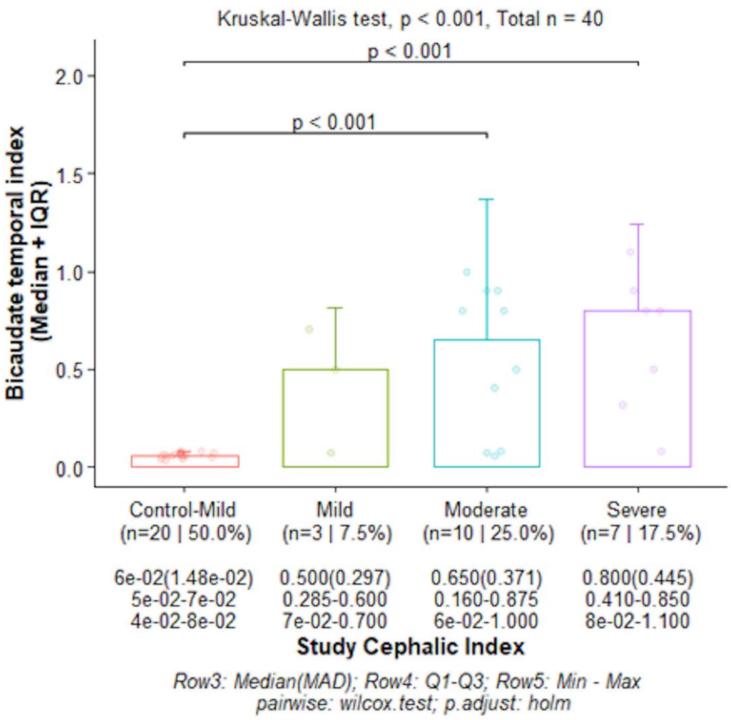

Fig. 10.- Post-hoc analysis of bicaudate temporal index in terms of the degree of severity in scaphocephaly compared to control patients.

the increase in ventricular volume is affected by the cranial deformity (Table 4). The third ventricle width was significantly larger in the severe scaphocephalic group compared to the control group, and the value increased with the degree of severity (Table 5) (Fig. 6).

The fourth ventricle width was found to be slightly larger in scaphocephaly patients compared to the control group (Table 2). This may be due to the restricted biparietal and bitemporal expansion, which results in compensatory growth in the occipital region, i.e., occipital protuberance and bossing, where the fourth ventricle is located (posterior cranial fossa). The present study illustrated that the fourth ventricle width increased with advancing age in scaphocephaly and normal individuals (Table 4). This is in accordance with what was previously reported in the literature, where a positive correlation between age and the width of the fourth ventricle was reported, and difference was statistically significant in healthy individuals (Patnaik et al., 2016; Jehangir et al., 2018). In relation to the degree of severity, the decrease in width from the mild to severe scaphocephaly groups may be due to the decrease in the transverse diameter of the skull in severe scaphocephaly, resulting in compression of the fourth ventricular space.

The fourth ventricle length is measured as the maximum A-P distance between the floor and the roof of the 4th ventricle (Gameraddin et al., 2015). In the present study, the length of the fourth ventricle was found to be shorter in scaphocephaly compared to normal (Table 2). Aldridge et al. (2005) reported that a posteroinferior shift of the hindbrain structures caused a decrease in the distance between the central sulcus and the sylvian fissure, resulting in constriction of the fourth ventricle. The A-P distance of the fourth ventricle increased with age in both study groups (Table 6). This is in accordance with the findings of Patnaik et al. (2016), who reported a weak positive correlation with age. In the current study, the fourth ventricle length was highest in the severe group of scaphocephaly, but still smaller than the control group.

The Evans index was significantly larger in scaphocephaly compared to the control group (Table 6). These results correlate with studies conducted by Usami et al. (2016) and Lu et al.

(2024), who demonstrated that the Evans index in scaphocephaly ranges from 0.25 to 0.30, indicating mild ventriculomegaly. The control group had a mean value of 0.25, similar to what has been reported in the literature (Sari et al., 2015; Jehangir et al., 2018; Kolsur et al., 2018; Dhok et al., 2020). The current study did not illustrate significant differences between males and females, corroborating the findings of Arusa et al. (2022) and Dhok et al. (2020). Regarding comparison by age, there were no significant differences in the age groups in the control and scaphocephaly groups; however, the ratio increased with advancing age (Table 8), supporting the findings of Jehangir et al. (2018) and Kolsur et al. (2018). In relation to the degree of severity, the Evans index was found to be significantly different in the severe scaphocephaly group; the ratio increased from mild to severe group (Table 9) (Fig. 7). Usami et al. (2016) reported that the Evans index ratio is directly proportional to the degree of severity of scaphocephaly, thus corroborating this finding.

The bifrontal index is the ratio of the maximum distance between the frontal horns of the bilateral lateral ventricles divided by the maximum internal diameter of the frontal bone. In the literature, it is reported that a value below 0.40 is considered normal, whilst a value above 0.50 indicates possible hydrocephaly (Wilk et al., 2011). This study reports a value of 0.33 in scaphocephaly, which is within the normal range of the bifrontal index. However, the value was significantly increased when compared to the normal patients (Table 6). This study reported the value to be higher in females than in males in both groups. These findings differed from those of Kolsur et al. (2018), who investigated the bifrontal index in normal populations and reported higher values in males than in females. The present study showed that the ratio increased with advancing age in the scaphocephaly group, but the difference was non-significant in consecutive age groups. However, in the control group, the ratio decreased as the age increased and was constant in 1-2 years; 3 years and 6+ years age group (Table 8). This is not in accordance with the study conducted by Kolsur et al. (2018), who found a positive correlation between the bifrontal index and age in healthy individuals. In relation to the cephalic index, the bifrontal index was significantly larger in the severe scaphocephalic group compared to the control group (Table 9) (Fig. 8). In severe cases of scaphocephaly, there is a decrease in the transverse diameter and an increase in the anteroposterior diameter, which ultimately leads to excessive growth in the structures found in the anterior aspect of the brain, such as the frontal horns of the lateral ventricle resulting in an increase in the bifrontal distance (Liu et al 2024).

The bicaudate index is defined as the ratio of the maximum distance between the bilateral lateral ventricles at the level of the head of the caudate nucleus to the maximum distance of the inner skull table at the same level (Arusa et al., 2022). The bicaudate index is an essential parameter to evaluate the ventricular volume and assessment of hydrocephalus (Dhok et al., 2020). In the current study, the bicaudate index was found to be significantly larger in scaphocephaly patients compared to the control group (Table 6). The mean value for the control group was similar to that reported by Dhok et al. (2020) in infants to adolescents, while a study by Arasu et al. (2022) reported a higher value compared to our findings. This study reported a higher value in females compared to males in both the scaphocephaly group and the unaffected individuals, while other studies found the value to be larger in males than in females; however, the difference was not statistically significant (Dhok et al., 2020; Arusa et al., 2022). According to Wilk et al. (2011), the bicaudate index decreased with age in normal subjects. However, in the scaphocephaly group, there was no trend found among the age groups (Table 8). The bicaudate index was found to be significantly larger in the severe group compared to the control group. This can be attributed to the decrease in the cephalic index in severe cases of scaphocephaly due to restricted transverse growth of the biparietal and bitemporal regions, allowing abnormal or excessive growth of the frontal region (frontal bossing) (Table 9) (Fig. 9).

The bicaudate temporal index is defined as the ratio of the minimum distance between the bicaudate nuclei to the maximum distance of the inner table of the skull (Wilk et al., 2011). The current study found the ratio to be significantly larger in scaphocephaly compared to the control group (Table 6). This may be due to the decrease in biparietal and bitemporal distances in scaphocephaly. Results for the control group were consistent with that reported in previous literature (Wilk et al., 2011; Kolsur et al., 2018). There was no significant difference among the age groups; however, the ratio decreased with the advancing age in both the control and the affected groups (Table 8). This is in accordance with the findings of Wilk et al. (2011). Meanwhile, Arasu et al. (2022) reported that the ratio increased as the age increased in unaffected individuals. Regarding severity, the ratio was reported to be significantly larger in the severe and moderate scaphocephalic groups compared to the control group, and the value increased as the degree of severity progressed from mild to severe (Table 9) (Fig. 10).

The Huckman number is defined as the sum of the maximum distance between the frontal horns of the lateral ventricles and the minimum bicaudate nuclei distance, and it is a useful parameter to evaluate the frontal horn width of the lateral ventricle diameter (Kolsur et al., 2018; Arusa et al., 2022). Literature reports that the Huckman number value in normal individuals ranges from 3 cm to 5 cm; a value greater than 5 cm indicates possible hydrocephalus (Wilk et al., 2011). In this study, the Huckman number was similar in the scaphocephaly and control groups (Table 2). However, when compared in relation to the degree of severity, the value was highest in the severe scaphocephaly group with a value of 4.10 cm. This indicates that mild ventriculomegaly is associated with scaphocephaly and can lead to hydrocephaly, especially in severe cases of scaphocephaly if the condition remains untreated and not monitored.

Various mechanisms have been suggested in the literature to explain the enlargement of the cerebral spaces, including abnormal skull shape as well as malabsorption of CSF (Usami et al., 2016). CSF absorption primarily occurs at the arachnoid villi (AV), which are located inferior to the superior sagittal sinus (SSS). The abnormal skull can cause compression to the SSS and AV, altering with CSF dynamics and result in enlarged ventricles. AV is considered immature in infancy thus limiting CSF absorption. The notable decrease in values with age such as the third ventricle width, bicaudate index, and bicaudate temporal index in the control cohort agrees with this theory. Meanwhile, in scaphocephaly the values increased with age, with children over six years exhibiting approximately double the bicaudate temporal index (0.80) compared to younger age groups (0.36).

The findings of the present study indicate that the ventricular system in scaphocephaly exhibits a significant variation from the normative anatomy. The AP expansion of the lateral ventricles, indicated by an increase in frontal horn length, corroborates previous findings by Aldridge et al. (2002) of the AP elongation in cortical and subcortical structures. Furthermore, mediolateral expansion of the frontal horns, illustrated by the elevated bifrontal index values, is consistent with the frontal bossing observed in scaphocephaly. Collectively, these findings support the concept that ventricular dilatation in scaphocephaly is associated with the cranial dysmorphia in scaphocephaly and subsequently results in cerebral and ventricular alteration.

Despite advancements in imaging technology, neuroradiologists and neurosurgeons continue to face diagnostic challenges in rare congenital craniofacial conditions like craniosynostosis (Baruah et al., 2020; Arusa et al., 2022). A thorough understanding of the anatomical changes in the skull and brain is crucial for surgeons to make accurate diagnoses and plan appropriate surgical interventions. Three-dimensional (3D) printing has emerged as a valuable tool in the study of the craniosynostoses, including scaphocephaly, offering a novel approach to understanding these changes (Schlund et al., 2024). Three-dimensional models are increasingly used in medical education and surgical training, enhancing long-term retention and improving understanding of craniofacial abnormalities (Al-Badri et al., 2022; Schlund et al., 2024). A recent study by Schlund et al. (2024) highlighted a positive correlation between the visuospatial abilities of medical students and their ability to recognize complex cranial disorders using 3D printed models of craniosynostotic skulls. The use of 3D printed models provides a more interactive approach to studying the anatomical changes in craniosynostosis, thus aiding clinicians in better visualizing the impact of cranial deformities on the ventricular system.

One of the primary limitations of this study was the small sample size in both scaphocephaly and control groups. The second limitation was the lack of age- and sex-matched control patients.

Further recommendations include the use of a larger sample size for both the scaphocephaly and control groups. Additionally, future studies should include pre- and post-operative CT scans to evaluate the effectiveness of corrective surgery on the ventricular system in scaphocephaly. Future studies may also incorporate 3D printing to aid in visualizing the relationship between scaphocephaly and its associated ventricular changes.

CONCLUSION

This study provides a morphometric analysis of the ventricular system and the changes that occur in the ventricles in patients with scaphocephaly. The results show that the cerebral ventricles are significantly larger in scaphocephaly when compared to the control group. The AP and mediolateral enlargement occur within the anterior aspect of the ventricular system (anterior horns of lateral ventricles), whilst AP constriction is observed in posterior aspect (fourth ventricle). The ventricular anatomy is also influenced by age, sex and severity of deformity. The present study reveals that the linear indices are greater in scaphocephaly patients within the older age groups, which is the opposite in non-affected individuals. Sex-related variations in linear dimensions are constant across scaphocephaly and unaffected patients, with males having higher values than females. The linear indices are in direct proportion with the degree of severity. In severe cases, the ventricles are excessively increased, indicating presence of ventriculomegaly. As such, intracranial pressure must be closely monitored, and corrective surgery should be considered as essential as in complex craniosynostosis cases. The findings of this study will aid neurosurgeons in better understanding the morphometric changes that occur in the ventricular system in scaphocephaly. This may assist in the early and accurate diagnosis of hydrocephalus that may occur due to the increased intracranial pressure in scaphocephaly, thereby enabling a more timely and effective treatment.

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AUTHORS' CONTRIBUTION

Angel Thandokuhle Cele: Project planning and development, data collection, data analysis, manuscript writing and editing. Vensuya Bisetty: Project planning and development, data collection, data analysis, manuscript writing and editing. Anil Madaree: Project planning and development, data collection. Rohen Harrichandparsad: Project planning and development, data collection. Indheresan Govindsamy Moodley: Project planning and development, data collection. Lelika Lazarus: Project planning and development, data collection, manuscript editing and supervision.

Ethical approval

Ethical clearance was obtained from the Biomedical Research Ethics Committee (BREC) of the University of KwaZulu-Natal (BREC/00004833/2022).

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