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Original Article

Anatomy Section

Ultrasonographic Nomograms of Foetal Fourth Ventricle Biometry and its Correlation with Transcerebellar Diameter and Gestational Age among Normal Foetuses: A Cross-sectional Study

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ABSTRACT

Introduction: The foetal fourth ventricle marks an important landmark for evaluating the development of the posterior fossa. Prenatal diagnosis of midbrain and hindbrain abnormalities is based on aberrant cerebellum and retrocerebellar space size and shape, with the most prevalent sign being an 'open fourth ventricle'.

Aim: To present the normal range of measurements of the foetal fourth ventricle and correlate the fourth ventricle biometry with Transcerebellar Diameter (TCD) and Gestational Age (GA) in normal foetuses.

Materials and Methods: This cross-sectional study included 260 pregnant women with low-risk pregnancies between 19 and 35 weeks of gestation, with the known Last Menstrual Period (LMP) confirmed by first trimester ultrasonography. The foetal heads were scanned in the axial plane. The TCD and fourth ventricle anteroposterior and transverse diameters were obtained ultrasonographically from the pregnant women who were recruited to the Department of Radiology, Rajarajeswari Medical College and Hospital, Bengaluru, India, between January 2021 and December 2023. The routine foetal biometric parameters, such as Biparietal Diameter (BPD), Head Circumference (HC), Abdominal Circumference (AC), and Estimated Foetal Birth Weight (EFBW), were also recorded. Pearson correlation coefficients were calculated to examine the strength of the linear relationship between each of the fourth ventricle parameters, GA, and TCD. Regression analysis was performed to determine the equation of the linear fitted function with each of the independent variables (GA, TCD). All statistical analyses were performed using Statistical Package for Social Sciences (SPSS) software, Version 22.0 (IBM, Armonk, New York).

Results: The mean and Standard Deviation (SD) of the fourth ventricle anteroposterior and transverse diameters are 2.122 mm (SD=0.309) and 5.648 mm (SD=1.975), respectively. The Pearson correlation coefficients of the fourth ventricle anteroposterior diameter for GA and TCD were r=0.917 and r=0.931, respectively. The coefficients of the fourth ventricle transverse diameter for GA and TCD were r=0.869 and r=0.884, respectively ($p<0.001$). The regression equations were plotted between GA and fourth ventricle anteroposterior diameter (r=0.917; $p<0.001$; y=0.406+(0.0716×GA (weeks) and transverse diameter (r=0.869; $p<0.001$; y=-4.753+(0.434×GA in weeks. A linear regression line was also plotted between TCD and fourth ventricle anteroposterior diameter (r=0.931; $p<0.001$; y=0.783+(0.0511×TCD (mm) and transverse diameter (r=0.884; $p<0.001$; y=-2.483+(0.310×TCD in mm.

Conclusion: The study established normal foetal fourth ventricle measurements and found strong correlations between GA and TCD. These results support their use as reliable markers of normal foetal brain development.

Keywords: Foetal biometry, First trimester, Malformations, Ultrasound

INTRODUCTION

The fourth ventricle is a fluid-filled canal that separates the brainstem and cerebellum. It extends from the aqueduct of sylvius to the foramen of magendie. The cerebellar peduncles form the lateral walls, giving it a "tent-like" shape. The cerebellar peduncles, medullary velum, and cerebellar nodules form the roof, while the dorsal surface of the pons and medulla oblongata forms the floor. The posterior superior recesses refer to the fourth ventricle's posterolateral expansions. The fourth ventricle develops from the rhombencephalon, which is the most caudal primary vesicle formed after the fusion of the neural fold and closure of the neuropore [1].

Recently, significant progress has been made in the understanding of supratentorial malformations and brain development [2]. However, the Posterior Cranial Fossa (PCF) has received relatively less attention, particularly the foetal fourth ventricle, which is a crucial landmark for assessing the development of the posterior fossa [3]. Recent advances in foetal imaging have enabled a more precise approach to the prenatal diagnosis of midbrain-hindbrain abnormalities. A reliable diagnosis requires the presence of visible symptoms of disease, such as a small TCD or an expanded posterior fossa, during routine examination. Diagnosis is frequently determined by a focused examination of the foetal brain using neurosonography or brain Magnetic Resonance Imaging (MRI) [4]. Rapid acquisition MRI allows for the evaluation of the foetal fourth ventricle as early as the late second trimester of pregnancy. Direct assessment of the fourth ventricle in the foetus during gestation is more indicative of normal development, particularly in mid sagittal MRI scans [5].

Although the anatomy of the fourth ventricle is not part of the routine assessment, an open fourth ventricle is a sonographic sign found during the second trimester, in which fourth ventricle (4V) funnels into the Cisterna Magna (CM) [6]. An open fourth ventricle is the most prevalent sign of midbrain and hindbrain abnormalities, and it indicates dysgenesis, agenesis, or upward displacement and rotation of the cerebellar vermis. These observations may be found temporarily in up to 10% of normal foetuses between 15 and

18 weeks [7]. Although both foetal MRI and ultrasonography can be used to estimate the fourth ventricle, only a few previous studies have focused on defining typical foetal biometric data of the fourth ventricle [8-10]. The fourth ventricle plays a pivotal role in prenatal diagnosis, especially anomalies affecting various Central Nervous Systems (CNS) [11-13]. Studying the normal appearance of the foetal fourth ventricle can aid in recognising prenatal posterior fossa abnormalities, as the size and shape of the ventricle typically alter early [6]. The well-known five axial planes of the brain can be used to detect the majority of prenatal brain abnormalities [14]. Relatively, the literature has very little information on the ultrasonographic features of the foetal fourth ventricle during gestation.

Thus, the goal of the study is to establish ultrasonographic nomograms of foetal fourth ventricle anteroposterior and transverse diameters between 18-35 weeks of gestation and correlate its dimensions (AP and Transverse) with GA, TCD, and also BPD. This information can also provide a basis for future investigations for normative data to assess aberrations in foetal fourth ventricle growth. The need for this study arises because, in India, a developing country with a large population, many women visit the hospital for the first time even during the third trimester and often do not recall their LMP accurately. As a result, estimating the foetus's GA becomes challenging. While there are numerous studies on this topic, few focus specifically on India, and many existing studies concentrate on only a specific trimester rather than covering the full range of the second and third trimesters [8,15-18]. Like all studies utilising diagnostic techniques, the TCD has limitations, even though it is a reliable predictor of GA [19-25]. Foetal growth patterns vary across populations due to genetic, nutritional, and environmental factors; the rate of cerebellar growth slows in late gestation, which may reduce the sensitivity of TCD in detecting small variations in GA. Poor foetal position, maternal obesity, or limited acoustic windows can lead to inaccurate measurements, and anomalies affecting the posterior fossa may artificially increase TCD measurements, leading to an overestimation of GA [26-28]. By considering the clinical background, understanding foetal growth patterns, and following the appropriate procedure, efforts were made to mitigate such challenges, and the accuracy of calculating GA was enhanced with the imaging department and clinical expertise.

MATERIALS AND METHODS

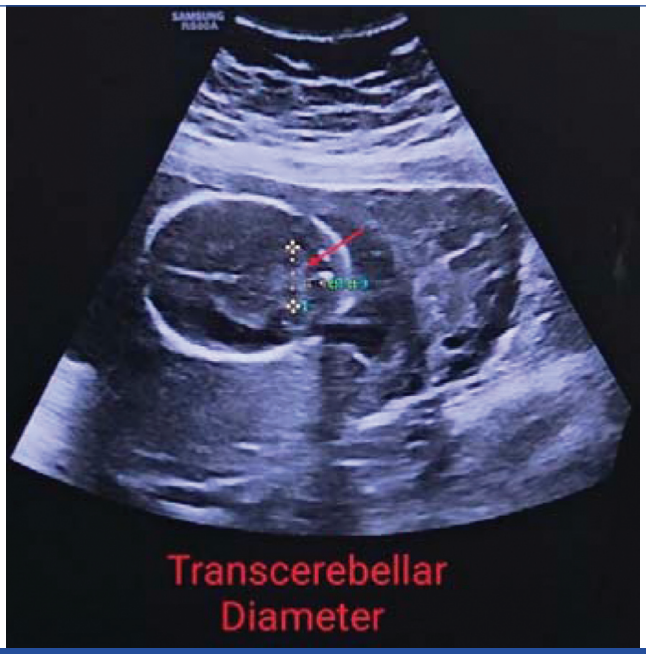
A cross-sectional study was carried out with 260 pregnant women seeking ultrasound for antenatal care between 19 and 35 weeks' gestation of singleton low-risk pregnancies from January 2021 to December 2023 at Rajarajeswari Medical College and Hospital, Bangalore, Karnataka, India after obtaining the approval of the Rajarajeswari Medical College institutional ethical committee (Approval number RRMCH-IEC/178/2019-20). Informed consent was taken from the prospective mothers explaining the study details in compliance with ethical standards and confidentiality.

Inclusion and Exclusion criteria: Pregnant women with a known GA based on the last menstrual cycle, confirmed by first trimester ultrasonography, with estimated foetal weight and BPD measurements within the normal range for GA, were included in the study. Pregnancies with maternal diseases such as diabetes, Pregnancy-Induced Hypertension (PIH)/pre-eclampsia, foetal chromosomal and structural anomalies, and growth-retarded foetuses were excluded from the study.

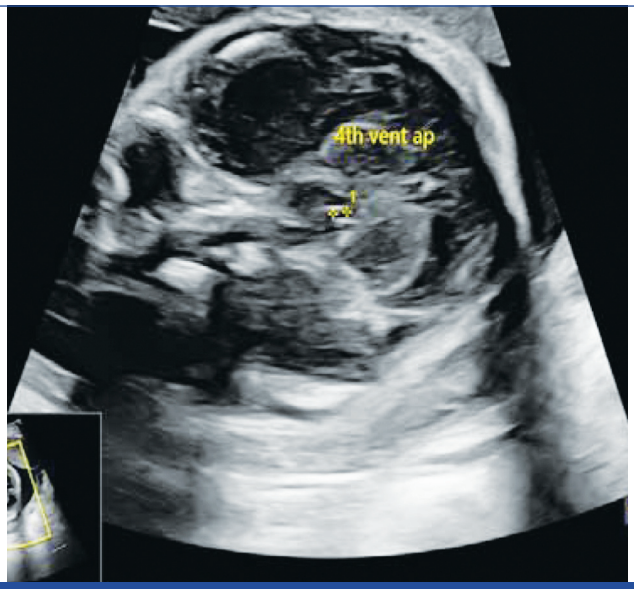
Sample size calculation: The sample size was estimated for a minimum correlation coefficient of 0.3 (positive or negative) among the dependent variables, with 90% power and a 1% significance level [29]. The correlation coefficient of 0.3 was selected as a moderate effect size based on Cohen's conventional criteria, supported by existing literature and representing a conservative and scientifically reasonable estimate for detecting associations in observational data. The estimated sample size was 222. Adding a 15% dropout rate, the sample size was rounded to 260. Sigma Plot 14.5 version (Systat Software Inc., San Jose, USA) was used for the sample size calculation [30].

Study Procedure

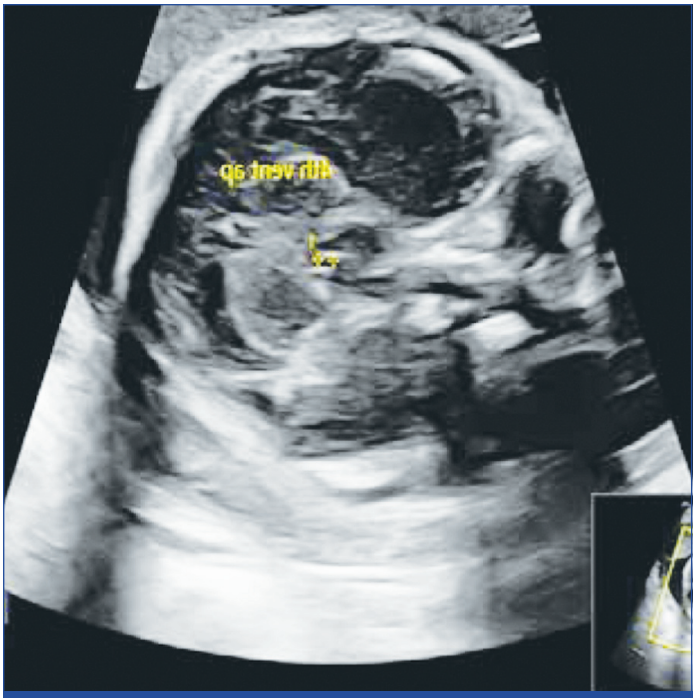
All measurements were taken by a single operator in axial planes. The 4V was depicted in the axial plane (caudal to the classic transcerebellar plane), where it appeared as a quadrangular anechoic space, and its largest diameters were visualised. The anteroposterior diameter was smaller than the maximum transverse diameter, as described previously by Baumeister LA et al., [8]. To measure the TCD, the transducer was rotated in the axial plane centred on the thalamus in the occipito-bregmatic view, and the widest diameter of the cerebellum was measured. Other routine biometric parameters, including HC, AC, femoral length, and EFBW, were also obtained to rule out intrauterine growth-retarded foetuses. The TCD [Table/Fig-1], fourth ventricle anteroposterior [Table/Fig-2], transverse diameter [Table/Fig-3], and BPD [Table/Fig-4] of the foetus were measured using the electronic callipers of Samsung RS80A and Siemens Juniper Acuson ultrasonography machines equipped with 1.5 MHz transabdominal transducers. Special focus was made on the PCF of the foetal brain to identify and measure the fourth ventricle and TCD.



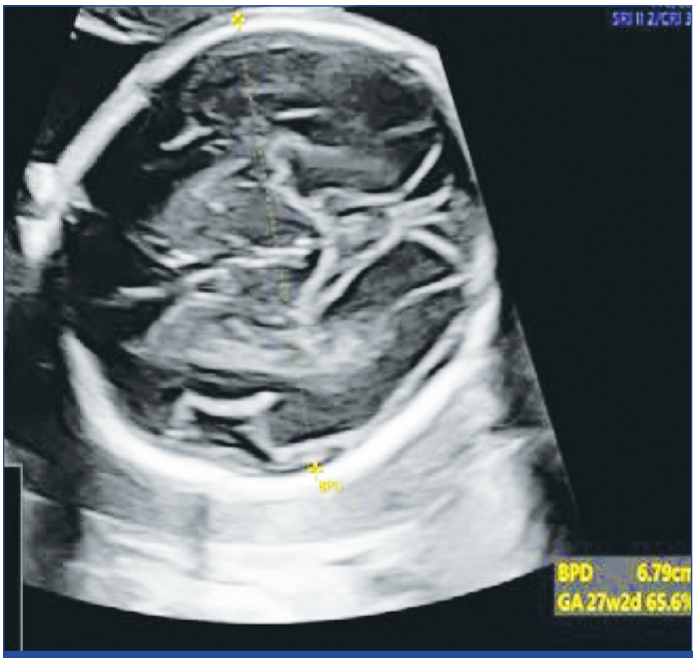
[Table/Fig-1]: 2D image in 27-week foetus showing the projection (arrow) of trans cerebellar diameter in axial plane.



[Table/Fig-2]: 2D image in 27-week foetus showing the projection (arrow) of fourth ventricle anteroposterior in axial plane.



[Table/Fig-3]: 2D image in 27-week foetus showing the projection (arrow) fourth ventricle transverse diameter in axial plane.



[Table/Fig-4]: 2D Image showing the Biparietal Diameter (BPD) in axial plane at 27 week gestation.

STATISTICAL ANALYSIS

All statistical analyses were performed using SPSS software, Version 22.0 (IBM, Armonk, New York). Means and standard deviations for the TCD, BPD, and the transverse and anteroposterior diameters of the fourth ventricle were also calculated. For each parameter of the fourth ventricle, regression analysis was conducted with the fourth ventricle's dimensions as the dependent variable (y) and GA, TCD, and BPD as independent variables. Percentile values for the transverse and anteroposterior diameters of the fourth ventricle, as well as the TCD, were determined for each GA group. The level of significance for statistical tests was considered at 1% ($p<0.01$).

RESULTS

A total of 260 foetuses between 19 and 35 weeks of gestation were scanned. The mean and standard deviation for the fourth ventricle's Anteroposterior (AP) diameter were 2.122 mm (SD=0.309), and for the transverse diameter, 5.648 mm (SD=1.975) [Table/Fig-5].

Parameters	Mean	SD
Gestational Age (GA) (weeks)	23.98	3.957
Transcerebellar Diameter (TCD) (mm)	26.2	5.627
Biparietal Diameter (BPD) (mm)	58.52	11.42
Fourth ventricle anteroposterior diameter (mm)	2.122	0.309
Fourth ventricle transverse diameter (mm)	5.648	1.975

[Table/Fig-5]: Descriptive data.

Pearson correlation coefficients for the fourth ventricle's anteroposterior diameter with GA, TCD, and BPD were r=0.917 ($p<0.001$), r=0.931 ($p<0.001$), and r=0.896 ($p<0.001$), respectively [Table/Fig-6]. For the transverse diameter, Pearson correlation coefficients with GA, TCD, and BPD were r=0.869 ($p<0.001$), r=0.884 ($p<0.001$), and r=0.865 ($p<0.001$) [Table/Fig-7].

Parameters compared	Correlation		Regression (y)	Regression coefficient (R2)
	r value	p-value		
4th ventricle AP diameter Vs GA	0.917	0.001	0.406+(0.0716 * GA)	0.840
4th ventricle AP diameter Vs TCD	0.931	0.001	0.783+(0.0511 * TCD)	0.867
4th ventricle AP diameter Vs BPD	0.896	0.001	0.705+(0.0242 * BPD)	0.802

[Table/Fig-6]: Showing correlation and regression of 4th ventricle AP diameter with GA, TCD, BPD.

Parameters compared	Correlation		Regression (y)	Regression coefficient (R2)
	r value	p-value		
4th ventricle Transverse diameter Vs GA	0.869	0.001	-4.753+(0.434 * GA)	0.755
4th ventricle Transverse diameter Vs TCD	0.884	0.001	-2.483+(0.310 * TCD)	0.782
4th ventricle Transverse diameter Vs BPD	0.865	0.001	-3.042+(0.149 * BPD)	0.748

[Table/Fig-7]: Showing correlation and regression of 4th ventricle transverse diameter with GA, TCD, BPD.

A significant, strong positive correlation ($p<0.001$) was observed between both the anteroposterior and transverse diameters of the fourth ventricle with GA, TCD, and BPD. [Table/Fig-8] presents nomograms for the fourth ventricle's anteroposterior and transverse diameters, including percentiles, means, and standard deviations for each GA.

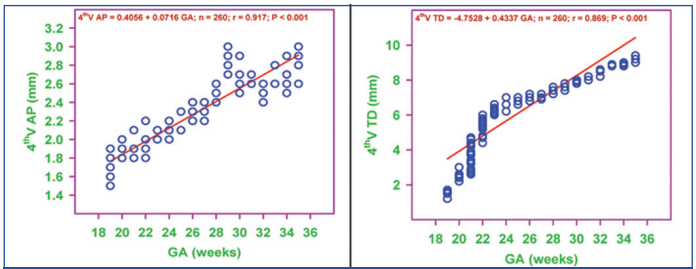
Linear regression equations were derived for the relationship between GA and the fourth ventricle's anteroposterior diameter ($y=0.406+0.0716\times GA$) and transverse diameter ($y=-4.753+0.434\times GA$) [Table/Fig-9]. Similarly, linear regression equations for the relationship between TCD and the fourth ventricle's anteroposterior diameter ($y=0.783+0.0511\times TCD$) and transverse diameter ($y=-2.483+0.310\times TCD$) were established [Table/Fig-10]. For BPD, the linear regression equations for the fourth ventricle's anteroposterior diameter ($y=0.705+0.0242\times BPD$) and transverse diameter ($y=-3.042+0.149\times BPD$) were determined [Table/Fig-11]. These analyses indicate a gradual increase in the diameters of the fourth ventricle with advancing GA, suggesting that fourth ventricle biometry can serve as a reliable factor in estimating GA.

DISCUSSION

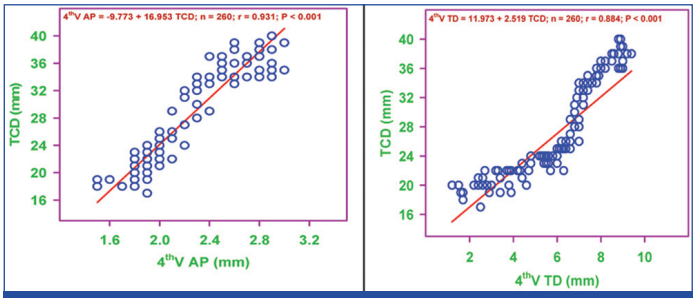
The standard second-trimester foetal ultrasound includes an axial view of the brain in the transcerebellar plane, essential for evaluating the PCF structures. Measurements of the TCD and CM aid in assessing these structures, as outlined in internationally recognised guidelines for basic foetal CNS evaluation [31,32]. Identifying the foetal fourth ventricle is crucial for diagnosing anomalies in the posterior fossa,

Gestational Age (GA)	n	AP diameter (mm)							Transverse diameter (mm)						
		Percentile					Mean	SD	Percentile					Mean	SD
		10	25	50	75	90			10	25	50	75	90		
19	8	1.5	1.5	1.7	1.9	1.9	0.175	0.062	1.2	1.2	1.6	1.7	1.7	0.220	0.078
20	28	1.9	1.8	1.9	1.9	2	0.072	0.014	2.2	2.4	2.4	2.6	2.6	0.181	0.034
21	46	1.8	1.8	1.9	1.9	1.9	0.071	0.011	3.1	3.4	3.8	4.2	4.4	1.642	0.242
22	38	1.9	1.9	1.9	2	2	0.081	0.013	4.8	5.3	5.5	5.7	5.8	0.347	0.056
23	42	2	2	2.1	2.1	2.1	0.049	0.008	6.2	6.3	6.4	6.6	6.6	0.165	0.025
24	10	2	2	2	2.1	2.2	0.084	0.027	6.2	6.6	6.6	6.6	6.9	0.189	0.060
25	16	2.1	2.3	2.3	2.3	2.3	0.068	0.017	6.6	6.8	6.8	6.8	7	0.115	0.029
26	20	2.2	2.2	2.3	2.4	2.4	0.085	0.019	6.8	6.8	6.8	7	7	0.121	0.027
27	9	2.2	2.2	2.3	2.4	2.4	0.078	0.026	6.9	6.9	7	7.2	7.2	0.124	0.041
28	5	2.4	2.4	2.6	2.6	2.6	0.089	0.040	7.2	7.3	7.4	7.5	7.6	0.141	0.063
29	7	2.7	2.8	2.9	2.9	3	0.098	0.037	7.4	7.6	7.8	7.8	7.8	0.157	0.060
30	7	2.5	2.5	2.6	2.7	2.9	0.140	0.053	7.8	7.8	7.9	8	8	0.100	0.038
31	3	2.6	2.6	2.7	2.7	2.7	0.058	0.033	8	8	8.2	8.2	8.2	0.115	0.067
32	5	2.4	2.4	2.5	2.6	2.6	0.084	0.037	8.2	8.2	8.5	8.5	8.6	0.187	0.084
33	3	2.6	2.6	2.8	2.8	2.8	0.115	0.067	8.8	8.8	8.8	8.9	8.9	0.058	0.033
34	8	2.5	2.5	2.5	2.8	2.9	0.177	0.063	8.8	8.8	8.9	8.9	9	0.076	0.027
35	5	2.6	2.7	2.9	2.9	3	0.152	0.068	9	9	9	9.3	9.4	0.179	0.080

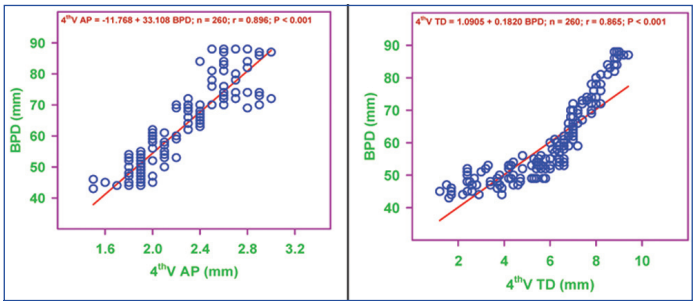
[Table/Fig-8]: Fourth ventricle anteroposterior and transverse diameter across the Gestational Age (GA).



[Table/Fig-9]: Showing relationship between Gestational Age (GA) and 4th ventricle anteroposterior diameter, transverse diameter.



[Table/Fig-10]: Showing relationship between Transcerebellar Diameter (TCD) and 4th ventricle anteroposterior diameter, transverse diameter.



[Table/Fig-11]: Showing relationship between Biparietal Diameter (BPD) and 4th ventricle anteroposterior diameter, transverse diameter.

such as cystic tumours, hydrocephalus, and conditions like Dandy-Walker malformation [33]. Ultrasonographically, the fourth ventricle is located in the midline, below the level of the thalami and anterior to the cerebellar hemispheres [34].

The foramen of Magendie serves as an outflow point in the lower part of the fourth ventricle. Any changes in the surrounding structures of the PCF can alter the height and angle of the fourth ventricle [12]. The fourth ventricle is thought to develop in close association with the development of surrounding structures, particularly the vermis, which is fully developed by 18 weeks of gestation.

Furthermore, the shape of the fourth ventricle can change as it may lose its usual morphological appearance when affected by certain disorders [35]. In general, increasing or decreasing the fourth ventricle's angle and height may suggest the presence of an anomaly in the posterior fossa [36]. Cystic malformations within the posterior fossa, such as Dandy-Walker malformation, Blake's pouch cyst, and posterior fossa arachnoid cyst, can cause changes in the shape of the fourth ventricle [6]. An enlarged fourth ventricle may represent a normal variant, as the caudal roof is not seen on ultrasonography until 16 weeks, creating a false appearance of communication between the fourth ventricle and the CM [37]. Some anomalies, such as Arnold-Chiari malformation, frequently decrease the height of the fourth ventricle. Pan H et al., discovered that the fourth ventricle's height increased significantly between 17 and 38 gestational weeks [5]. They found that the height and angle of the fourth ventricle increased linearly and corresponded with GA. The height of the fourth ventricle increased from 2 mm to 7 mm.

A statistically significant linear correlation ($p<0.001$) was observed between the anteroposterior and transverse diameters of the fourth ventricle with GA, as well as with the transcerebellar and BPDs. A linear regression line of the fourth ventricle parameters modelled as a function of GA, TCD, and BPD was observed.

The findings align with existing literature, particularly in terms of the relationship between the fourth ventricle's dimensions and GA [38-40]. However, differences in reported dimensions highlight the importance of standardising measurement techniques and considering the influence of imaging modalities. Baumeister LA et al., examined 310 second and third-trimester foetuses to define the normal appearance of the foetal fourth ventricle and ascertain its frequency of depiction at different GAs. Their study found that the fourth ventricle was seen in 221 of the 310 foetuses (71.3%) and was most consistently demonstrated in the middle of the second trimester. The mean anteroposterior dimension of the fourth ventricle was 3.5 mm ±1.3, and the mean width was 3.9 mm ±1.7 [8]. These values are notably larger than those observed in the current research. This discrepancy may be attributed to differences in GA ranges, measurement techniques, or population characteristics.

Goldstein I et al., developed ultrasonographic nomograms for the foetal fourth ventricle to aid in detecting abnormalities of the posterior fossa. Their study found a first-degree correlation between GA and the anteroposterior diameter of the fourth ventricle (r=0.894; p<0.0001), its width (r=0.657; p<0.0001), its circumference (r=0.843; p<0.0001), and its area (r=0.844; p<0.0001). The development of similar nomograms in the current research aligns with Goldstein I et al., approach, offering a valuable tool for clinical assessment. However, direct comparisons of specific measurements would require access to the detailed nomograms presented in their study [7].

Pan H et al., measured the normal foetal fourth ventricle biometry using MRI mid-sagittal images. Their study found that the fourth ventricle's height increased significantly between 17 and 38 gestational weeks. They found that the height and angle of the fourth ventricle increased linearly and corresponded with GA. The height of the fourth ventricle increased from 2 mm to 7 mm. The use of ultrasound for measurement in the current research may yield different results compared to MRI-based studies due to the inherent differences in imaging modalities. Direct comparisons would require matching specific GAs and measurement techniques [5].

The study by Goldstein I et al., also observed that isolated early fourth ventricle enlargement often normalises by 20 weeks, suggesting it may be a normal variant requiring follow-up rather than immediate intervention [7]. Therefore, the findings clearly indicate a gradual and consistent change in ultrasonographic appearances of the foetal anteroposterior and transverse diameters with increasing GA.

By developing reference ranges for the fourth ventricle's transverse and anteroposterior dimensions between 19 and 35 weeks of gestation, the findings are essential for improving prenatal treatment. This research not only provides grounds for accurate foetal monitoring but also serves as a stepping stone for future research on the developmental pathway of the fourth ventricle and its role in foetal neurological well-being. The results provide normative data for the growth of the foetal fourth ventricle throughout gestation, demonstrating a linear growth function of first-degree correlation.

Limitation(s)

Reflecting on the present study, several limitations should be considered. As a cross-sectional study, it does not track changes within the same foetus over time. Conducted at a single centre in Bengaluru, the findings may not be applicable to other populations with different genetic, nutritional, or environmental factors. All imaging interpretations were made by a single expert, which could introduce bias. The study relied solely on ultrasound, which is less accurate than MRI for assessing detailed brain structures. Additionally, the study focused on foetuses between 19 and 35 weeks, limiting its applicability to other gestational periods. Factors such as maternal obesity and foetal position may have influenced measurements, though they were not fully accounted for.

CONCLUSION(S)

Ultrasonographic measurements of the foetal fourth ventricle, TCD, and BPD demonstrate a strong correlation with advancing GA and other routinely assessed biometric parameters. These findings establish normative reference ranges for the transverse and anteroposterior diameters of the fourth ventricle between 19 and 35 weeks of gestation, which are instrumental in developing future nomograms for the fourth ventricle. Future research should focus on validating these ultrasound-derived nomograms by comparing them with MRI-based measurements across a broader GA spectrum, including the first and second trimesters. Additionally, incorporating a more diverse sample population can enhance the generalisability of the findings. Longitudinal studies examining the correlation between fourth ventricle dimensions and neurodevelopmental outcomes could provide valuable insights into the clinical significance of these measurements. By addressing these aspects, future research can refine the utility of fourth ventricle biometry in prenatal diagnostics.

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