

## Normal Values of Third Ventricular Width of Preterm Infants

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### ABSTRACT

**Objectives:** Although the third ventricle width reference ranges obtained by cranial ultrasonography in term infants are known in the literature. There is no adequate up-to-date data regarding the reference ranges of third ventricle width in premature infants. In our study, we aimed to obtain the normal reference values of third ventricle width and the third ventricle related parameters in preterm infants (gestational age [GA]<38 weeks).

**Materials and Methods:** In our study 156 early preterm infants (GA<32 weeks) and 64 moderately-late preterm infants (GA≥32 and <38weeks) were included. Weights and head circumference of all infants were measured before cranial ultrasonography (C-US). The right and left lateral ventricle anterior horn width (AHW), ventricular index (VI) and third ventricle width were recorded through C-US. Study data was divided into 2 groups as early preterm infants and moderately-late preterm infants.

**Results:** Third ventricle was successfully measured in all preterm infants. While the frequency of cesarean section operations was significantly higher, weights and head circumferences were significantly lower ( $p<0.05$ ) in early preterm infants. R-AHW, L-AHW, R-VI, L-VI values were significantly higher in moderately-late preterm infants compared to early preterm infants ( $p<0.05$ ). Mean±SD, median, minimum and maximum third ventricle diameters in early preterm infants were  $1.27\pm 0.33$ mm, 1.20mm, 0.50mm and 1.90mm respectively. Through univariate analysis, GA, R-AHW, L-AHW, R-VI, L-VI values were found to have an association with third ventricle diameters. Linear regression analysis revealed that only GA and R-AHW were independently associated with third ventricle (beta: 0.611,  $p<0.001$  and beta: 0.141,  $p=0.011$ , respectively).

**Conclusion:** The third ventricle width obtained through C-US is significantly lower in early preterm infants than in moderately late term infants and is independently associated with GA values. The results of our study are critical to the identification of third ventricle dilation in preterm infants in a clinical environment.

**Key words:** Third ventricle width, cranial ultrasonography, gestational age

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### INTRODUCTION

Premature births encapsulate 11.1% of all births worldwide [1]. Developed intensive care conditions and treatment protocols increase survival; however premature infants face many complications. Periventricular / intraventricular hemorrhage is a common complication that causes brain damage

in premature infants [2]. This situation is seen in 25-30% of very low birth weight preterm infants (<1500 gr) and the incidence reported in extremely low birth weight preterm infants (<1000 gr) increases up to 45% [3].

Cranial ultrasonography (C-US) is the most preferred

method in the early evaluation of the cerebral parenchyma and ventricular system; it is easy and fast to access, cheap and widespread use, non-invasive, and lack of radiation. C-US is a reliable method in the evaluation of congenital or acquired intracranial pathologies in premature and term infants [4]. Because premature infants are very sensitive to hydrocephalus due to intraventricular hemorrhage, it is important to measure ventricular width by C-US to diagnose hydrocephalus, to evaluate the necessity of intervention and to evaluate clinical symptoms due to intracranial pressure increase [5]. Therefore, it is very important to determine the normal reference values of the ventricular system and to follow the ventricular system width.

There are many data on the normal reference value of the third ventricle obtained by C-US in term infants and 1.6 to 2.6 mm is accepted as the normal reference range [5-7]. However, in the literature, to the best of our knowledge there is limited data about the third ventricle width reference intervals in premature infants [7].

In this study, we aimed to investigate the normal reference values of third ventricle width in preterm infants and to determine the parameters associated with third ventricle.

## MATERIALS and METHODS

The study included 156 early preterm infants (GA <32 weeks) and 64 moderately-late preterm infants (GA  $\geq$  32 and < 38 weeks) in the neonatal intensive care unit. C-US examinations were performed on the 7-10th days in premature infants with a portable US device. The patients without intracranial pathology were included in the study. Infants with unknown gestational age, central nervous system anomalies, perinatal asphyxia, intrauterine infection, seizures, intracranial and intraventricular hemorrhage were not included in the study. This study was followed by the recommendations of the ethical principles published in the Declaration of Helsinki, developed by the World Medical Association (WMA), and study protocol was reviewed and approved by Ethical Committee of Adana Health Practice and Research Center (Decision date and number: 04/07/2018 and 215). Informed consents were obtained from the parents. Demographic data were recorded. Weight and head circumference of all cases were measured. All preterm infants underwent C-US scan by using high-resolution US device Aloka Noble (Hitachi Aloka Noble, Hitachi Health Care Americas,

Twinsburg, Ohio, USA) and 9-2 MHz sector probe. C-US examination was performed in the neonatal intensive care unit at the bedside while the infant was in the supine position. Anterior fontanel was used as an acoustic window for gray-scale B-mode examination and frozen images. Right and left ventricular index (R-VI and L-VI) evaluations were made by measuring the distance between the lateral wall of the lateral ventricle anterior horn and falx at the level of foramen Monroe in the coronal plane. The right and left anterior horn width (R-AHW and L-AHW) evaluation was performed by measuring the widest distance between the medial and lateral walls of the lateral ventricle anterior horn in the coronal plane. The width of the third ventricle was measured at the thalamus level in the coronal plane (Figure 1). All C-US examinations were performed by the same radiologist who has more than 5 years of experience in C-US studies and performs at least 500 C-US per year.

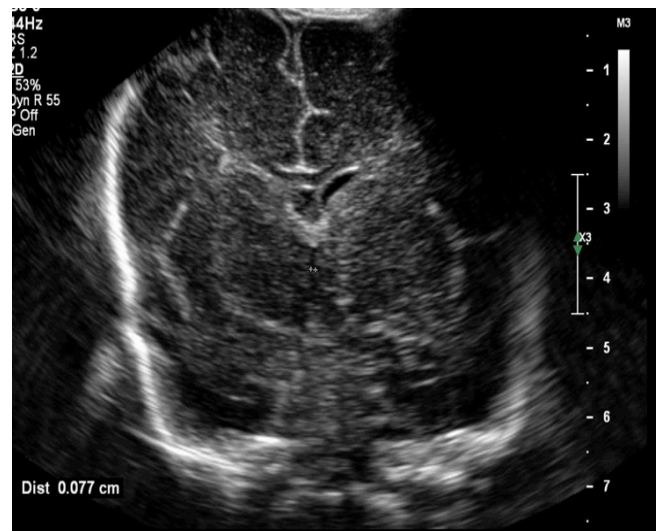


Figure 1: In 27-week early preterm infant's third ventricle was measured 0.77mm

All analyzes were performed using SPSS 22,0 (Chicago, IL, USA) statistical software package. Whether the distribution of continuous variables was normal was assessed by Kolmogorov-Smirnov test. Continuous variables in-group data were expressed as mean  $\pm$  standard deviation. Categorical variables were indicated by numbers and percentages. Student- t test was used to compare continuous variables between groups. In the comparison of categorical variables, "chi-square ( $\chi^2$ )" test was used. Parameters associated with the third ventricular width were determined with univariate Pearson's

and Spearman's correlation analyses. Statistically significant parameters were included in a linear regression analysis, and the parameters having the closest association with the third ventricular width were identified.  $P < 0.05$  was considered statistically significant.

## RESULTS

Third ventricle measurements were successfully obtained from all preterm infants. Study data were divided into 2 groups as early preterm infants and moderately-late preterm infants. The number of early preterm infants of 22, 23, 25, 26, 27, 28, 29, 30 and 31 gestational weeks were 2, 2, 10, 14, 18, 24, 32, 30 and 22, respectively. The number of moderately-late preterm infants of 32, 33, 34, 35, 36 and 37

weeks were 6, 6, 14, 14, 8 and 18, respectively.

Gestational age of moderately-late preterm infants was significantly higher compared to early preterm infants ( $36.1 \pm 1.57$  vs.  $29.4 \pm 2.1$ ,  $p < 0.001$ ); genders were similar in both groups (female/male 40/24 vs 88/68,  $p=0.249$ ). The frequency of caesarean section was significantly higher in early preterm infants (91% vs. 53.1%,  $p < 0.001$ ), while weight and head circumference were significantly lower ( $1.411 \pm 0.360$  kg vs.  $2.757 \pm 0.510$  kg,  $p < 0.001$  and  $27.2 \pm 1.51$  mm vs.  $34.6 \pm 1.56$  mm,  $p < 0.001$ , respectively).

Width of the third ventricle and R-AHW, L-AHW, R-VI, L-VI were significantly higher in moderately-late preterm infants than in early preterm infants (Table 1). The third ventricle widths of preterm infants according to GA were shown in Figure 2.

Table 1. Ultrasonography measurements of infants

	Moderate and late preterm infants n=64	Early preterm infants n=156	p
Left lateral ventricle anterior horne (mm)	$2.61 \pm 0.70$	$2.31 \pm 0.62$	0.037
Right lateral ventricle anterior horne (mm)	$2.62 \pm 0.79$	$2.30 \pm 0.60$	0.040
Left ventricle index (mm)	$13.2 \pm 1.85$	$11.3 \pm 1.60$	<0.001
Right ventricle index (mm)	$13.1 \pm 1.81$	$11.5 \pm 1.57$	<0.001
Third ventricle (mm) (mean $\pm$ SD) (median) (minimum- maximum)	$1.65 \pm 0.38$ 1.75 0.90- 2.20	$1.27 \pm 0.33$ 1.20 0.50 - 1.90	<0.001

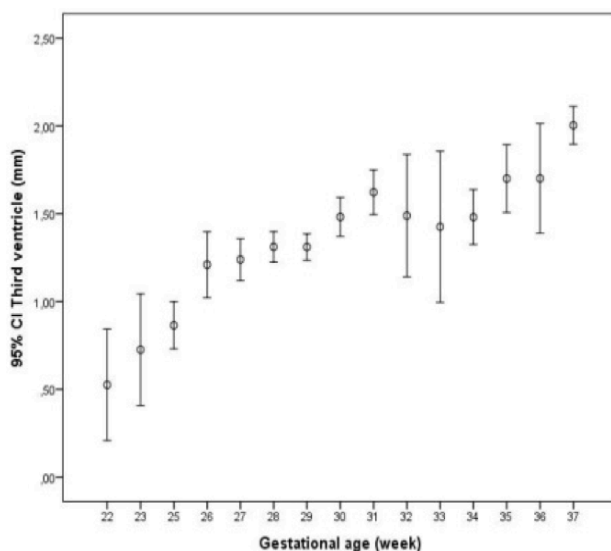


Figure 2: Boxplot chart for third ventricle width in preterm infants according to gestational weeks.

When the infants included in the study were grouped according to GA into 5 groups (<26 weeks, 26-27 weeks, 28-29 weeks, 30-31 weeks and  $\geq 32$  weeks), it was observed that third ventricle width increased as gestational age increased. Mean values of the third ventricle were found to be  $0.76 \pm 0.21$  mm,  $1.19 \pm 0.28$  mm,  $1.25 \pm 0.21$  mm,  $1.48 \pm 0.31$  mm, and  $1.65 \pm 0.38$  mm, respectively.

Demographic and C-US parameters associated with the third ventricle in the univariate analyses were summarized in Table 2. Linear regression analysis was performed with these parameters, which were significantly associated with the third ventricle (Table 2). From these parameters, only GA and R-AHW values were found to be independently associated with third ventricle (Table 2). The relationship

between the third ventricle and GA was shown in Figure 3.

Table 2. The parameters associated with third ventricle and linear regression analysis for parameters significantly correlated with third ventricle in premature infants

For third ventricle	Univariate analyze		Multivariate analyze	
	p	r	p	$\beta$
Gestational age (week)	<0.001	0.667	<0.001	0.610
Weight (kg)	<0.001	0.623	0.832	0.027
Head circumference (mm)	<0.001	0.585	0.284	0.129
Left lateral ventricle anterior horne (mm)	<0.001	0.341	0.631	0.051
Right lateral ventricle anterior horne (mm)	<0.001	0.373	0.011	0.141
Left ventricle index (mm)	<0.001	0.403	0.150	0.190
Right ventricle index (mm)	<0.001	0.431	0.256	0.164

\*  $R^2_{Adjusted} = 0.667$

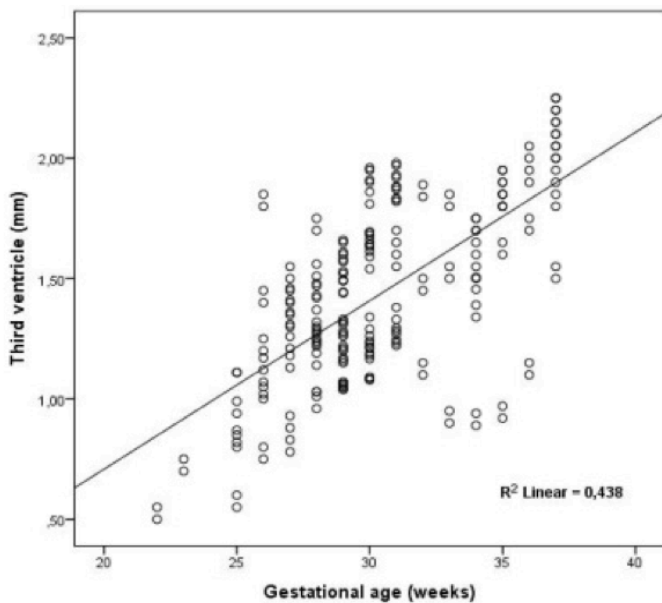


Figure 3: Scatter/dot graphics for third ventricle and gestation weeks: Third ventricle diameter was significantly related with gestational weeks in preterm newborns.

DISCUSSION

The most important finding of our study was that the third ventricle value obtained by C-US was significantly lower in early preterm infants than in moderately-late preterm infants and this decrease was independently related with GA. Although there are recent studies about R-AHW, L-AHW, R-VI, L-VI

values in preterm infants in the literature; third ventricular width are not available [5, 6]. Only few studies in the last decade have data on third ventricle width in preterm infants [7, 8]. We believe that this study is important in terms of the evaluation of the third ventricle with new model and high-resolution devices and probes. 90% of spontaneous intra cerebral hemorrhages in premature infants are in the germinal matrix tissue, resulting severe morbidity and even mortality due to the severity of bleeding [9]. The incidence of intraventricular hemorrhage with GMB is 20% in low birth weight premature infants [4]. Post-hemorrhagic ventricular dilatation (PVHD) risk increases with severe GMB-IVH, lower gestational age and severe problems of prematurity [10]. It is usually observed in infants with stage III GMB-IVH or PVHI (stage IV GMB-IVH). The risk of PVHD development for Stage I, II, III GMB and PVHI is 1, 4, 25 and 28%, respectively [11]. For this reason, the GMB diagnosis and assessment and treatment of ventricular dilatation is important for the neurological development of premature infants. C-US is the most preferred method for evaluating cerebral parenchyma and ventricular system in newborns, especially in premature infants, and helps objectively in determining germinal matrix bleeding and post hemorrhagic ventricular dilatation [9, 12]. Especially in high-risk infants, it is important to assess the size of the ventricle initially

and the subsequent changes due to the possible progressive ventricular dilatation [13]. Cerebral ventricular width measurement and its standardization are very important especially in children and it is difficult to diagnose hydrocephalus clinically in the early stage of the disease [13]. In addition to the diagnosis of hydrocephalus, cerebral ventricular system width can be followed after ventricular shunt operation and shunt failure can be detected at an early stage [14].

The third ventricle is located between two cerebral hemispheres, in the midline, inferior to the corpus callosum and the corpus of the lateral ventricles, superior to the sella turcica, and between hypothalamus and thalamus. It is connected to the lateral ventricles through the foramen Monroe at the anterior-superior edge and to the fourth ventricle through the aqueductus Sylvius at the posterior edge. There is no study in the last decade regarding the width of the third ventricle in preterm infants and there are limited reference values in the literature. In a study conducted by Sondhi et al. [7] a decade ago, it was reported that the width of the third ventricle in preterm infants was 1.25 - 2.0 mm and increased in accordance with GA. A similar study was carried out in 2000 and the third ventricle width in preterm infants (GA < 33 weeks) was found to be in the range of 0.9 - 2.6 mm [8]. To the best of our knowledge, our study is the most recent study in which the third ventricle width is evaluated in early preterm infants and normal reference range values are given. In early preterm infants, the third ventricle mean  $\pm$  SD, median, minimum and maximum widths were  $1.27 \pm 0.33$  mm, 1.20 mm, 0.50 mm and 1.90 mm respectively. The results of our study were determined by latest model and high-resolution probes, and narrower third ventricle width was obtained compared to previous studies. The width of

the widest third ventricle in preterm infant was also measured as 1.9 mm. In our study, the third ventricle width was examined with R-AHW, L-AHW, R-VI, L-VI, and was significantly higher in moderately-late preterm infants compared to early preterm infants, similar to the other studies [5-8].

## LIMITATIONS

The lower number of participants in the study and conducted in one center are the limitations of our study. Also, our study was performed in preterm infants with normal C-US evaluation and could not be used in infants with pathological findings. Only one radiologist performed neonatal C-US and another radiologist did not evaluate the same cases, inter-observer variability could not be evaluated. A close relationship was found between the third ventricle and GA, but the number of infants <26 weeks was low, mainly due to the presence of pathological C-US findings in most infants <26 weeks. Our study should be evaluated with new studies including more infants with the same characteristics.

## CONCLUSION

Third ventricle width obtained by C-US is significantly lower in early preterm infants than in term babies and this decrease is independently associated with GA. In our study, it was considered that these data are important for the detection of third ventricle enlargement in preterm infants with abnormal C-US and our data could be used clinically. However, this finding should be confirmed by further studies with more participants.

## CONFLICT of INTEREST

We have no conflict of interest for this study.



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