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Nomogram of corpus callosum length and thickness in Turkish population

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Abstract

Objectives: Central nervous system (CNS) malformations constitute an important part of congenital anomalies and corpus callosum anomalies are highly associated with other CNS abnormalities. Starting from this point of view we conducted a retrospective study providing reliable reference charts for accurate fetal corpus callosum measurements.

Materials and Methods: The corpus callosum length (CCL) and thickness (CCT) were measured in the midsagittal plane. The CCL was measured from the most anterior part of the genu to the most posterior part of the splenium (outer-outer), the thickness of the body was measured as well.

Results: Study included 1152 patients. 95.6% of the detailed ultrasonographies were performed between 19-21 gestational weeks and 611(63.0%) were performed at 20th gestational week. The mean values of the CCL and CCT measurements were from 16.9 mm to 25.5 mm and from 1.3 mm to 2.0 mm, respectively with increasing gestational weeks. Third percentile for CCL was 14.6 mm, 16.2 mm and 17.9 mm for 19th, 20th and 21th gestational weeks, respectively and median CCL values were 17.7mm, 19.5 mm and 21.7 mm for 19th, 20th and 21th gestational weeks respectively.

Conclusion: Our study demonstrates that defining and using corpus callosum length and thickness charts characteristic for our population may improve diagnostic accuracy of corpus callosum presence and structure. Objective measurements of CC may help to identify developmental anomalies of CNS and enable better prenatal counseling.

Introduction

Central nervous system (CNS) malformations constitute an important part of congenital anomalies. Visualization of fetal brain is an essential part of fetal ultrasonographic evaluation and is generally performed as a part of detailed ultrasonography at mid-gestation (18-22 weeks). According to International Society of Ultrasound in Obstetrics and Gynecology (ISUOG) guidelines, screening should include evaluation of head shape, lateral ventricles, cavum septi pellucidi, thalami, cerebellum, cisterna magna and the spine [1]. However, ultrasonographic evaluation of Corpus Callosum Length (CCL) and Corpus Callosum Thickness (CCT) is not routine and performed mostly in patient basis.

Incidence of corpus callosum agenesis ranges from 0.05% to 3%, according to the investigated populations [2]. CC anomalies are highly associated with other CNS abnormalities, up to 80% of the cases [3-5]. In 30-45% of cases, genetic etiologies such as chromosomal anomalies (10%) and genetic syndromes (20-35%) can be identified. Malformations of corpus callosum such as a total/partial absence, hypoplasia, and dysgenesis are potential risk factors for developmental delays [6]. The thick corpus callosum, which is rarely mentioned, has also been associated with brain abnormalities that have some relevance especially to autism or developmental delays in some literature [7, 8]. Although current guidelines have not recommended visualizing corpus callosum routinely, it is important to deduce the absence of CC by visualizing indirect signs such as absence of cavum septi pellucidi (CSP), cerebral ventricle abnormalities, widening of the interhemispheric fissure, pericallosal artery alterations, radial arrangement of cerebral sulci around the third ventricle [9, 10]. However, direct visualization of CC would be more advantageous in order to demonstrate the integrity of fetal CNS and determine the candidates for a further neurodevelopmental follow-up. Moreover there are differences in various nomograms in different populations [9, 11] and this highlights the need of population-based nomograms in CC measurements.

As a tertiary perinatology center, we routinely perform fetal neurosonography and evaluation of CCL and CCT is

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an essential part of this examination. Starting from this point of view we conducted a retrospective study providing reliable reference charts for accurate fetal corpus callosum measurements by prenatal 2D ultrasonography in our population.

Material and Methods

This is a retrospective study which was conducted in Başkent University Ankara Hospital, Division of Perinatology. We reviewed all anomaly scans performed by a single expert (SE) between the years 2017 and 2020. Study was approved by the Institutional Ethics Commitee (KA20/187).

Evaluation of corpus callosum was mostly performed between 19-22 weeks during routine second trimester anomaly scan. All examinations were done using Voluson E10 ultasound machine with a 4 to 8-MHz transabdominal transducer as default.

The CC was visualized and measurements were performed in a midsagittal plane as demonstrated in prior studies [12, 13]. CCL was measured from the most anterior part of the genu to the most posterior part of the splenium (outer-outer); the thickness of the body was measured, as well.

Exclusion criteria were pregnancy ≤17th gestational weeks, abnormal karyotype, presence of any structural(brain or other) and chromosomal anomalies, patients with history of teratogen use, patients with multiple gestation, and patients with suspicious dating. Inclusion criteria were singleton pregnancy without any structural (brain or other) and chromosomal anomalies between 18 to 24 weeks.

During the study period, 1267 detailed ultrasonographies were performed. Distribution of excluded 115 patients was as follows: 47 patients due to multi-ple gestation, 8 according to suspicious dating, 23 due to chromosomal abnormality, 29 due to any structural abnormality, and in 8 patients due to lack of measurement of both CCT and CCL (only observed). Age, obstetric history, gestational age, use of artificial reproductive techniques and ultrasonographic measurements were obtained from patient records.

Statistical Analysis

Data were analyzed using SPSS for Windows v.15.0 (SPSS,Inc., Chicago, IL, USA). Descriptive and frequency analysis were performed. The percentile function of frequency analysis was used to determine the specific percentile points for 19 to 21 gestational weeks. Percentile analysis were not performed for other gestational weeks due to limited number of patients numbers.

Results

The median age of patients was 32 (Range: 18-46). Median of gravida was 2 and 678 (58.9%) of the patients were nulliparous. Detailed ultrasonographies were performed between mostly between 19-21 gestational weeks (95.6%) and 611(63.0%) were performed at 20th gestational week. CC agenesis was detected in 4 patients (‰7). General patient characteristics are summarized in Table 1.

Table 1. General Characteristics of Patients

	Median	Range
Age (Years)	32	18-46
Gravida	2	1-8
Artificial Reproductive Technique	Number of Patients	%
Absent	904	78.5
Present	248	21.5
Distribution of Gestational Age		
18	9	.8
19	320	27.8
20	611	53.0
21	171	14.8
22	29	2.5
23	9	.8
24	3	.3

Table 2. Corpus Callosum Length (mm) according to gestational age

Gestational Week	Mean	Std. Dev.	Min.	Max.
18	16.9	2.6	14.0	22.0
19	17.9	2.0	13.3	24.0
20	19.6	2.1	15.0	26.0
21	21.8	1.9	16.8	27.7
22	23.4	2.0	19.7	27.0
23	25.3	2.3	22.5	29.0
24	25.5	3.4	22.3	29.1

The mean values of the CCL and CCT measurements were from 16.9±2.6 mm to 25.5±3.4 mm and from 1.3±0.2 mm to 2.0±0.2 mm, respectively with increasing gestational weeks. Table 2 and 3 shows the means and ranges of corpus callosum measurements.

Corpus Callosum length and thickness percentiles are shown in table 4 and 5. Third percentile for CCL was 14.6 mm, 16.2 mm and 17.9 mm for 19th, 20th and 21th gestational weeks, respectively and median CCL values were 17.7mm, 19.5mm and 21.7mm for 19th, 20th and 21th gestational weeks respectively.

Discussion

Normal dimension ranges for various structures of fetal brain were priorly defined whereas corpus callosum measurement is not a routine in clinical practice. However, development of corpus callosum could be an indicator of fetal brain development and maturation [13]. Therefore, in this study we retrospectively evaluated the fetal gestational age specific corpus callosum length and thickness in our Turkish population in second trimester and established

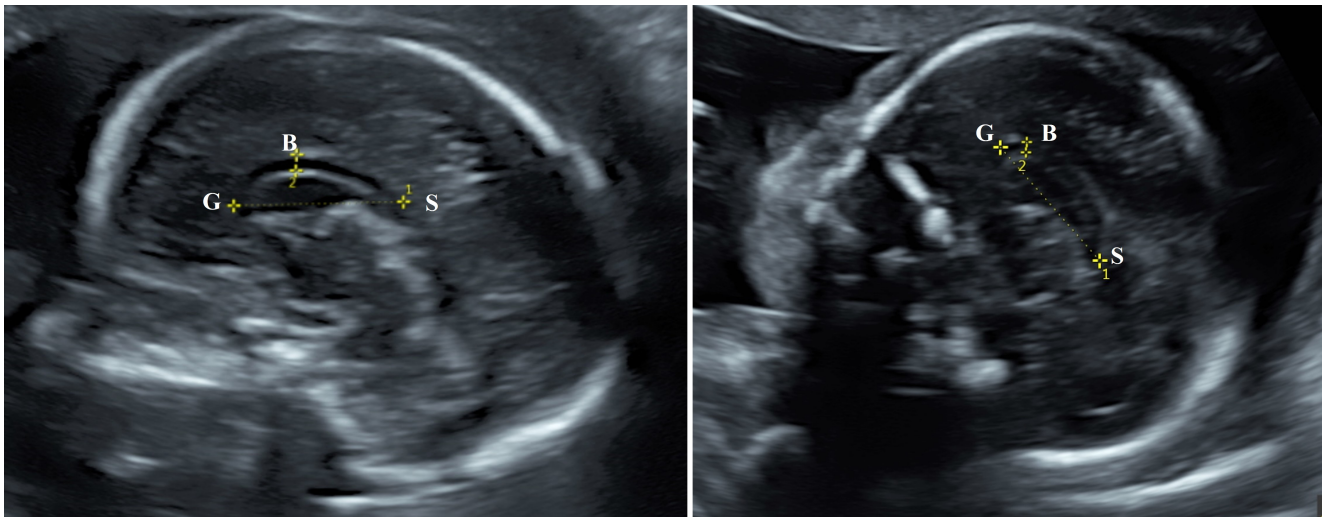

Figure 1. Figure Legend: The measurement technique of CCL and CCTCalipers are placed in inner edges of callosal sulcus: genu (G), body (B) and splenium (S).

Table 3. Corpus Callosum Thickness (mm) according to gestational age

Gestational Week	Mean	Std. Dev.	Min.	Max.
18	1.3	0.2	1.0	1.7
19	1.4	0.3	1.0	2.4
20	1.5	0.3	1.0	2.4
21	1.6	0.4	1.1	2.9
22	1.5	0.3	1.2	2.2
23	1.7	0.3	1.2	2.2
24	2.0	0.2	1.8	2.1

Table 4. Gestational Age based Corpus Callosum Length Percentiles (mm)

	Percentiles							
Gestational Week	1	3	5	10	25	50	95	97
19	13.8	14.6	15.1	15.5	16.5	17.7	21.5	21.9
20	15.7	16.2	16.4	17.0	18.1	19.5	23.1	24.0
21	17.2	17.9	18.6	19.2	20.4	21.7	24.9	25.2

reference charts for fetal corpus callosum length derived between 19 and 22 weeks.

CC agenesis is seen in about 1:4000 live births and it is frequently associated with other CNS (e. g., cortical developmental disorders, callosal lipoma, intracranial cysts) or extra-CNS anomalies (e. g., eyes, face, cardiovascular) [14]. Therefore investigation of presence or absence of CC is an essential part of fetal ultrasonographic examination. Usually, indirect signs such as absence of the cavum septi pellucidi, ventriculomegaly or colpocephaly are used for corpus callosum investigation [10] however, these may also not be present or apparent or may not be diagnosed depending on the ultrasonographic view. Point of view, that is why we routinely measure corpus callosum along with other brain structures, such as cavum septum pellucidum, anterior and posterior horns of lateral ventricles, cerebellum, vermis, cisterna magna and nuchal fold thickness in our clinic.

Table 5. Gestational Age based Corpus Callosum Thickness Percentiles (mm)

	Percentiles							
Gestational Week	1	3	5	10	25	50	95	97
19	1.0	1.0	1.0	1.1	1.2	1.4	2.0	2.0
20	1.0	1.1	1.1	1.2	1.3	1.5	2.1	2.1
21	1.1	1.1	1.1	1.2	1.3	1.6	2.2	2.4

Final shape of corpus callosum assumes by 18-20 weeks of gestation, so ideally it can be visualized by fetal ultrasonography at the beginning 20th week of gestation [9, 15, 16]. Thus we've focused on this time interval in this study. It may also be visualized in later gestational weeks but it would be difficult to obtain optimal views to visualize CC especially in vertex presentations.

CC development evaluation has been evaluated in Caucasian population [9, 11]. Malinger et al. reported the ranges and change of CC measurements during pregnancy. They revealed a nearly 17 mm in length at 18th gestational week and this increased to about 44 mm at term [11]. It was also priorly shown that CCT increases until 19-21st week of gestation, however CCL grows during whole pregnancy [9]. Zhang et al. reported ranges between 16-39 weeks for Chinese population [17]. In a very recent study from Turkey, Alemdaroglu et al. presented very similar results with our study which supports value of population-based nomograms on CC measurements [18]. In our study, there was a linear association between CC length measurement and gestational week and that was consistent with the previously published studies.

Fetal corpus callosum measurement can be performed with 2-dimensional (2D), 3-dimensional (3D) sonography [9, 11, 16]. In our study we determined the percentiles according to 2-dimensional measurements. It is applicable and present in most of the settings. Also the technique is easy to learn and perform; a good sagittal view of the anteflexed fetal head is appropriate for CC evaluation.

High number of patients and standard measurement by the same expert were the strengths of the study. Main limitation was thought as the retrospective structure. We reported our findings in measurements during 19-22 gestational weeks at when most of the fetal anomaly scans are performed. Our number of patients in 18th gestational week was low and therefore we excluded these patients. A well-designed prospective future study with larger sample sizes from various ethnic origins carried out by a single operator using strict criteria and technique for CC measurement could be more reliable in determining variations of CCT and CCL between populations.

In conclusion, our study demonstrates that defining and using corpus callosum length and thickness charts characteristic for our population may improve diagnostic accuracy of corpus callosum presence and structure. Knowledge of normal CC appearance and objective measurements may help identify developmental anomalies and enable accurate prenatal counseling.

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