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REVIEW ARTICLE

What is Known about Corpus Callosum Prenatally?

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ABSTRACT

The corpus callosum is the main commissure of the fetal brain and can be displayed with two-dimensional (2D) and three-dimensional (3D) ultrasound. However, only 3D ultrasound provides the operator with the possibility to adjust the three orthogonal planes of the brain in that way that the entire corpus callosum is shown precisely in the median plane.

The aim of this article is to provide the most recent information on the assessment of the fetal corpus callosum by means of 3D ultrasound. Different topics are highlighted, such as advantage of 3D ultrasound over 2D ultrasound, indications for displaying the fetal corpus callosum, demonstration of the normal and abnormal corpus callosum and biometric measurements of the fetal corpus callosum by 3D ultrasound. Furthermore the question is raised whether fetal magnetic resonance imaging (MRI) can give additional information to the 3D ultrasound examination and whether the diagnosis resulting from 3D neurosonography gives us the chance for a better counseling of parents who are confronted with the diagnosis of a fetal corpus callosum pathology.

Keywords: Corpus callosum, Corpus callosum pathology, Fetus, Prenatal counseling, 3D ultrasound

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INTRODUCTION

The corpus callosum receives its name from its anatomical compactness and represents the major telencephalic commissure between the two brain hemispheres.[1] It is considered to be complete at 150 to 200 mm crown rump length.[2,3]

Each hemisphere of the brain is specialized in controlling movements and feeling in the opposite half of the body, as well as in processing certain types of information, such as language or spatial orientation. Thus, to coordinate movements or to process complex information, the hemispheres must communicate with each other.

The adult form of the corpus callosum is achieved by 18 weeks of gestation and its height will increase with myelination. During the 3rd month after birth, there is a weeding out of the callosal axons which confines contacts between the hemispheres to certain cortical zones.[4]

While the entire structure develops prior to birth, its effectiveness and efficiency increase until adolescence. The anterior and posterior corpus callosum sectors are among the most rapidly developing white matter structures in humans.[5,6] By the time a child is approximately 12 years of age, the corpus callosum functions essentially as it will do in adulthood, allowing rapid interaction between the two sides of the brain. Parents report that children with absent corpus callosum and intact early motor development (i.e., sitting and walking within the normal age range) are significantly likely to display clinically relevant behavior problems when they reach the 6- to 11-year-old age range. They may exhibit somatic complaints, attention problems, aggressive behavior, social problems, and thought problems.[6]

PRENATAL DEMONSTRATION OF CORPUS CALLOSUM

Fetal neurosonography with imaging of the corpus callosum can be performed with two-dimensional (2D)[7-9] and three-dimensional (3D) ultrasound.[10-14] Clear sonographic visualization of the corpus callosum requires scanning planes that are difficult to obtain *in utero* with 2D ultrasound. Due to its arch shape, the structure cannot be demonstrated using standard axial planes, while coronal planes enable the visualization on screen of only a small portion at a time.[10]

In contrast to 2D sonography, 3D ultrasound provides many advantages in imaging of the fetal brain, because the different cerebral planes can be shown using various display modes. With the help of these different display modes, including the 3D orthogonal-plane mode, parallel-plane mode, and surface mode,[15] it has become possible to obtain not only a detailed view of the fetal face,[16] but also to enable a rapid and easy evaluation of intracranial structures such as normal and abnormal corpus callosum,[13,14,17,18] cavum septi pellucidi, cortical development (Figs 1A and B), and their relationship to the fetal gender.[12,19-21]

Sonographically, the corpus callosum is considered to be fully developed when it overlies the quadrigeminal plate of the mesencephalon in the median view of the fetal brain.[17,22] The corpus callosum is displayed as a hypoechoic band, demarcated superiorly and inferiorly

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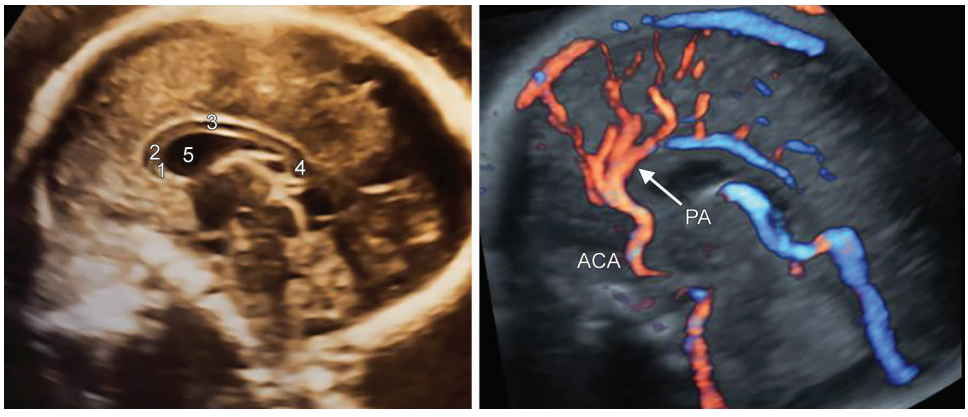


Figs 1A and B: (A) Three-dimensional surface-rendered median plane of the fetal brain at 31 gestational weeks with demonstration of the corpus callosum with the segments rostrum (1), genu (2), body (3), splenium (4), and the cavum septi pellucidi (5), (B) Three-dimensional sonoangiogram at 31 weeks of gestation with demonstration of the anterior cerebral artery (ACA) and the pericallosal artery (PA)

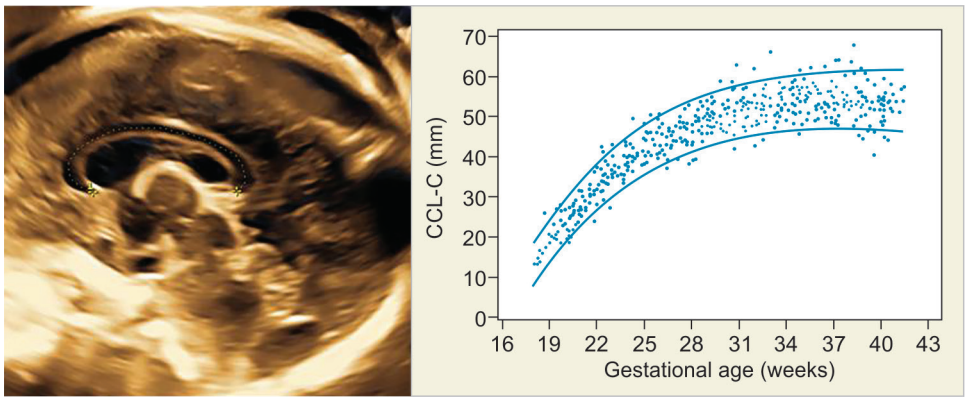
by two echogenic lines. The presence of hyperechogenicity signifies possible pathology, mainly callosal lipoma.[10,18]

BIOMETRIC MEASUREMENTS OF CORPUS CALLOSUM *IN UTERO*

Two-dimensional ultrasound measurements of the corpus callosum are reported by Malinger and Zakut in 1993[8] and Achiron and Achiron in 2001.[9] However, their data are limited to a small number of fetuses for each gestational week, which does not permit to determine precise charts for normal development. Moreover, the height (=thickness) of the corpus callosum is measured just in a mid-coronal plane only and not in the four corpus callosum segments: Rostrum, genu, body, and splenium. Malinger and Zakut[8] observed a twofold increase in the height (=thickness) of the corpus callosum. In contrast, Achiron and Achiron[9] reported a threefold increase in the height (=thickness) and a 10-fold increase in the length. They explained that this difference is due to the fact that the measurements performed by Malinger and Zakut[8] began at 18 to 19 weeks' gestation, while the study of Achiron and Achiron[9] started as early as 16 weeks of gestations. The latter authors further reported that 50% of the total height (=thickness) was achieved at 21 to 22 weeks of gestation, which correlates with the first phase of neuronal migration. Both of these studies proposed and documented a linear growth of the corpus callosum. In contrast, a nonlinear growth for the corpus callosum was reported by two other studies. In the first study, the measurements were performed with 2D ultrasound.[23] In the second study, the measurements were performed with magnetic resonance imaging (MRI), and the authors described the observed growth as a polynomial growth which reflects both linear growth and folding.[24] In our recently published study[17], we observed a nonlinear growth and approximately a fourfold increase in all corpus callosum lengths, a threefold increase in the rostrum height (= thickness), a fourfold increase in the genu height (=thickness), a twofold increase in the body height (=thickness), and a threefold increase in the splenium height (=thickness) (Figs 2A and B). The growth patterns of the rostrum and the body height seem to be similar. They show a fast development until 24, resp. 22, weeks of gestation, to be followed by stagnation after this period. The growth patterns of the genu and the splenium are also similar.[17]

Regarding the echogenicity of the corpus callosum, it was observed as a hypoechoic structure with a clear demarcation from the cavum septi pellucidi and cavum vergae throughout the entire observation period.[17]

Surprisingly, in the paper of Correa et al[25] and Pilu et al,[26] 3D reconstructed images demonstrated the corpus callosum as a hyperechoic structure and also the corpus callosum could not be differentiated clearly from the cavum septi pellucidi. Rizzo et al in 2010[27] attempted to create charts for normal corpus callosum measurements from 3D sonographic volumes acquired transabdominally from an axial view. They reported charts for corpus callosum or corpus callosum–cavum septi pellucidi complex, with the latter visualized as a single comma-shaped echogenic structure. Since lipomas of the corpus callosum are rare, the possibility of an artifact causing the hyperechogenicity has to be considered. This type of artifact may be due to the simultaneous use of 3D voxel reconstruction in conjunction with speckle reduction imaging[10] and represents the interface between the cingulated gyrus, the cingulated sulcus, cerebrospinal fluid, and the blood flow in the callosal arteries. A curvilinear lipoma shows similar characteristics on 3D imaging, but does not usually interfere with the 2D visualization of the corpus callosum.[10]



Figs 2A and B: (A) Three-dimensional surface-rendered view of the fetal corpus callosum at 27 gestational weeks, illustrating the measurement of the curved corpus callosum length (CCL-C = 48.4 mm), (B) Individual measurements and calculated 90% reference band of the CCL-C in relation to the gestational age (18–41 weeks) (n = 466 cases). The lines represent the 5th, 50th, and 95th percentiles[17]

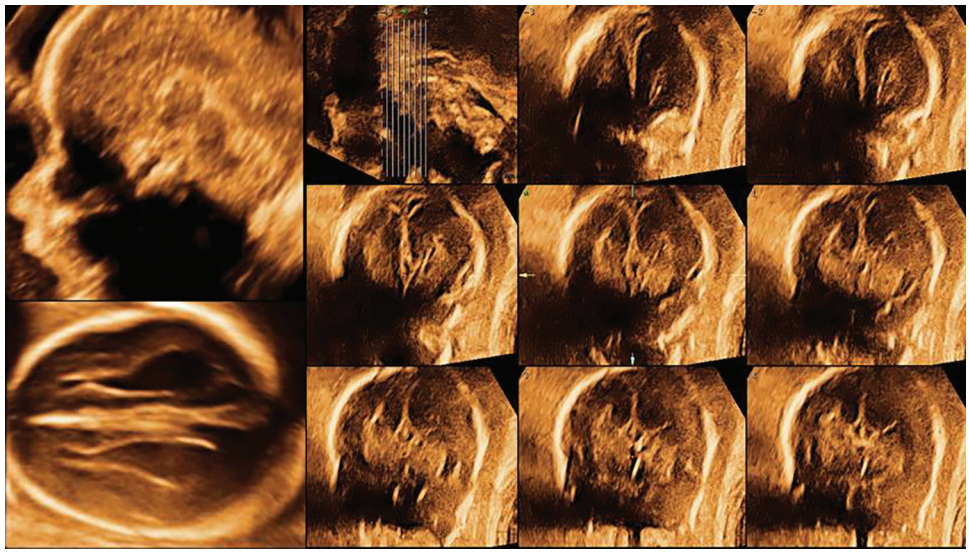
In 2012, Araujo Júnior et al[28] reported measurements of the outer length and area of the corpus callosum from 20 to 33 weeks of gestation, using the transfrontal view obtained by 3D ultrasonography. They believe that the area of the corpus callosum could be a more reliable parameter for identifying small changes in the size of the organ and helpful in the evaluation of partial agenesis. In cases of abnormally thin or thick corpus callosum, the availability of reference ranges for corpus callosal length and the height of the four different parts of the structure is very helpful, as already demonstrated by pathological cases.[17,18]

PATHOLOGIES OF THE CORPUS CALLOSUM *IN UTERO*

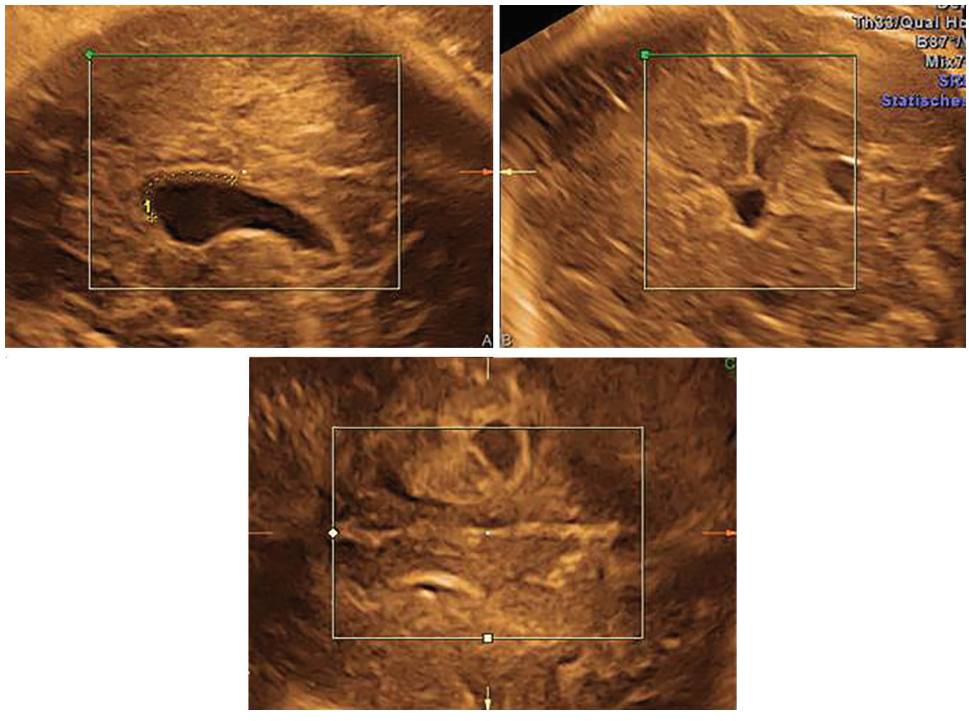
Abnormalities of the corpus callosum include agenesis, partial agenesis, hypoplasia, hyperplasia, and lipoma with enhanced echogenicity.[18] According to our sonographic experience, we defined the corpus callosum pathologies as follows[18]:

- Agenesis of the corpus callosum was diagnosed when the corpus callosum could neither be detected in the median plane nor in the axial and coronal views (Figs 3A to C).
- Partial agenesis of the corpus callosum was diagnosed when at least one of the anatomical segments was missing, while the height was within the normal range and all three lengths of the corpus callosum were less than the 5th percentiles according to our growth charts[17] (Figs 4A to C).
- Hypoplasia was diagnosed when all anatomical segments were present and the height of at least one corpus callosum segment was less than the 5th percentile according to our growth charts[17], independent of the length range.
- Hyperplasia was defined when all anatomical segments were present and the height of at least one corpus callosum segment was found above the 95th percentile according to our growth charts[17], while all three lengths were normal or out of the normal range (Figs 5A and B).
- A combination of hypo- and hyperplasia (=mixed abnormal thickening) was diagnosed when all anatomical segments were present and the height of at least one segment was found above the 95th percentile and another segment below the 5th percentile, independent of the length range.
- A lipoma was diagnosed when the corpus callosum was found with enhanced echogenicity (Fig. 6).

Prenatal diagnosis of complete agenesis of the corpus callosum is feasible by expert sonography from 18 to 20 weeks of gestation onward and relies on the recognition of direct and/or indirect signs[7,29-32] (Figs 3A to C). Although the prenatal diagnosis of complete agenesis was first described by Comstock et al in 1985,[33] until today it continues to be regarded as a malformation of uncertain prevalence and clinical significance. Direct sonographic signs consist of the demonstration of the absence of the corpus callosum in the median and coronal views of the fetal brain (Figs 3A and C). The median plane shows absent corpus callosum structure and an atypical radiating appearance of the median sulci, which converge toward the third ventricle. In the majority of cases, the cingulated gyrus is absent or may be incomplete.[31] Indirect signs include the so-called teardrop-shaped ventricles[34] (Fig. 3B) as well as colpocephaly,[35] which is characterized by dilatation of the atria and occipital horns of the lateral ventricles. All of these signs were consistently observed in our series of fetuses with corpus callosum agenesis. Additional sonographic findings are diagnosed due to the presence of underlying chromosomal anomalies or



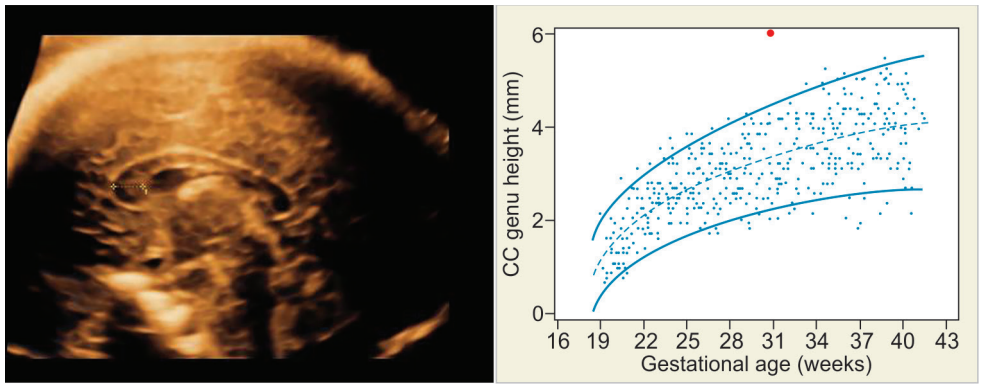
Figs 3A to C: (A) Three-dimensional surface-rendered median plane of a fetal brain at 22 weeks gestation demonstrating complete agenesis of the corpus callosum with an upward displacement of the third ventricle, (B) three-dimensional surface-rendered image of a fetal brain with agenesis of the corpus callosum at 19 gestational weeks. The axial plane reveals the "teardrop"-shaped lateral ventricles, and (C) three-dimensional tomographic display of a fetal brain with complete agenesis of the corpus callosum (coronal planes). The parallel section planes are similar to those seen in computed tomography or magnetic resonance imaging at 24 weeks' gestation



Figs 4A to C: Three-dimensional multiplanar imaging of a fetal brain with partial agenesis of the corpus callosum at 34 weeks of gestation. The curved corpus callosum length is only 19 mm: (A) displays the median plane, (B) the coronal plane, and (C) the axial plane of the fetal brain

genetic syndromes.[36,37] In our series of corpus callosum agenesis, over 75% of the cases had additional sonographic findings and a poor prognosis.[18]

Partial agenesis of the corpus callosum results from growth arrest which occurs between 12 and 18 weeks of gestation and usually involves the dorsal part of the splenium, with the more anterior part being preserved.[22] It remains uncertain whether partial agenesis of the corpus callosum represents a true malformation or is the consequence of a disruptive event. In our study[18], the measurements of all three corpus callosum lengths were below the 5th percentile (Fig. 4).



Figs 5A and B: (A) Three-dimensional surface view of the median plane of a fetal brain at 31 gestational weeks demonstrating hyperplasia of the genu segment of the corpus callosum (5 mm); (B) Individual measurements and calculated 90% reference band for the genu height (= thickness) (Genu-H) of the corpus callosum in relation to the gestational age (18–41 weeks) (n = 466 cases).[17] The lines represent the 5th, 50th, and 95th percentiles. The red dot demonstrates the case with hyperplasia of the genu

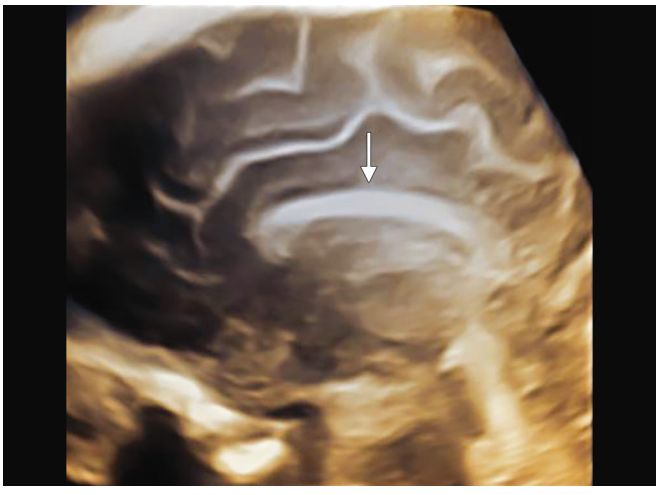


Fig. 6: Fetus at 38 weeks of gestation with lipoma of the corpus callosum. The three-dimensional surface-rendered image of the median plane of the brain shows the corpus callosum as a hyperechoic structure (→)

Hypoplasia of the corpus callosum is related to a decrease in thickness or to a decrease in both thickness and length. Hypoplasia occurs as a result of the late destruction of the corpus callosum owing to a metabolic, infectious, or ischemic origin.[38] In contrast to a primary malformation, callosal hypoplasia is more likely to depend upon an external factor affecting the number and size of callosal axons.[38] Prenatal diagnosis is still challenging and relies on a clear demonstration of the corpus callosum structure in the median plane, as well as on a precise measurement that can be compared with normal values observed at the corresponding gestational age.[7,18]

In cases of hyperplasia of corpus callosum, the knowledge of growth charts of corpus callosum length and height of the four different segments of the corpus callosum is of great importance (Figs 5A and B).[17,18]

The same is true in cases showing mixed abnormal thickening, that is, a combination of hypo- and hyperplasia of the corpus callosum.[18]

When a lipoma of the corpus callosum is present, the entire corpus callosum can be observed with enhanced echogenicity (Fig. 6).[18]

In prenatal diagnosis, the pericallosal artery (Fig. 1B) is an important landmark for the normal and abnormal development of the corpus callosum. With the help of the glass body-render mode, a combination of 3D gray values and 3D color Doppler technique, the pericallosal artery can be displayed as it runs between the two cerebral hemispheres on the upper margin of corpus callosum.[39,40] It is accepted that changes in the course of the pericallosal artery are an additional finding in corpus callosum pathologies.[26,41] Therefore, it is important to know the normal variants of the pericallosal artery *in utero*.[39]

Although we are able to demonstrate structural abnormalities of the corpus callosum accurately with 3D ultrasound and the new reference ranges for the different corpus callosum measurements, the precise prognosis in the different corpus callosum anomalies continues to be challenging.[42]

CONCLUSION

The corpus callosum represents an important landmark for the normal development of the fetal brain. Demonstration of the normal and abnormal corpus callosum in the median plane is precisely possible with 3D ultrasound. Due to the complex anatomy of the fetal brain, it is helpful to have reference views and gestational age-related tables and charts of the dimensions of the corpus callosum to diagnose partial agenesis and hypo- and hyperplasia of the corpus callosum correctly. Due to the high association of corpus callosum anomalies with fetal syndromes, it is important to search always for additional pathological fetal findings.

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