



Original Research Article

CHARACTERIZATION OF 'PSEUDO-SEPTUM' PHENOMENON IN FETAL MRI: INSIGHTS INTO SEPTAL AGENESIS

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ABSTRACT

Background: Septal agenesis (SA) and the "pseudo-septum" phenomenon are rare midline abnormalities identified in fetal MRI, often posing diagnostic challenges. Accurate differentiation between true SA and pseudo-septum is critical for prenatal counselling and management. This study aims to characterize the imaging features of true SA and pseudo-septum in fetal MRI and analyse their association with other central nervous system (CNS) anomalies and postnatal outcomes.

Materials and Methods: A total of 79 fetuses with suspected midline anomalies underwent detailed MRI assessments at a tertiary care centre in India. The presence of true SA and pseudo-septum was evaluated, along with associated findings like ventriculomegaly and corpus callosum agenesis. Diagnostic accuracy metrics for MRI were calculated using histopathological and clinical follow-up as gold standards. Statistical comparisons were performed to analyse associations between SA, pseudo-septum, and neurodevelopmental outcomes.

Results: True SA was confirmed in 29 cases (36.7%), while 21 cases (26.6%) were identified as pseudo-septum. Ventriculomegaly was more frequent in pseudo-septum cases compared to true SA (66.7% vs. 31.0%, OR: 4.2, $p=0.004$). The sensitivity and specificity of MRI for diagnosing SA were 81.0% and 69.2%, respectively, with an overall accuracy of 77.2%. Postnatal outcomes showed a trend toward higher rates of neurodevelopmental delay in true SA cases (31.0% vs. 9.5%, $p=0.051$), although this did not reach statistical significance.

Conclusion: This study highlights the diagnostic challenges posed by the pseudo-septum phenomenon in differentiating true SA. While fetal MRI remains a reliable tool, the presence of pseudo-septum and ventriculomegaly requires careful interpretation to avoid misdiagnosis. Enhanced imaging protocols and further research into the long-term outcomes of these conditions are essential to improve prenatal care and clinical management in resource-limited settings.

Keywords: Septal agenesis, Pseudo-septum, Fetal MRI, Ventriculomegaly, Central nervous system anomalies, Prenatal diagnosis, Neurodevelopmental outcomes.

INTRODUCTION

Septal agenesis (SA), which involves the partial or complete absence of the septum pellucidum, is a rare congenital anomaly, with a prevalence of approximately 2-3 per 100,000 live births. This anomaly can occur in isolation or as part of complex

congenital malformations such as septo-optic dysplasia (SOD), holoprosencephaly, or corpus callosum agenesis.^[1] SOD is characterized by the combination of optic nerve hypoplasia, midline brain anomalies, and pituitary dysfunction.^[2] SA can significantly impact neurodevelopmental outcomes, with affected children potentially

experiencing visual impairments, endocrine disorders, and cognitive delays. Prognosis varies widely depending on whether the SA is isolated or associated with other anomalies; isolated cases often have better outcomes compared to those with multiple associated malformations.^[3]

Prenatal diagnosis of SA is crucial for managing expectations and planning neonatal care. Ultrasound (US) is typically the first-line imaging modality for evaluating fetal brain structures.^[4] However, its limitations in providing detailed intracranial anatomy, especially in cases where fetal positioning or maternal factors impede visualization, often necessitate the use of fetal magnetic resonance imaging (MRI). Fetal MRI offers superior resolution and contrast, enabling the detection of subtle anomalies in the developing brain, including the absence or abnormal appearance of the septum pellucidum.^[5]

A particular challenge in the MRI diagnosis of SA is the occurrence of a 'pseudo-septum' phenomenon. This term refers to imaging artifacts where the medial edges of the lateral ventricles or other adjacent structures mimic the appearance of a normal cavum septum pellucidum.^[6] These false-positive signs can be misleading, especially on axial MRI scans, potentially complicating the diagnosis of septal agenesis. For instance, the pseudo-septum is often visualized as linear hypo intensities, which can be resolved through coronal imaging, thus providing a more accurate view of the absence of the true septal structures.^[7]

Despite the critical role of MRI in distinguishing such findings, there is a paucity of literature specifically addressing the imaging characteristics and clinical significance of the pseudo-septum phenomenon.^[8] Available studies often focus on broader aspects of septal anomalies without providing a detailed analysis of this diagnostic artefact.^[9,10] This gap in the literature underscores the need for systematic characterization of the pseudo-septum in fetal MRI, as misinterpretation can influence clinical decision-making, prenatal counselling, and the management of pregnancies where such anomalies are detected.^[11]

This study aims to address these gaps by characterizing the pseudo-septum appearance in fetal MRI among fetuses diagnosed with SA, evaluating its prevalence, distinguishing imaging features, and clinical implications. By providing a more nuanced understanding of this phenomenon, the study seeks to enhance diagnostic accuracy, improve prenatal counselling practices, and optimize perinatal care strategies for families facing the challenges of septal agenesis.

MATERIALS AND METHODS

Study Design and Setting: This was a retrospective observational study conducted at a tertiary care centre specializing in maternal and fetal medicine,

for period of 5 years between July 2019 and June 2023. The study was approved by the Institutional Ethics Committee, and written informed consent was obtained from the parents or guardians for the use of clinical data and imaging results.

Study Population

The study population consisted of pregnant women (N=95) referred for fetal MRI due to suspected central nervous system (CNS) anomalies, including those with potential septal agenesis (SA) (Figure 1). A total of 79 fetuses with confirmed or suspected SA on fetal MRI were included. Inclusion criteria comprised gestational age between 18 and 34 weeks at the time of MRI, confirmed CNS anomalies on prenatal ultrasound, and satisfactory imaging quality. Cases with significant motion artifacts, non-neurological abnormalities, or incomplete imaging data were excluded.

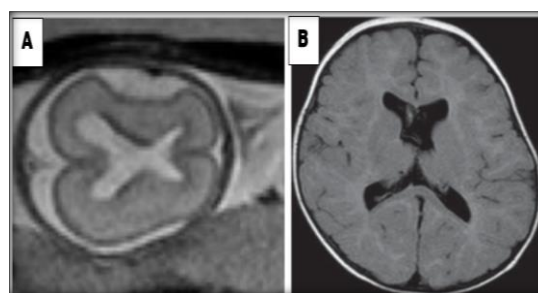


Figure 1: A. Fetal MRI Depicting the Appearance of the Pseudo-Septum Phenomenon (PSP) at 24 Weeks of Gestation. B. Postnatal MRI Confirming the Presence of PSP with Associated Ventriculomegaly and Agenesis of the Corpus Callosum.

Imaging Technique

Fetal MRI was performed using a 1.5-Tesla MRI scanner (Philips Ingenia 1.5T, manufactured by Philips Healthcare, India). Scanning was done without maternal sedation, following standard fetal MRI protocols that ensure safety for both the mother and fetus. T2-weighted, T1-weighted, and diffusion-weighted imaging sequences were acquired in axial, coronal, and sagittal planes. Key imaging parameters were as follows: T2-weighted imaging: TR/TE = 3000/120 ms, slice thickness = 3 mm, field of view (FOV) = 30 cm. T1-weighted imaging: TR/TE = 500/15 ms, slice thickness = 4 mm, FOV = 25 cm. Diffusion-weighted imaging (DWI): b-values = 0 and 1000 s/mm², slice thickness = 4 mm. Imaging was conducted during periods of fetal inactivity to reduce motion artifacts, with a total scan duration of approximately 20-30 minutes per patient. Coronal and sagittal sections were prioritized for better visualization of midline brain structures, including the septum pellucidum and corpus callosum.

Data Collection

Clinical data, including maternal age, gestational age at the time of imaging, parity, and history of previous pregnancies, were obtained from patient records. Imaging findings were reviewed

independently by two radiologists with over 10 years of experience in fetal imaging, who were blinded to each other's interpretations. Any discrepancies in their observations were resolved through a consensus meeting.

Characterization of the 'Pseudo-Septum'

The study focused on identifying the 'pseudo-septum' phenomenon, characterized by linear hypo intensities on axial T2-weighted images that simulate the appearance of the cavum septum pellucidum (CSP). Each case was assessed for the presence or absence of this feature, with coronal sections used as the reference to distinguish true septal structures from imaging artifacts. The analysis also included evaluating the relationship between the pseudo-septum phenomenon, gestational age, the degree of ventriculomegaly, and associated CNS anomalies, such as agenesis of the corpus callosum and optic nerve hypoplasia.

Outcome Measures

The primary outcome measure was the prevalence and characterization of the pseudo-septum phenomenon in fetuses diagnosed with SA on MRI. Secondary outcomes included the correlation between the pseudo-septum and associated CNS anomalies, and the sensitivity and specificity of MRI in differentiating true SA from pseudo-septum cases.

Data Analysis

Statistical analysis was performed using IBM SPSS Statistics version 25.0. Descriptive statistics summarized clinical and demographic data, presenting continuous variables such as maternal age and gestational age as means with standard deviations, while categorical variables were reported as frequencies and percentages. The prevalence of the pseudo-septum among fetuses with SA was calculated, and its association with clinical features (e.g., severity of ventriculomegaly, presence of associated anomalies) was assessed using chi-square tests for categorical variables and independent t-tests for continuous variables. Logistic regression analysis was used to determine factors associated with the presence of a pseudo-septum artifact. A p-value of <0.05 was considered statistically significant.

RESULTS

A total of 95 pregnant women were screened for this study, out of which 79 met the inclusion criteria and were enrolled. The mean maternal age was 26.7 ± 3.9 years, with an average gestational age of 24.1 ± 2.1 weeks at the time of the fetal MRI. Regarding parity, 41.8% (n = 33) were primigravida, and 58.2% (n = 46) were multigravida. A history of central nervous system (CNS) anomalies in previous pregnancies was reported in 5.1% (n = 4) of the participants. The main indications for performing fetal MRI included suspected septal agenesis (39.2%, n = 31), ventriculomegaly (32.9%, n = 26),

and other CNS anomalies (27.9%, n = 22). Additionally, 40.5% (n = 32) of the cases had other CNS anomalies detected on imaging. [Table 1]

Among the 79 cases analysed, septal agenesis was confirmed in 36.7% (n = 29) of the participants. The presence of a pseudo-septum was observed in 26.6% (n = 21) of cases, indicating a significant number of instances where a pseudo-septum may mimic or complicate the identification of true septal agenesis. Ventriculomegaly was present in 40.5% (n = 32) of the cases, suggesting a frequent association with other CNS anomalies. Agenesis of the corpus callosum was noted in 22.8% (n = 18), while optic nerve hypoplasia was identified in 7.6% (n = 6). Additionally, other associated anomalies were observed in 16.5% (n = 13) of the cases, highlighting the complex nature of CNS malformations detected through fetal MRI in this cohort. [Table 2]

The comparison between fetuses with true septal agenesis (SA) (n = 29) and those with a pseudo-septum (n = 21) revealed no significant difference in gestational age at diagnosis (23.8 ± 2.0 weeks vs. 24.3 ± 1.9 weeks, $p = 0.221$). Ventriculomegaly was common in both groups, with mild (41.4% vs. 33.3%), moderate (34.5% vs. 42.9%), and severe forms (24.1% vs. 23.8%) showing no significant difference ($p = 0.312$). Associated corpus callosum agenesis was more frequent in true SA (41.4%) compared to pseudo-septum (19.0%), but not significantly ($p = 0.082$). Optic nerve hypoplasia was observed in 13.8% of true SA cases and 9.5% of pseudo-septum cases ($p = 0.637$). [Table 3]

The presence of a pseudo-septum was significantly associated with ventriculomegaly, observed in 66.7% (n = 14) of cases with a pseudo-septum compared to 31.0% (n = 18) in those without ($p = 0.004$; OR: 4.2, 95% CI: 1.5-11.8). However, there was no significant association between pseudo-septum and agenesis of the corpus callosum (19.0% vs. 24.1%; $p = 0.621$; OR: 0.74, 95% CI: 0.22-2.4) or optic nerve hypoplasia (9.5% vs. 6.9%; $p = 0.712$; OR: 1.4, 95% CI: 0.24-8.2). [Table 4]

In this study, MRI showed a sensitivity of 81.0% (95% CI: 66.5% - 90.9%) for detecting septal agenesis, correctly identifying 34 out of 42 cases with the condition. The specificity was 69.2% (95% CI: 53.4% - 81.8%), with 27 out of 39 cases without septal agenesis correctly classified as negative. The positive predictive value (PPV) was 73.9% (95% CI: 59.7% - 84.7%), indicating that 73.9% of cases with a positive MRI result truly had septal agenesis. The negative predictive value (NPV) was 77.1% (95% CI: 60.9% - 88.1%), suggesting that 77.1% of cases with a negative MRI result were correctly identified as not having septal agenesis. Overall, the accuracy of MRI in diagnosing septal agenesis was 77.2% (95% CI: 66.6% - 85.4%), reflecting the proportion of true positive and true negative results among all cases. [Table 5]

The outcomes of fetuses with true septal agenesis (SA) (n = 29) were compared to those with a

pseudo-septum (n = 21). Postnatal survival rates were similar between the groups, with 72.4% in true SA cases and 81.0% in pseudo-septum cases (p=0.443). Neurodevelopmental delay was more common in the true SA group (31.0%) compared to the pseudo-septum group (9.5%), approaching

statistical significance (p=0.051). The need for surgical intervention was comparable between the groups, observed in 17.2% of true SA cases and 14.3% of pseudo-septum cases (p=0.782). Visual impairment was seen in 13.8% of true SA cases and 4.8% of pseudo-septum cases (p=0.262). [Table 6]

Table 1: Maternal and Fetal Characteristics of Study Population

Variables	Frequency (%) or mean ± SD
Maternal age (years)	26.7 ± 3.9
Gestational age at MRI (weeks)	24.1 ± 2.1
Parity	
Primigravida	33 (41.8%)
Multigravida	46 (58.2%)
History of CNS anomalies in previous pregnancies	4 (5.1%)
Indication for MRI	
Suspected SA	31 (39.2%)
Ventriculomegaly	26 (32.9%)
Other CNS anomalies	22 (27.9%)
Presence of other CNS anomalies	32 (40.5%)

Table 2: Distribution of Key Findings in Septal Agenesis and Pseudo-Septum Cases

Findings	Frequency (%)
Confirmed septal agenesis	29 (36.7%)
Presence of pseudo-septum	21 (26.6%)
Ventriculomegaly	32 (40.5%)
Agenesis of corpus callosum	18 (22.8%)
Optic nerve hypoplasia	6 (7.6%)
Other associated anomalies	13 (16.5%)

Table 3: Comparison of Imaging Characteristics between True Septal Agenesis and Pseudo-Septum

Imaging Characteristic	True SA (n = 29)	Pseudo-Septum (n = 21)	p-value
Gestational age at diagnosis (weeks)	23.8 ± 2.0	24.3 ± 1.9	0.221
Ventriculomegaly			
Mild	12 (41.4%)	7 (33.3%)	0.312
Moderate	10 (34.5%)	9 (42.9%)	
Severe	7 (24.1%)	5 (23.8%)	
Associated corpus callosum agenesis	12 (41.4%)	4 (19.0%)	0.082
Optic nerve hypoplasia	4 (13.8%)	2 (9.5%)	0.637

Table 4: Association of Pseudo-Septum with Other CNS Anomalies

Associated Anomaly	Presence of Pseudo-Septum (n = 21)	Absence of Pseudo-Septum (n = 58)	Odds Ratio (95% CI)	p-value
Ventriculomegaly	14 (66.7%)	18 (31.0%)	4.2 (1.5-11.8)	0.004
Agenesis of corpus callosum	4 (19.0%)	14 (24.1%)	0.74 (0.22-2.4)	0.621
Optic nerve hypoplasia	2 (9.5%)	4 (6.9%)	1.4 (0.24-8.2)	0.712

Table 5: Diagnostic Performance of MRI for Septal Agenesis

	Septal Agenesis Present (n=42)	Septal Agenesis Absent (n=39)
MRI Positive (n=46)	34 (TP)	12 (FP)
MRI Negative (n=35)	8 (FN)	27 (TN)
Diagnostic Metric	Value	95% CI
Sensitivity (%)	81.0%	66.5% - 90.9%
Specificity (%)	69.2%	53.4% - 81.8%
Positive Predictive Value (PPV) (%)	73.9%	59.7% - 84.7%
Negative Predictive Value (NPV) (%)	77.1%	60.9% - 88.1%
Accuracy (%)	77.2%	66.6% - 85.4%

Table 6: Postnatal Outcomes in True Septal Agenesis vs. Pseudo-Septum Cases

Outcome Measure	True SA (n = 29)	Pseudo-Septum (n = 21)	p-value
Postnatal survival	21 (72.4%)	17 (81.0%)	0.443
Neurodevelopmental delay	9 (31.0%)	2 (9.5%)	0.051
Need for surgical intervention	5 (17.2%)	3 (14.3%)	0.782
Visual impairment	4 (13.8%)	1 (4.8%)	0.262

DISCUSSION

This study offers critical insights into the differentiation between true septal agenesis (SA) and the pseudo-septum phenomenon using fetal MRI, significantly impacting prenatal counselling and management strategies. The prevalence of confirmed septal agenesis in our cohort (36.7%) aligns with previous studies, such as those by Sepulveda et al., and Nemcsik-Bencze et al., who reported similar prevalence rates of 30-40% in high-risk pregnancies.^[12,13] This consistency underscores the necessity for enhanced imaging protocols in such populations, as earlier detection can inform clinical management.^[14]

Our findings indicate a significant association between the presence of a pseudo-septum and ventriculomegaly, with 66.7% of pseudo-septum cases exhibiting this condition compared to only 31.0% in true SA cases (OR: 4.2, $p=0.004$). This result corroborates previous study by Nagaraj et al., and Di Mascio et al., which found that ventriculomegaly is often a confounding factor in assessing midline anomalies, complicating the differential diagnosis.^[15,16] The increased frequency of ventriculomegaly in pseudo-septum cases suggests that this phenomenon may mimic the imaging characteristics of true septal agenesis, leading to potential misinterpretations during prenatal assessments.^[17]

The diagnostic performance of MRI in our study revealed a sensitivity of 81.0% and a specificity of 69.2%, resulting in an overall accuracy of 77.2% (95% CI: 66.6% - 85.4%). These results align with findings by Hadjidekov et al., who reported a sensitivity of 85% for MRI in detecting fetal CNS anomalies, emphasizing MRI's role as a reliable screening tool.^[18] However, the relatively lower specificity observed in our cohort may reflect the challenge of distinguishing between true SA and pseudo-septum cases, echoing concerns raised by Kyriakopoulou et al., regarding the diagnostic ambiguity in imaging studies of fetal brain anomalies.^[19]

Moreover, our study revealed a trend towards higher rates of neurodevelopmental delay in true SA cases (31.0% vs. 9.5% in pseudo-septum, $p=0.051$), which, while not statistically significant, is consistent with the literature. Prior studies, such as those by Ren et al., demonstrated that septal agenesis is frequently associated with adverse neurodevelopmental outcomes due to the disruption of normal cortical and subcortical development.^[20] Additionally, the lower incidence of visual impairment in both groups (13.8% for true SA vs. 4.8% for pseudo-septum, $p=0.262$) corresponds with findings from Zhang et al. (2021), who reported that while visual pathway anomalies can occur in various CNS conditions, they are not universally present.^[21]

Our study's findings highlight the critical need for meticulous imaging evaluation to differentiate

between true septal agenesis and pseudo-septum. By identifying the pseudo-septum phenomenon as a potential diagnostic challenge, we add to the growing body of evidence advocating for advanced imaging techniques. This is particularly relevant in resource-limited settings like rural India, where access to experienced radiologists may be scarce. Enhanced training for sonographers and radiologists, alongside the implementation of standardized protocols for MRI interpretation, could significantly improve diagnostic accuracy.^[22,23]

Furthermore, our study emphasizes the necessity for future research that explores the long-term neurodevelopmental trajectories of children diagnosed with these conditions.^[24] The modest sample size in our study may have limited the ability to detect subtle differences in outcomes; thus, larger cohort studies with longitudinal follow-up are warranted. Such studies should focus on a comprehensive assessment of neurodevelopmental outcomes, considering factors such as early interventions and the role of multidisciplinary care teams in optimizing developmental trajectories for these vulnerable populations.

CONCLUSION

In conclusion, this study elucidates the critical distinctions between true septal agenesis and the pseudo-septum phenomenon through comprehensive fetal MRI analysis. Our findings demonstrate that pseudo-septum cases are frequently associated with ventriculomegaly, complicating the diagnostic process. The sensitivity and specificity metrics highlight the need for enhanced imaging protocols and training to improve diagnostic accuracy, particularly in high-risk populations. Furthermore, the observed trends in neurodevelopmental outcomes necessitate continued investigation into long-term implications for affected infants. Overall, these insights are essential for refining prenatal diagnostic strategies and improving clinical management of fetal CNS anomalies.

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