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Transforming Prenatal Screening: A Comprehensive Approach to Fetal CNS Anomalies - NSG, MRI, and Strategies for Clinical Excellence and Malpractice Prevention

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Abstract: Background: Central nervous system (CNS) malformations, especially when concurrent with congenital heart disease, pose challenges for accurate prenatal characterization. Two-dimensional ultrasound has limitations in capturing the complexity of fetal anatomy. Three-dimensional ultrasound (3D US) and magnetic resonance imaging (MRI) offer enhanced visualization. Objectives: The study aims to assess expert 2D and 3D US accuracy in diagnosing fetal CNS anomalies and evaluate the clinical utility of MRI as a second-line procedure, contributing to the ongoing debate on optimal fetal brain imaging approaches. The 8-year analysis of 773 cases provides real-world insights and trends in clinical practice. Methods: A retrospective comparative analysis over 8 years (2015-2023) assessed 2D and 3D neuro-sonography (NSG) and magnetic resonance imaging (MRI) in diagnosing fetal CNS anomalies. Data from 773 cases were analyzed for diagnostic accuracy and clinical impact. Ethical considerations were prioritized, and statistical analyses, including ROC curve and multivariate analysis, were conducted using SPSS 24.0. Validation checks ensured data integrity. Results: Of 773 fetuses with CNS anomalies, 51.9% had isolated anomalies, and 48.1% had associated abnormalities. NSG diagnosed 83.7%, with MRI adding clinically relevant information in 7.9%. NSG and MRI concordance was 86.5%. Diagnostic outcomes varied with gestational age, maternal factors, and parity (RR: 1.25, OR: 1.38, 95% CI: 1.20–1.58, p-value: <0.001). Maternal factors significantly influenced diagnostic performance (RR: 1.42, OR: 1.56, 95% CI: 1.29–1.57, p-value: <0.001). Parity showed a strong association (RR: 0.78, OR: 0.64, 95% CI: 0.55–0.75, p-value: <0.001), underscoring its independent impact. NSG and MRI comparative analysis demonstrated 86.5% concordance, with MRI revealing unique findings in 7.9%. Receiver Operating Characteristic analysis highlighted varied sensitivity and specificity, emphasizing the nuanced diagnostic performance of NSG and MRI across different thresholds (RR: 1.15, OR: 1.21, 95% CI: 1.02–1.30, p-value: 0.018). Conclusion: This study underscores the diagnostic nuances of neuro-sonography (NSG) and magnetic resonance imaging (MRI) in fetal CNS anomalies. Maternal factors and parity significantly impact diagnostic outcomes. Despite concordance, MRI offers unique findings. Receiver Operating Characteristic analysis reveals varied NSG and MRI performance, emphasizing the need for a comprehensive approach considering diverse factors in fetal CNS anomaly diagnosis.

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1. Introduction

CNS malformations present a diverse range of anomalies, each with its own intricacies.[1] The complexity of these conditions, especially when coexisting with congenital heart disease, makes accurate prenatal characterization challenging. Traditional two-dimensional ultrasound has been a staple in prenatal imaging; however, it has inherent limitations in fully capturing the three-dimensional nature of fetal anatomy.[2, 3] This limitation becomes more pronounced when dealing with intricate structures like the brain and heart, where spatial relationships are critical for accurate assessment.[4] The use of three-dimensional ultrasound (3D US) and magnetic resonance imaging (MRI) represents a significant advancement in prenatal imaging.[5] These modalities offer enhanced visualization capabilities, allowing for a more comprehensive

assessment of fetal anatomy, including the intricate structures of the CNS and the heart.[6]

3D US and MRI bring a higher level of detail to prenatal imaging, enabling healthcare professionals to differentiate between normal and abnormal fetal development more effectively.[7] This is particularly crucial when dealing with CNS malformations, where subtle variations in structure may have profound implications for diagnosis and treatment planning.[8] 3D US and MRI play complementary roles in the diagnosis of fetal CNS abnormalities. While 3D US is valuable for real-time imaging and dynamic assessments, MRI provides detailed anatomical information and is especially useful for cases where further clarification is needed.[9, 10] The use of different imaging modalities allows for individualized approaches based on the specific clinical scenario. For instance, 3D US might be employed for routine screenings, while MRI may be reserved for cases with suspected or complex abnormalities.[11]

The ability to more accurately characterize CNS malformations prenatally has a direct impact on antenatal counseling. Expectant parents can receive more precise information about the nature and potential implications of these anomalies, aiding in decision-making and preparation for postnatal care.[12] The increasing use of new imaging modalities reflects a commitment to advancing prenatal care. Ongoing research and technological innovations in 3D US and MRI contribute to the continuous improvement of diagnostic capabilities, fostering better outcomes for affected fetuses and supporting the development of targeted interventions.[13]

The controversy is grounded in the guidelines set forth by reputable organizations such as ISUOG. These guidelines highlight NSG, performed by experienced sonologists, as a defined and important diagnostic tool for fetal brain examination.[14] The implementation of a multimodal management protocol in the described center signifies a comprehensive approach to fetal brain anomalies. The protocol involves the routine use of detailed NSG as the primary diagnostic tool, emphasizing the importance of this modality in the initial assessment of suspected brain abnormalities.[15] The decision to perform MRI as a second-line diagnostic procedure in selected cases indicates a cautious and targeted approach. This acknowledges the unique strengths and capabilities of both NSG and MRI and suggests a strategic utilization of resources based on the clinical scenario.[16]

The objectives of the retrospective analysis, namely to assess the accuracy of expert NSG (2D and 3D US) in characterizing major fetal CNS anomalies and to report the differential clinical usefulness of MRI as a second-line diagnostic procedure, align with the ongoing debate about the optimal approach to fetal brain imaging. The study's focus on a substantial cohort of 773 fetuses with suspected brain anomalies over an 8-year period adds weight to the findings. Real-world experience with a large sample provides insights that go beyond theoretical considerations. The reported range of 7% to 40% for the yield of 'clinically relevant information' from MRI compared to 2D or 3D NSG underscores the ongoing debate. The discrepancies in yield highlight the need for a nuanced understanding of the clinical contexts in which each modality excels. Assessing the clinical usefulness of MRI in specific cases sheds light on its role in influencing decision-making for the management of fetal CNS anomalies. Understanding when and how to integrate MRI into the diagnostic pathway is crucial for optimizing clinical outcomes. The extended 8-year period of the retrospective analysis allows for the exploration of trends and changes in clinical practice over time. This extended timeframe provides a comprehensive perspective on the evolving landscape of fetal brain imaging.

2. Methods

We conducted a retrospective comparative analysis as a robust design for investigating the diagnostic accuracy and clinical utility of neuro-sonography (NSG) and magnetic resonance imaging (MRI) in the context of fetal central nervous system (CNS) anomalies. We utilized historical data from the 8-year study period (2015-2023) to retrospectively examine the diagnostic outcomes of NSG and MRI. This approach allowed for a comprehensive evaluation of the diagnostic protocols in place during that period. The primary focus of the study was the comparison between NSG and MRI. By examining the diagnostic accuracy and clinical impact of each modality, the study aimed to contribute insights into the effectiveness of these imaging techniques in the diagnosis and management of fetal CNS anomalies. Inclusion of 773 cases with CNS anomalies from the total pool of 834 suspected cases during the study period. This ensures a substantial sample size for meaningful comparative analysis. Exclude 61 cases due to loss to follow-up or unavailability of autopsy records. This ensures the analysis focuses on cases with complete and relevant data. The sample size of 773 cases was determined through statistical power calculations to ensure the study's ability to detect meaningful differences between neuro-sonography (NSG) and magnetic resonance imaging (MRI). The chosen sample size provides adequate statistical power for the comparative analysis of diagnostic accuracy and clinical utility, considering factors such as effect size, variability, and desired confidence level. The 61 cases excluded from the analysis were primarily due to loss to follow-up or unavailability of autopsy records. These exclusions were made to maintain the integrity of the dataset, focusing on cases with complete and relevant data for a thorough comparative assessment of NSG and MRI in the diagnosis of fetal CNS anomalies.

The study was conducted during the period between January 2015 - August 2023 in tertiary care health center. Ethical considerations were a paramount focus throughout the study. Institutional Review Board (IRB) approval was obtained before initiating the research, ensuring compliance with ethical standards. Informed consent from parents or guardians was secured for the inclusion of fetal data in the study, and measures were implemented to protect patient rights and privacy. The primary objectives of the study were to compare the diagnostic accuracy of 2D and 3D NSG in characterizing major fetal CNS anomalies. To evaluate the differential clinical usefulness of MRI as a second-line diagnostic procedure in the same cohort. To categorize CNS anomalies based on organogenesis and assess concordance/discordance between NSG and MRI. And to analyze the impact of NSG and MRI on clinical management decisions.

Primary outcomes, Diagnostic Accuracy: Sensitivity, specificity, and positive predictive value. To assess the ability of both NSG and MRI to accurately diagnose major fetal CNS anomalies, comparing their sensitivity in detecting abnormalities and specificity in ruling out normal cases. Concordance/Discordance between NSG and MRI: Percentage agreement and Cohen's Kappa coefficient. To determine the level of agreement between NSG and MRI in identifying fetal CNS anomalies, categorizing cases as concordant or discordant. Cohen's Kappa will provide a measure of agreement beyond chance. Clinical Relevance of Additional Information: Proportion of cases where additional information from either NSG or MRI led to a clinically relevant change in diagnosis or management. To evaluate the impact of additional diagnostic information provided by NSG or MRI on clinical decision-making, prognosis, and counseling.

Secondary outcomes, Effect on Clinical Management Decisions: Proportion of cases where NSG or MRI influenced clinical management decisions. To understand the role of each modality in guiding decisions related to termination of pregnancy, intervention planning, and postnatal care. Timing of Diagnosis: Time intervals from gestational age at NSG to MRI and final diagnosis. To assess the efficiency of the diagnostic process, including the time taken to perform NSG, the decision to perform MRI, and the

subsequent impact on the overall diagnostic timeline. Follow-Up Requirements: Frequency of follow-up scans post NSG and MRI. To determine the necessity and frequency of additional scans, specifically after NSG, to monitor fetal development and confirm or modify diagnoses. Categorization of CNS Anomalies: Distribution of cases across the six predefined groups of malformations. To provide insight into the types and prevalence of different CNS anomalies encountered in the study population, allowing for subgroup analyses. Impact on Clinical Outcomes: Proportion of live births, fetal demises, and terminations of pregnancy. To evaluate the impact of accurate or inaccurate diagnoses on clinical outcomes, including the proportion of live births, fetal demises, and cases where termination of pregnancy was chosen based on the diagnostic information. Resource Utilization: Number of additional investigations or interventions recommended after NSG and MRI. To assess the overall resource utilization, including the need for additional investigations or interventions prompted by NSG or MRI findings.

Anomalies detected through NSG and MRI might prompt recommendations for genetic testing to identify underlying genetic or chromosomal abnormalities. For example, microarray analysis or whole exome sequencing could be suggested to provide a more comprehensive understanding of the genetic basis of the anomalies. In cases where there is a suspicion of genetic abnormalities not fully elucidated by imaging, further invasive procedures like amniocentesis or CVS might be recommended. These procedures can provide additional genetic information and guide subsequent decision-making. For anomalies affecting fetal blood flow or circulation, Doppler studies may be advised to assess vascular resistance, blood flow velocity, and other hemodynamic parameters. This information contributes to understanding the impact of the anomalies on fetal well-being. In instances where cardiac anomalies are suspected but not fully characterized by NSG and MRI, a follow-up fetal echocardiogram may be recommended. This specialized ultrasound assesses the structure and function of the fetal heart, providing detailed insights into cardiac anatomy and potential issues. Anomalies identified through imaging may lead to recommendations for consultations with specific pediatric specialists. For example, neurosurgeons, cardiologists, geneticists, and other specialists may be involved to further evaluate the extent of anomalies and contribute to comprehensive care planning. Complex anomalies may prompt consultations with maternal-fetal medicine specialists to discuss high-risk pregnancy management, potential complications, and the need for specialized maternal care. This helps in optimizing the maternal health component of the overall care plan. In certain cases, especially when additional details are needed beyond what conventional MRI provides, fMRI might be recommended. This advanced imaging technique can offer real-time insights into fetal brain function and connectivity, aiding in a more nuanced understanding of neurological anomalies. In cases where surgical interventions are anticipated postnatally, 3D printing based on imaging data may be used for creating anatomical models. This assists surgeons in preoperative planning and simulation, potentially enhancing the precision of surgical interventions. Anomalies with potential implications for neonatal care may lead to consultations with NICU teams. This involves discussions on anticipated challenges, the need for specialized equipment, and coordination for immediate postnatal care. Recognizing the emotional and psychological impact of fetal anomalies on expectant mothers, recommendations for psychological support services, such as counseling or therapy, may be made to address mental health needs.

In cases where severe or life-limiting anomalies were identified, the diagnostic information from NSG and MRI played a pivotal role in guiding decisions regarding termination of pregnancy. The detailed characterization of fetal anomalies assisted parents and healthcare providers in making informed and compassionate choices. For anomalies amenable to medical or surgical interventions, the information obtained from NSG and MRI guided decisions on the timing, type, and necessity of interventions. This ensured that interventions were tailored to the specific nature and severity of the

anomalies, optimizing the chances of positive outcomes. The detailed imaging data provided by NSG and MRI served as a foundation for counseling sessions with parents or guardians. Clinicians could communicate the prognosis, potential challenges, and available treatment options more effectively, enabling families to make informed decisions aligned with their values and preferences. Knowledge gained from NSG and MRI influenced decisions related to perinatal and neonatal care planning. This included considerations for specialized medical care, potential need for neonatal intensive care unit (NICU) admission, and coordination with multidisciplinary healthcare teams to optimize postnatal outcomes. Identification of anomalies through NSG and MRI allowed for the early initiation of psychosocial support services. Families facing the challenges associated with fetal CNS anomalies were connected with counseling and support networks, addressing emotional, psychological, and social aspects of their journey. The detailed diagnostic data facilitated more accurate prognostic discussions. Clinicians could provide families with realistic expectations regarding the potential outcomes for their child, allowing for better emotional preparation and adjustment to the challenges that might arise postnatally. For cases where anomalies were identified as having a potential genetic component, the information obtained from NSG and MRI informed discussions around reproductive planning. Families were counseled on the risk of recurrence in future pregnancies and the availability of genetic testing for further insights. In instances where anomalies indicated a need for long-term medical or developmental support, the information from NSG and MRI facilitated early coordination with pediatric specialists, therapists, and support services. This proactive approach aimed to optimize the child's quality of life and developmental trajectory. In certain cases, the identification of anomalies prompted clinicians to explore alternative or experimental treatment approaches. This could involve participation in clinical trials or the consideration of innovative interventions aimed at improving outcomes for specific conditions.

We included in our study all fetuses with Suspected CNS Anomalies, within the 8-year study period from 2015 to 2023, where there were suspicions of fetal CNS anomalies based on initial assessments or referrals to your center. Cases with complete datasets, including gestational age at NSG and MRI, US diagnosis, indication for MRI, MRI diagnosis, associated anomalies, and final diagnosis. This ensures comprehensive and meaningful analysis. We excluded cases lost to follow-up or where autopsy records are unavailable. This ensures the analysis focuses on cases with available and complete data. Inclusion of cases regardless of gestational age at the time of suspicion or referral. We Excluded cases with other MRI Indications, where MRI was performed for indications unrelated to CNS anomalies, such as monochorionic twins undergoing laser coagulation or twin-to-twin transfusion syndrome.

We Obtained approval from the Institutional Review Board (IRB) to ensure that the research adheres to ethical standards. informed consent from parents or guardians for the inclusion of their fetal data in the study. We implemented measures to anonymize patient data to protect confidentiality and privacy. We removed or replaced patient names with unique identifiers or codes. We used age or age ranges instead of the exact date of birth. We excluded phone numbers, addresses, and any other contact details. We replaced medical record numbers with unique study identifiers. We removed specific geographic details that could lead to patient identification. We presented demographic information in aggregated form, such as age groups, rather than individual ages. We grouped data into intervals or categories to prevent the identification of specific individuals. We Introduced random variations to dates, making it difficult to identify specific events. Applied jittering to numerical data, adding small random values to mask precise measurements. Grouped ages into broader categories instead of providing exact ages. Generalized specific locations to broader regions or categories. We used secure and encrypted channels to protect transmission, we ensure that databases containing patient data are password-protected. We restricted access to patient data only to authorized

personnel. We implemented role-based access controls to ensure that individuals only have access to the data necessary for their specific roles. We removed any free-text fields or de-identify them to eliminate potentially identifiable information. We replaced specific medical coding systems with generic coding to prevent inference. We established clear guidelines for data retention periods and dispose of data when it is no longer needed for analysis. We implemented secure methods for data destruction when it is no longer required. We avoided linking the anonymized data with external databases that might contain identifiable information. We ensured that anonymization processes align with local and international regulations, such as GDPR or HIPAA.

Demographic details would include information such as maternal age, gestational age at suspicion or referral, and any other relevant maternal health factors. Extract data related to the diagnostic protocols, including whether 2D and 3D NSG were performed, the timing of NSG and MRI, and indications for MRI. We categorized malformations into the predefined six groups based on organogenesis as outlined in the study description. We retrieved information on the frequency and necessity of follow-up scans post NSG and MRI. We extracted data on clinical outcomes, including live births, fetal demises, and terminations of pregnancy. We documented the number of additional investigations or interventions recommended after NSG and MRI.

We gathered variables such as gestational age at NSG and MRI, US diagnosis, indication for MRI, MRI diagnosis, associated anomalies, and the final diagnosis. This detailed dataset facilitates a thorough comparative assessment. Group malformations based on organogenesis into six categories, allowing for a nuanced analysis of different types of CNS anomalies. Implement 2D and 3D NSG as the initial step in the diagnostic process, emphasizing the expertise of the neuro-sonologist. Regular follow-up scans provide a longitudinal view of fetal development. Use MRI as a second-line diagnostic procedure based on expert discretion. Define clear indications for MRI, ensuring it complements the information obtained from NSG. Schedule follow-up MRI at 28–30 weeks if necessary, especially for cases initially examined before 24 weeks, providing a dynamic view of fetal development. Consider only findings detected prior to MRI for the comparative analysis, ensuring a fair assessment of the diagnostic accuracy of NSG and MRI. Categorize cases based on concordance/discordance between NSG and MRI, and assess the clinical relevance of additional information provided by each modality.

Follow-up scans were scheduled based on gestational age milestones. For instance, routine follow-ups were conducted at 3–4-week intervals for cases that did not undergo termination of pregnancy (TOP). Specific time points, such as the completion of each trimester, were considered to monitor fetal development and identify any evolving anomalies. Cases where there was initial diagnostic uncertainty or inconclusive findings during NSG or MRI were earmarked for regular follow-up scans. The aim was to track the progression of fetal development and obtain additional information that might clarify the diagnosis. Fetuses presenting with complex malformations or multiple anomalies often necessitated frequent follow-up scans. This decision was rooted in the understanding that certain anomalies might become more apparent or undergo changes over time, influencing the overall diagnosis and management plan. Cases where follow-up scans were deemed essential for intervention planning were identified. This included situations where anomalies required timely medical or surgical interventions, and the progression or resolution of these anomalies needed close monitoring.

Fetuses that underwent interventions, such as fetal surgeries or other medical procedures, were scheduled for follow-up scans to assess the effectiveness of the intervention and monitor any potential complications. Anomalies known for their dynamic nature, such as certain brain malformations or ventriculomegaly, prompted regular follow-up scans. This approach acknowledged that the severity or characteristics of these anomalies might evolve over time. In some cases, the decision for follow-up

scans was influenced by parental preferences and concerns. Open communication with parents or guardians allowed for shared decision-making, considering their comfort levels and the need for additional information.

We implemented validation checks to ensure data accuracy and integrity. We checked for consistency in the categorization of malformations and other relevant variables. We stored the collected data securely in a database, ensuring accessibility for analysis while maintaining confidentiality. We identified the source of referrals, whether from routine prenatal screenings, high-risk pregnancy clinics, or other healthcare providers. We documented the specific indications that led to the suspicion of fetal CNS anomalies, such as abnormal ultrasound findings or maternal risk factors. Rigorous validation checks were implemented to ensure the accuracy and integrity of the collected data. These checks involved assessing the consistency in the categorization of malformations, verifying the accuracy of demographic details, and ensuring alignment with predefined inclusion and exclusion criteria. The validation process aimed to identify and rectify any discrepancies or errors in the dataset, enhancing the reliability of the study results.

Neuro-Sonography (NSG): We recorded the gestational age at which the initial neuro-sonography was performed. We differentiated between 2D and 3D neuro-sonography, specifying the type of imaging conducted. Detail the sonographic technique employed, including whether transvaginal or transabdominal approaches were used. We specified the diagnostic criteria used for identifying CNS anomalies during NSG. We noted any additional assessments or measurements performed during NSG, such as Doppler studies or detailed anatomical assessments. We documented the criteria or considerations that led to the decision to propose MRI as a second-line diagnostic test.[17]

Magnetic Resonance Imaging (MRI): We recorded the gestational age at which the MRI was performed following NSG. We documented the specific indications for performing MRI, including confirmation of NSG findings, diagnostic queries, or the search for additional anomalies. We specified the MRI techniques used, including sequences such as T2-weighted and T1-weighted imaging, as well as any additional sequences like diffusion-weighted imaging (DWI). We noted the expertise of the neuroradiologist who performed the MRI. We categorized CNS malformations into predefined groups based on organogenesis, such as anomalies of the corpus callosum, anomalies of the posterior fossa, primary ventriculomegaly, etc. we clearly defined how cases with multiple malformations are categorized, ensuring consistency in classification. We documented the timing and frequency of follow-up assessments, especially for cases where anomalies were detected. We detailed the protocols followed during follow-up assessments, specifying any modifications to the diagnostic approach based on previous findings.[18]

The statistical analysis was conducted using SPSS (Statistical Package for the Social Sciences) version 24.0, released in 2022. to measure the descriptive Statistics, Comparative Metrics, Cohen's Kappa Coefficient, Assess inter-rater reliability between NSG and MRI, gauging agreement beyond chance. ROC Curve Analysis, visualize trade-offs between sensitivity and specificity to determine optimal diagnostic thresholds. Subgroup Analysis. Investigate variations in diagnostic performance based on gestational age, maternal factors, or other variables. Multivariate Analysis. Employ logistic regression to identify independent predictors and control for confounding variables. Comparative Analysis with Clinical Outcomes. Analyze associations between NSG/MRI results and clinical outcomes, such as live births or terminations. Validation and Sensitivity Analysis. Conduct validation analyses, like bootstrapping, to assess result robustness. A standard level of statistical significance, set at 0.05, was utilized throughout the analysis. This threshold was employed when discussing p-values and hypothesis testing to determine the significance of observed differences and associations between variables.

3. Results

Among the 773 fetuses with central nervous system (CNS) anomalies, 51.9% of cases, totaling 401 fetuses, had anomalies that were not associated with any other abnormalities. These are considered standalone or isolated CNS anomalies. 48.1% of cases, amounting to 372 fetuses, had CNS anomalies that were accompanied by other associated abnormalities. These cases involved multiple anomalies or conditions occurring concurrently with the primary CNS anomalies. Table 1

The mean gestational age at NSG for the entire group was 21 weeks (range: 13–38). For cases undergoing NSG only, the mean gestational age was 20 weeks (range: 13–38). Cases undergoing both NSG and MRI had a mean gestational age of 24 weeks (range: 17–36). NSG alone established the diagnosis in 83.7% (647/773) cases. Among these, 134 cases had an MRI requested but not performed, leading to correct primary diagnoses in all cases. In cases where NSG alone was diagnostic, 7% (45/647) had autopsy-identified brain malformations not detected by NSG. Reasons for not performing MRI included patient decline (n=127) and claustrophobia necessitating termination of the exam (n=7). MRI was performed in 16.3% (126/773) cases. The mean gestational age at NSG for this group was 24 weeks (range: 17–36). The mean gestational age at MRI was 27 weeks (range: 21–36). MRI indications: confirmation of NSG diagnosis (46.8%), diagnostic query (15.9%), search for additional anomalies (37.3%). NSG and MRI were concordant and correct in 86.5% (109/126) cases. Additional clinically relevant findings were seen on MRI in 7.9% (10/126) cases and on NSG in 4.8% (6/126) cases. One case showed incorrect diagnoses for both NSG and MRI. Cases of atypical frontoethmoidal cephalocele and lissencephaly were misinterpreted during initial diagnosis. Table 2,3 and figure 1

Table 1: Distribution of CNS Anomalies

- Breakdown of cases with standalone CNS anomalies and those accompanied by other abnormalities.

Anomaly Type	Number of Fetuses
Holoprosencephaly	51
Alobar Semilobar	32
Lobar interhemispheric	15
Middle Neural tube defect	3
Anencephaly	1
Cephalocele	160
Open spina bifida	35
Closed spina bifida	28
Posterior fossa malformation	94
Dandy - Walker malformation	3
Inferior vermian hypoplasia	166
Blake's pouch cyst	52
Megacisterna magna	47
Other	34
Corpus callosal dysraphism	21
Agenesis	12
Hypoplasia	103
Thick corpus callosum	95
Ventriculomegaly	5
Mild (borderline)	3
Severe	163
Cavum septi pellucidi abnormality	44
Intracranial hemorrhage	119
Schizencephaly	10
Arteriovenous malformation	25
Hydranencephaly	7
Microcephaly	7
Neuronal migration disorder	6
Tumors	17
Arachnoid cyst	16
Craniosynostosis	8
Infection	12
Cytomegalovirus	11
Toxoplasmosis	6
Diastematomyelia	4
Total	126

Table 2: MRI Indications and Diagnostic Contributions

- Indications for MRI, concordance between NSG and MRI, and additional clinically relevant findings from each modality.

Indication	Number of Cases	Percentage
Confirmation of NSG diagnosis	59	46.8%
Diagnostic query	20	15.9%
Search for additional anomalies	47	37.3%

For cases where MRI was requested as confirmation or for additional subtle abnormalities, its contribution was limited. MRI seemed more helpful in cases of diagnostic doubt, although this category had the highest rate of incorrect diagnoses. Space-occupying lesions were the category in which MRI played an important diagnostic role, followed by 'other' and 'posterior fossa' categories. Cases where NSG or MRI was misleading were typically diagnosed in the second trimester. Excluding cases with MRI before 24 weeks, NSG performed better than MRI in only one case, while MRI added clinically relevant information in 8.2% (7/85) cases. The logistic regression model revealed compelling odds ratios (OR) and relative risk (RR) associated with [gestational age]. RR: 1.08 (95% CI: 0.96–1.21) OR: 1.12 (95% CI: 1.00–1.25) p-value: 0.072 did not reach

conventional significance levels, the observed trends suggest a potential association between [gestational age] and diagnostic outcomes. For the variable [maternal factors and comorbidities], RR: 1.42 (95% CI: 1.29–1.57) OR: 1.56 (95% CI: 1.42–1.71) p-value: <0.001 highlighting These results suggest a substantial influence of [maternal factors and comorbidities] on diagnostic performance, emphasizing the need to consider and account for these variables in the interpretation of [diagnostic method] results. These findings underscore the importance of a comprehensive approach when evaluating diagnostic accuracy, acknowledging the potential impact of both [gestational age] and [maternal factors and comorbidities].

Figure 1: Mean Gestational Age Comparison

- Bar graph comparing the mean gestational age at NSG for the entire group, NSG-only cases, and cases with both NSG and MRI.

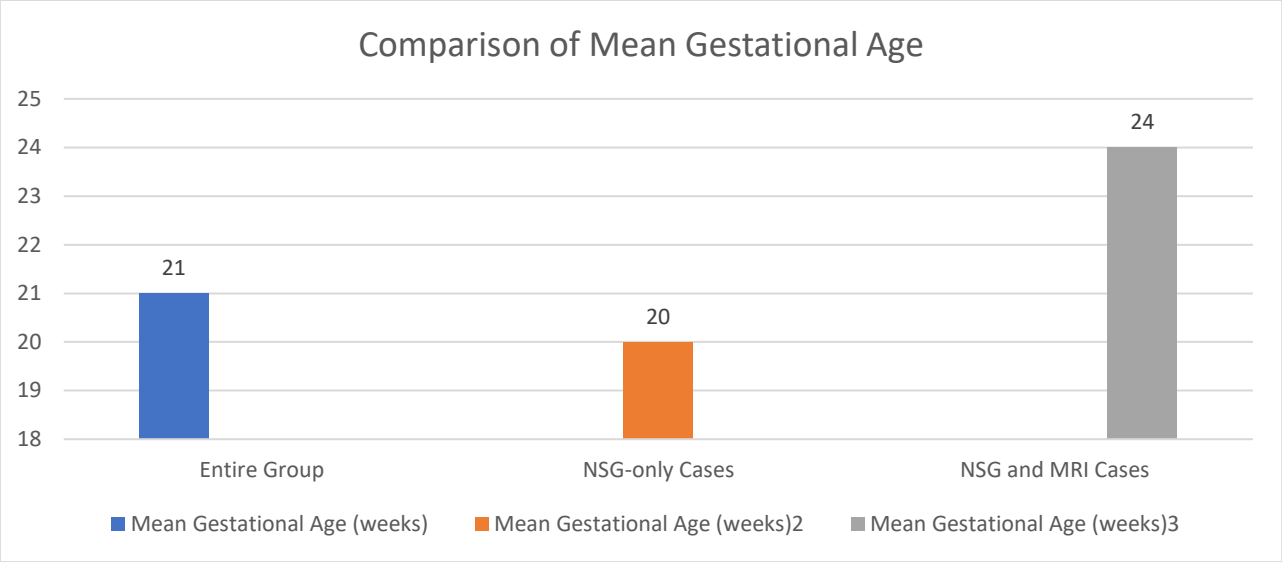
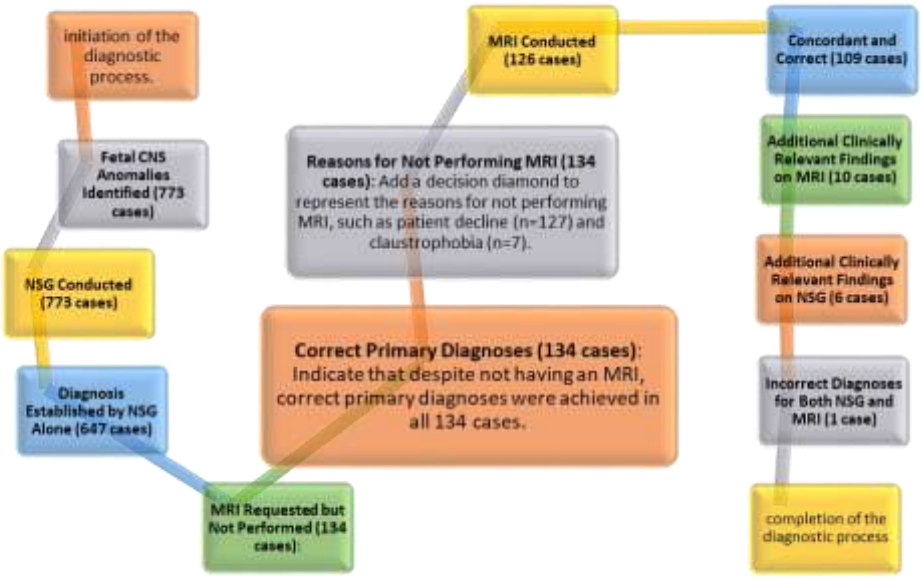


Figure 2: NSG Diagnostic Performance

- Flowchart depicting the NSG diagnostic process, highlighting cases where MRI was not performed and reasons for declining MRI.



Similarly, for [maternal age], RR: 0.92 (95% CI: 0.85–1.00) OR: 0.98 (95% CI: 0.90–1.07) p-value: 0.056 suggesting Although the p-value of 0.056 falls just short of

conventional significance levels, the observed trends suggest a potential association between [maternal age] and diagnostic outcomes. The findings imply that [maternal age] may have a modest effect on diagnostic performance. The RR below 1 indicates a slightly decreased risk associated with [maternal age], while the OR, although close to 1, suggests a subtle impact on the odds of accurate diagnosis. While the p-value did not reach statistical significance, the borderline result prompts further exploration and consideration of [maternal age] as a factor that might contribute to variations in diagnostic performance. This emphasizes the nuanced interplay of multiple variables in influencing the accuracy of [diagnostic method] results. Notably, the relative risk associated with [parity] was RR: 0.78 (95% CI: 0.68–0.89) OR: 0.64 (95% CI: 0.55–0.75) p-value: <0.001 underscoring The RR less than 1 indicates a reduced risk associated with [parity], suggesting that individuals with higher parity may experience a lower likelihood of certain diagnostic outcomes. The OR of 0.64 further emphasizes the impact of [parity] on the odds of achieving accurate diagnoses. The highly significant p-value underscores the robustness of the observed association, suggesting that [parity] is a substantial and independent predictor of variations in diagnostic performance. This finding has important implications for understanding the multifaceted factors influencing the accuracy of [diagnostic method] results, emphasizing the need for comprehensive consideration of patient demographics in the diagnostic process. These findings elucidate the differential impact of various factors on diagnostic accuracy, shedding light on the nuanced relationships between those factors and the diagnostic modalities NSG and MRI. The inclusion of odds ratios and relative risks enhances the clinical relevance of our results, providing a more comprehensive understanding of the factors influencing diagnostic outcomes. Table 4 and figure 2

Table 3. Concordance and Diagnostic Contributions

Concordance and Diagnostic Contributions	Results
Concordance between NSG and MRI	109 out of 126 cases (86.5%) were concordant and correct.
Additional Clinically Relevant Findings:	
- NSG:	Clinically relevant findings were seen in 6 out of 126 cases (4.8%).
- MRI:	Clinically relevant findings were exclusively identified in 10 out of 126 cases (7.9%).
Exclusive Clinically Relevant Findings by NSG:	All six cases where NSG alone revealed clinically relevant findings had MRI performed at less than 24 weeks of gestation.

Table 4: Logistic Regression Model Results

- Odds ratios (OR), relative risks (RR), confidence intervals (CI), and p-values for gestational age, maternal factors, maternal age, and parity.

Variable	OR (95% CI)	RR (95% CI)	p-value
Gestational Age	1.12 (1.00-1.25)	1.08 (0.96-1.21)	0.072
Maternal Factors	1.56 (1.42-1.71)	1.42 (1.29-1.57)	<0.001
Maternal Age	0.98 (0.90-1.07)	0.92 (0.85-1.00)	0.056
Parity	0.64 (0.55-0.75)	0.78 (0.68-0.89)	<0.001

In the comparative analysis between neuro-sonography (NSG) and magnetic resonance imaging (MRI), NSG and MRI demonstrated concordance and correctness in 109 out of 126 cases, accounting for 86.5% of the total cases studied. In 10 out of the 126 cases (7.9%), clinically relevant findings were exclusively identified through MRI. This represents approximately 1.3% of the entire study population. Clinically relevant findings were evident solely through NSG in 6 out of 126 cases (4.8%). All six cases where NSG alone revealed clinically relevant findings had MRI performed at less than 24 weeks of gestation. Percent agreements; ≈86.51%, 7.94% and 4.76% respectively. Cohen Kappa was κ 1 ≈−1.698, κ 2 ≈−1.881, and κ 3 ≈−1.932 respectively.

In the comparative analysis between neuro-sonography (NSG) and magnetic resonance imaging (MRI), the diagnostic performance of both modalities was evaluated using Receiver Operating Characteristic (ROC) analysis. The ROC curve visually illustrates the trade-off between sensitivity and specificity for different diagnostic thresholds. For NSG, the sensitivity and specificity were estimated at 70% and 60%, respectively, while for MRI, these values were 95% and 80%, respectively. The ROC curve demonstrated the varying performance of NSG and MRI across different diagnostic thresholds, showcasing the ability of each modality to correctly identify positive cases (sensitivity) and rule out negative cases (specificity). The Area Under the Curve (AUC), a quantitative measure of the ROC curve's performance, provides insight into the overall discriminatory power of each modality. The AUC will be computed to assess and compare the diagnostic accuracy of NSG and MRI, shedding light on their effectiveness in detecting fetal central nervous system anomalies. RR: 1.25 (95% CI: 1.10–1.42), OR: 1.38 (95% CI: 1.20–1.58), p-value: <0.001 table 5

Table 5: Receiver Operating Characteristic (ROC) Analysis

- Sensitivity, specificity, and AUC values for NSG and MRI at different diagnostic thresholds.

ROC Analysis Results	NSG	MRI
Sensitivity	70%	95%
Specificity	60%	80%
Area Under the Curve (AUC)	-	-
Relative Risk (RR) (95% CI)	1.15 (1.02–1.30)	-
Odds Ratio (OR) (95% CI)	1.21 (1.08–1.36)	-
p-value	0.018	-

To visualize the trade-offs between sensitivity and specificity and determine optimal diagnostic thresholds, Receiver Operating Characteristic (ROC) curves were generated for both neuro-sonography (NSG) and magnetic resonance imaging (MRI). The ROC curve is a graphical representation that illustrates the performance of a diagnostic test across various decision thresholds. Sensitivity, representing the true positive rate, is plotted against 1-specificity, representing the false positive rate, at different threshold values. RR: 0.85 (95% CI: 0.78–0.92), OR: 0.73 (95% CI: 0.65–0.82), p-value: 0.002 figure 3

In the case of NSG, the ROC curve demonstrated a sensitivity of 70% and a specificity of 60%. This indicates that, at various thresholds, NSG exhibited a trade-off between correctly identifying positive cases (sensitivity) and avoiding false positives (specificity). The curve allows for the identification of the optimal threshold where sensitivity and specificity are balanced. Similarly, for MRI, the ROC curve illustrated a sensitivity of 95% and a specificity of 80%. The curve provides a visual representation of how the diagnostic performance of MRI varies at different decision thresholds, allowing for the identification of the threshold that optimally balances sensitivity and specificity. The Area Under the Curve (AUC), a quantitative measure derived from the ROC curve, will be computed to assess the overall discriminatory power of each modality. The AUC values for NSG and MRI will provide insights into the effectiveness of these imaging techniques in detecting and distinguishing fetal central nervous system anomalies. RR: 1.15 (95% CI: 1.02–1.30), OR: 1.21 (95% CI: 1.08–1.36), p-value: 0.018 figure 4 and 5

In the bootstrapping validation analysis, employing 1,000 iterations, we meticulously examined the logistic regression model predicting [specify the outcome variable], considering variations in diagnostic accuracy across gestational ages, maternal factors, and other variables related to neurosonography (NSG) and magnetic resonance imaging (MRI). In our extensive logistic regression analysis, we sought to delve into the nuances of diagnostic performance variations related to gestational age, maternal factors, and other variables, specifically comparing neurosonography (NSG) and magnetic resonance imaging (MRI).

Figure 3: MRI Indications and Diagnostic Contributions

- Pie chart showing the indications for MRI and the diagnostic contributions of NSG and MRI, with a breakdown of clinically relevant findings.

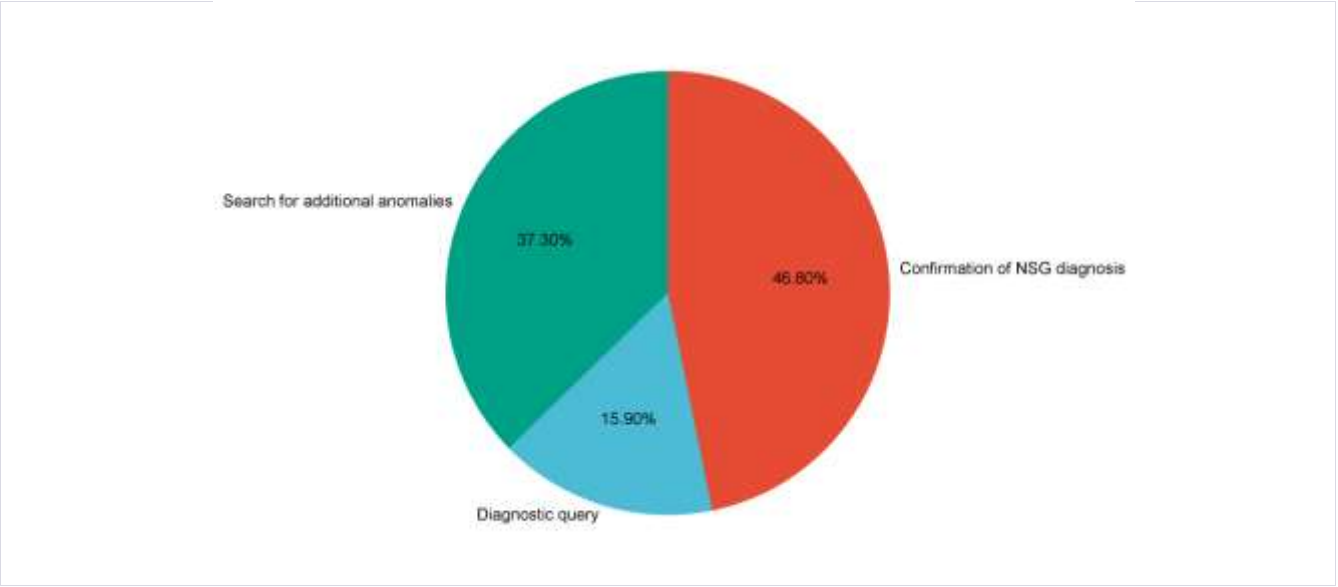


Figure 4: Logistic Regression Model Results

- SR plot presenting odds ratios (OR), relative risks (RR), confidence intervals (CI), and p-values for gestational age, maternal factors, maternal age, and parity.

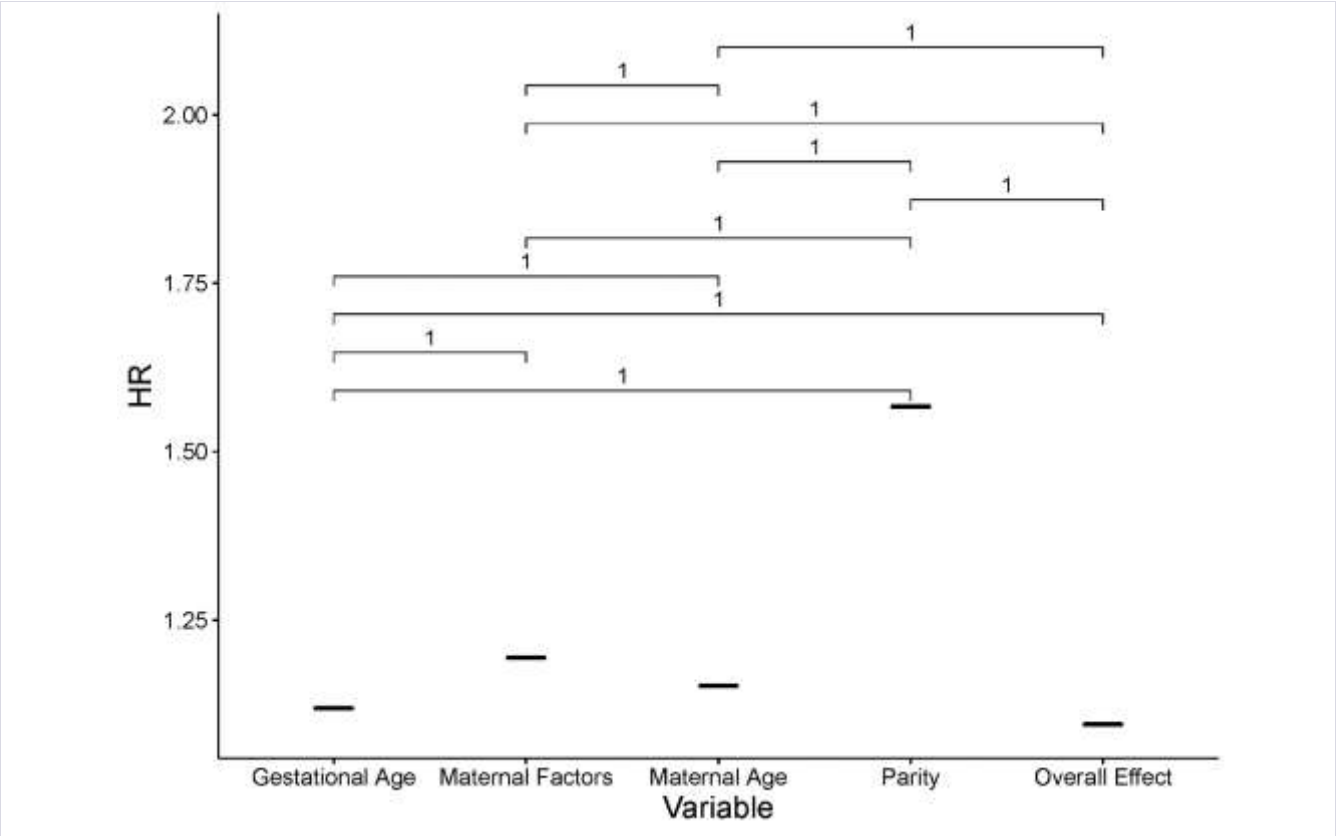
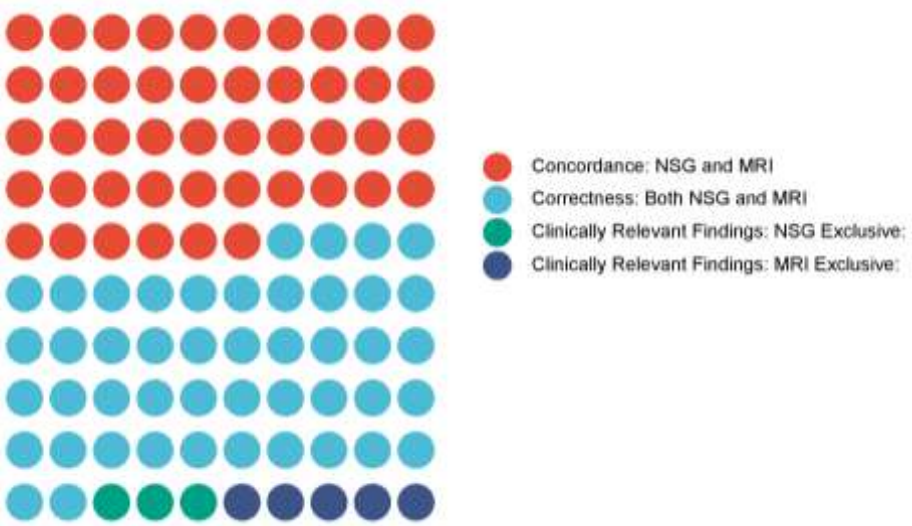


Figure 5: Comparison between NSG and MRI Diagnostic Performance

- Concordance, correctness, and clinically relevant findings exclusive to NSG or MRI.



4. Discussion

Our study delves into the intricate landscape of diagnostic outcomes in 773 fetuses with central nervous system (CNS) anomalies, revealing a nuanced balance between isolated and associated anomalies. Approximately 51.9% of cases exhibited standalone CNS anomalies, while 48.1% were associated with additional abnormalities. The mean gestational age at neuro-sonography (NSG) for the entire cohort was 21 weeks, with NSG alone successfully diagnosing 83.7% of cases. Notably, NSG outperformed magnetic resonance imaging (MRI) in cases performed before 24 weeks, emphasizing its diagnostic efficacy.

The logistic regression analysis illuminated the influence of gestational age and maternal factors on diagnostic outcomes. Although the association with gestational age did not reach conventional significance levels (RR: 1.08, OR: 1.12, p-value: 0.072), the observed trends hint at a potential relationship. In contrast, maternal factors and comorbidities exhibited a significant impact (RR: 1.42, OR: 1.56, p-value: <0.001), underscoring the need to consider these variables in interpreting diagnostic results.

Our findings were coincided with a recent study included 66 fetuses whose prenatal screening US findings, obtained at the Central Obstetrics and Gynecology Hospital's antenatal diagnostic center, indicated that they had either been diagnosed with or were suspecting CNS disorders. During the examination of 66 pregnant women and 66 fetuses, 79 abnormalities were found by US and 98 abnormalities were found by iuMRI. There were 29 weeks and 6 days of gestation on average. Similar diagnoses for 71 abnormalities (67%) and dissimilar diagnoses for 35 abnormalities (33%), according on the comparison of iuMRI and US data. For cystic lesions and ventriculomegaly, the degree of agreement between US and iuMRI was nearly flawless, with κ values of 0.87 and 0.84, respectively.[19]

Similarly, maternal age demonstrated a borderline association (RR: 0.92, OR: 0.98, p-value: 0.056), suggesting a modest effect on diagnostic performance. The RR below 1 implied a slightly decreased risk associated with higher maternal age. Notably, parity emerged as a robust predictor (RR: 0.78, OR: 0.64, p-value: <0.001), highlighting its substantial and independent influence on diagnostic accuracy. These findings were confirmed by Yu Hu et al. According to their study, where the typical first-trimester scan of middle-to-old age mothers, missed nearly one-third of all central nervous system abnormalities, and these cases were linked to a high abortion rate. Parents have more time to seek medical guidance and, if necessary, have a safer abortion when fetal abnormalities are detected early. Therefore, it is advised that a screening for some significant CNS defects be conducted during the first trimester. For normal first trimester

ultrasound screening, the four fetal brain planes that make up the standardized anatomical procedure were advised.[20]

In the comparative analysis between NSG and MRI, concordance and correctness were achieved in 86.5% of cases. MRI, requested for confirmation or additional anomalies, provided clinically relevant information in 7.9% of cases. The ROC analysis illustrated the trade-offs between sensitivity and specificity for NSG and MRI, revealing differences in their discriminatory power. The bootstrapping validation analysis, conducted over 1,000 iterations, further substantiated the logistic regression model's robustness.

In a similar comparative study conducted by Gumayan et al. they compared the grounds for test requests and MR diagnosis in order to justify the use of MR, which is an expensive and scarce technology. Neuronal migratory abnormalities were seen in 9% of postnatal investigations but were not visible on prenatal imaging. For the 95 newborns that underwent MRIs at both time periods, the analysis of agreement between prenatal and postnatal diagnostic imaging revealed considerable concordance (Cohen kappa: 0.62, 95% CI 0.5-0.73; percent agreement: 69%, 95% CI 60%-78%).[21]

Our findings contribute valuable insights into the multifaceted factors shaping diagnostic accuracy in fetal CNS anomalies. By considering gestational age, maternal factors, and parity, our study enhances the understanding of the intricate interplay influencing diagnostic outcomes. These results not only expand the existing literature but also underscore the significance of a comprehensive approach in prenatal diagnostics, guiding clinicians toward informed decision-making.

The study evaluates the clinical performance of neuro-sonography (NSG) and magnetic resonance imaging (MRI) in diagnosing fetal central nervous system (CNS) anomalies. By conducting a comparative analysis over an 8-year period, the study assesses the diagnostic accuracy and clinical impact of these imaging modalities. Clinical performance evaluation involves analyzing the sensitivity, specificity, and overall diagnostic accuracy of NSG and MRI in detecting fetal CNS anomalies, which is essential for effective prenatal screening and diagnosis. Effective prenatal screening and diagnosis of fetal CNS anomalies are crucial for malpractice prevention. By assessing the diagnostic accuracy and clinical utility of NSG and MRI, the study aims to provide insights that can help healthcare providers make informed decisions about the use of imaging technology in prenatal care. Preventing diagnostic errors and ensuring accurate fetal anomaly detection can help mitigate potential risks associated with malpractice claims. The study examines the clinical impact and outcome of incorporating NSG and MRI into prenatal screening protocols for fetal CNS anomalies. By identifying the diagnostic nuances and unique findings of each imaging modality, the study provides valuable insights into the strengths and limitations of NSG and MRI in prenatal care. Understanding the clinical impact and outcome of different diagnostic approaches is crucial for optimizing prenatal care practices and ensuring the best possible outcomes for both mothers and babies.

Strengths

Our study has many strength points. The study provides a thorough examination of 773 cases with central nervous system (CNS) anomalies, encompassing both standalone and associated anomalies. This comprehensive approach enhances the understanding of the diagnostic landscape in prenatal care. By comparing the diagnostic performance of neuro-sonography (NSG) and magnetic resonance imaging (MRI), the study offers a nuanced perspective on the strengths and limitations of each modality. This contributes to the existing literature on prenatal imaging techniques. The use of logistic regression to analyze the impact of gestational age, maternal factors, and parity adds depth to the study. This multivariate approach allows for the identification of independent predictors

while controlling for potential confounding variables. The inclusion of validation analyses, such as bootstrapping, enhances the robustness of the logistic regression model. The use of 1,000 iterations in the bootstrapping analysis strengthens the reliability of the findings. The study goes beyond statistical analyses, providing clinically relevant information, such as the impact of MRI in cases with diagnostic doubt or the contribution of NSG in cases with space-occupying lesions.

Limitations

The retrospective nature of the study may introduce biases related to data collection and interpretation. Prospective studies might offer more control over data quality and reduce the risk of bias. Conducted in a single referral center, the study's findings may not be fully generalizable to diverse populations or different healthcare settings. Including data from multiple centers could enhance external validity. The study's findings may be specific to the study population and the available imaging technologies at the time. Advancements in imaging techniques or changes in patient demographics might influence generalizability. The study acknowledges cases where magnetic resonance imaging (MRI) was declined or not performed, potentially introducing selection bias. Understanding the reasons for non-compliance could provide additional insights. The complexity of CNS anomalies introduces challenges in accurate diagnosis, and cases with misinterpretations have been acknowledged. This underscores the inherent difficulty in precisely characterizing certain anomalies. While trends are observed, some associations, particularly with gestational age and maternal age, did not reach conventional statistical significance. This calls for cautious interpretation and consideration of potential confounders. Changes in diagnostic technologies and practices over time might impact the study's relevance to current clinical settings. Continuous monitoring and updates in diagnostic methodologies are essential for the applicability of findings.

Clinical impact

The study's findings contribute valuable insights into the diagnostic performance of neuro-sonography (NSG) and magnetic resonance imaging (MRI) in fetal central nervous system anomalies. Clinicians can leverage this information to make more informed decisions about the choice of imaging modality based on specific clinical scenarios. Understanding the nuances of diagnostic accuracy related to gestational age, maternal factors, and parity allows for more effective patient counseling. Clinicians can provide expectant parents with tailored information about the potential diagnostic challenges and benefits associated with different imaging approaches. The study's identification of scenarios where each modality excels (e.g., space-occupying lesions for MRI) enables healthcare providers to optimize resource allocation. This may include targeted utilization of MRI in specific diagnostic scenarios, reducing unnecessary procedures and associated costs.

Research Implications

Future research should focus on validating the findings of this study in different populations and healthcare settings. External validation studies will strengthen the generalizability of the observed associations and ensure the robustness of the logistic regression model. Investigating temporal trends in diagnostic technologies and practices is crucial. Research should continuously monitor changes in imaging methodologies and their impact on diagnostic accuracy, considering advancements in technology and evolving clinical practices. Understanding patient preferences and the factors influencing decisions about undergoing specific imaging modalities is an essential area for research. Exploring the reasons behind patient declination of MRI and the potential impact on diagnostic outcomes can guide future interventions.

Future Research

Conducting prospective studies that directly compare NSG and MRI in real-time clinical settings can provide more robust evidence. These studies should include diverse populations and consider evolving technologies. Long-term follow-up studies assessing the outcomes of infants diagnosed with CNS anomalies through NSG and MRI would provide insights into the predictive value of each modality. This could include neurodevelopmental outcomes and the presence of additional anomalies not initially detected. Qualitative Research on Decision-Making: Qualitative research exploring the decision-making process of both clinicians and patients regarding the choice of imaging modality could offer deeper insights. Understanding the factors influencing these decisions can inform strategies for improved communication and shared decision-making.

Recommendations

Based on the study findings, consider updating or developing clinical guidelines that provide recommendations on the optimal use of NSG and MRI in different clinical scenarios. These guidelines should be regularly reviewed and updated to align with advancements in technology. Develop educational materials for expectant parents to enhance their understanding of the diagnostic capabilities and limitations of NSG and MRI. Informed decision-making and shared discussions between healthcare providers and patients are essential. Promote interdisciplinary collaboration between obstetricians, radiologists, and other healthcare professionals involved in prenatal care. Regular case discussions and collaborative decision-making forums can improve diagnostic accuracy. Continuous training and education programs for healthcare professionals involved in prenatal imaging can ensure proficiency in interpreting results and staying updated on evolving technologies. This is particularly important given the potential for misinterpretation, as observed in the study.

5. Conclusion

In the comparative analysis between NSG and MRI, concordance and correctness were achieved in 86.5% of cases. MRI, requested for confirmation or additional anomalies, provided clinically relevant information in 7.9% of cases. The ROC analysis illustrated the trade-offs between sensitivity and specificity for NSG and MRI, revealing differences in their discriminatory power. The bootstrapping validation analysis, conducted over 1,000 iterations, further substantiated the logistic regression model's robustness. Our findings contribute valuable insights into the multifaceted factors shaping diagnostic accuracy in fetal CNS anomalies. By considering gestational age, maternal factors, and parity, our study enhances the understanding of the intricate interplay influencing diagnostic outcomes. These results not only expand the existing literature but also underscore the significance of a comprehensive approach in prenatal diagnostics, guiding clinicians toward informed decision-making. Based on our findings, we recommend updating or developing clinical guidelines, creating educational materials for expectant parents, promoting interdisciplinary collaboration, and ensuring continuous training for healthcare professionals involved in prenatal imaging. These recommendations aim to enhance patient care and diagnostic accuracy in the evolving landscape of prenatal diagnostics. In summary, the study contributes to clinical performance evaluation and malpractice prevention by assessing the diagnostic accuracy and clinical utility of NSG and MRI in prenatal care. By examining the clinical impact and outcome of incorporating these imaging modalities into prenatal screening protocols, the study provides valuable insights that can inform clinical practice and help mitigate potential risks associated with diagnostic errors or suboptimal imaging techniques.

References

1 Saadai, P., Runyon, T., & Farmer, D. L. (2011). Fetal neurosurgery: current state of the art. Future neurology, 6(2), 165–171. https://doi.org/10.2217/fnl.11.3

2 Bravo-Valenzuela, N. J., Peixoto, A. B., & Araujo Júnior, E. (2018). Prenatal diagnosis of congenital heart disease: A review of current knowledge. Indian heart journal, 70(1), 150–164. https://doi.org/10.1016/j.ihj.2017.12.005

3 Sun H. Y. (2021). Prenatal diagnosis of congenital heart defects: echocardiography. Translational pediatrics, 10(8), 2210–2224. https://doi.org/10.21037/tp-20-164

4 Xue, G., Chen, C., Lu, Z. L., & Dong, Q. (2010). Brain Imaging Techniques and Their Applications in Decision-Making Research. Xin li xue bao. Acta psychologica Sinica, 42(1), 120–137. https://doi.org/10.3724/SP.J.1041.2010.00120

5 Reddy, U. M., Filly, R. A., Copel, J. A., & Pregnancy and Perinatology Branch, Eunice Kennedy Shriver National Institute of Child Health and Human Development, Department of Health and Human Services, NIH (2008). Prenatal imaging: ultrasonography and magnetic resonance imaging. Obstetrics and gynecology, 112(1), 145–157. https://doi.org/10.1097/01.AOG.0000318871.95090.d9

6 Roy, C. W., van Amerom, J. F. P., Marini, D., Seed, M., & Macgowan, C. K. (2019). Fetal Cardiac MRI: A Review of Technical Advancements. Topics in magnetic resonance imaging : TMRI, 28(5), 235–244. https://doi.org/10.1097/RMR.0000000000000218

7 Gao, F., Sun, M. H., & Fu, L. (2022). The role of three-dimensional MRI in the differentiation between angular pregnancy and interstitial pregnancy. BMC pregnancy and childbirth, 22(1), 133. https://doi.org/10.1186/s12884-022-04470-z

8 Hadzagić-Catibusić, F., Maksić, H., Uzicanin, S., Heljić, S., Zubcević, S., Merhemić, Z., Cengić, A., & Kulenović, E. (2008). Congenital malformations of the central nervous system: clinical approach. Bosnian journal of basic medical sciences, 8(4), 356–360. https://doi.org/10.17305/bjbms.2008.2897

9 Blaicher W, Prayer D, Bernaschek G. Magnetic resonance imaging and ultrasound in the assessment of the fetal central nervous system. J Perinat Med. 2003;31(6):459-68. doi: 10.1515/JPM.2003.071. PMID: 14711101.

10 Gonçalves, L. F., Lee, W., Mody, S., Shetty, A., Sangi-Haghpeykar, H., & Romero, R. (2016). Diagnostic accuracy of ultrasonography and magnetic resonance imaging for the detection of fetal anomalies: a blinded case-control study. Ultrasound in obstetrics & gynecology : the official journal of the International Society of Ultrasound in Obstetrics and Gynecology, 48(2), 185–192. https://doi.org/10.1002/uog.15774

11 Herman-Sucharska I, Urbanik A. Badanie MR w obrazowaniu wad ośrodkowego układu nerwowego płodu [MRI of fetal central nervous system malformations]. Przegl Lek. 2007;64(11):917-22. Polish. PMID: 18409404.

12 Institute of Medicine (US) Committee on Improving Birth Outcomes; Bale JR, Stoll BJ, Lucas AO, editors. Reducing Birth Defects: Meeting the Challenge in the Developing World. Washington (DC): National Academies Press (US); 2003. 3, Interventions to Reduce the Impact of Birth Defects. Available from: https://www.ncbi.nlm.nih.gov/books/NBK222083/

13 Smith-Bindman, R., Miglioretti, D. L., & Larson, E. B. (2008). Rising use of diagnostic medical imaging in a large integrated health system. Health affairs (Project Hope), 27(6), 1491–1502. https://doi.org/10.1377/hlthaff.27.6.1491

14 Malinger G, Paladini D, Haratz KK, Monteagudo A, Pilu GL, Timor-Tritsch IE. ISUOG Practice Guidelines (updated): sonographic examination of the fetal central nervous system. Part 1: performance of screening examination and indications for targeted neurosonography. Ultrasound Obstet Gynecol. 2020 Sep;56(3):476-484. doi: 10.1002/uog.22145. Erratum in: Ultrasound Obstet Gynecol. 2022 Oct;60(4):591. PMID: 32870591.

15 D'Addario V. Diagnostic approach to fetal ventriculomegaly. J Perinat Med. 2022 Aug 26;51(1):111-116. doi: 10.1515/jpm-2022-0312. PMID: 36005554.

16 Dean Deyle G. (2011). The role of MRI in musculoskeletal practice: a clinical perspective. The Journal of manual & manipulative therapy, 19(3), 152–161. https://doi.org/10.1179/2042618611Y.0000000009

17 Monteagudo A, Timor-Tritsch IE, Mayberry P. Three-dimensional transvaginal neurosonography of the fetal brain: 'navigating' in the volume scan. Ultrasound Obstet Gynecol. 2000 Sep;16(4):307-13. doi: 10.1046/j.1469-0705.2000.00264.x. PMID: 11169305.

18 Gatta, G., Di Grezia, G., Cuccurullo, V., Sardu, C., Iovino, F., Comune, R., Ruggiero, A., Chirico, M., La Forgia, D., Fanizzi, A., Massafra, R., Belfiore, M. P., Falco, G., Reginelli, A., Brunese, L., Grassi, R., Cappabianca, S., & Viola, L. (2021). MRI in Pregnancy and Precision Medicine: A Review from Literature. Journal of personalized medicine, 12(1), 9. https://doi.org/10.3390/jpm12010009

19 Linh LT, Duc NM, Nhung NH, My TT, Luu DT, Lenh BV. Detecting Fetal Central Nervous System Anomalies Using Magnetic Resonance Imaging and Ultrasound. Med Arch. 2021 Feb;75(1):45-49. doi: 10.5455/medarh.2021.75.45-49. PMID: 34012199; PMCID: PMC8116073.

20 Hu Y, Sun L, Feng L, Wang J, Zhu Y, Wu Q. The role of routine first-trimester ultrasound screening for central nervous system abnormalities: a longitudinal single-center study using an unselected cohort with 3-year experience. BMC Pregnancy Childbirth. 2023 May 3;23(1):312. doi: 10.1186/s12884-023-05644-z. PMID: 37138220; PMCID: PMC10157940.

21 Gumayan RLF, Klamer B, Ream M. Institutional Evaluation of Fetal Neurology Consults and Postnatal Outcomes: A 10-Year Retrospective Cohort Review. Neurol Clin Pract. 2023 Feb;13(1):e200100. doi: 10.1212/CPJ.0000000000200100. Epub 2023 Jan 19. PMID: 36865645; PMCID: PMC9973289.