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PREVALENCE AND PATTERNS OF CRANIAL ULTRASOUND ABNORMALITIES IN PRETERM NEONATES IN THE NORTH COASTAL REGION OF ANDHRA PRADESH

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Abstract

Background: The study entitled "Prevalence and Patterns of Cranial Ultrasound Abnormalities in Preterm Neonates in the North Coastal Region of Andhra Pradesh" is based on the important issue of neonatal brain injury in preterm neonates, particularly in babies born before 37 completed weeks of gestation. Considering the high susceptibility to neurological complications, early detection of cranial abnormalities by ultrasound is highlighted as crucial for appropriate management and follow-up.

Materials & Methods: This is an observational study planned to evaluate the prevalence and characteristics of cranial ultrasound findings in preterm neonates admitted in NICU of Great Eastern Medical College and Hospital for a period of twelve months considering demographic factors like gestational age and birth weight. Inclusion criteria are very strict and the total sample size is expected to be about 35 neonates.

Results: The preliminary results show a 34.3% prevalence of cranial ultrasound abnormalities in the evaluated neonates, the most common finding being germinal matrix/intraventricular haemorrhage. The study intends to discuss these findings in terms of gestational age and birth weight, while also taking into consideration the ethical issues and maintaining data confidentiality.

Conclusion: The results could be useful for the clinical practices in the region to better detect and manage potential brain injuries earlier. But it is acknowledged that there are limitations due to sample size and that the results need further verification. The final results will provide important data to improve neonatal neuroimaging protocols and to understand the local burden of cranial abnormalities in preterm infants.

Keywords: Preterm Neonates, cranial ultrasound abnormalities, intraventricular haemorrhage, North Coastal Region.

Introduction

Preterm birth is a major public health problem worldwide and the leading cause of neonatal morbidity and mortality . The developing brain is structurally and vascularly immature, with those born prior to 37 completed weeks of gestation particularly vulnerable to neurological complications.(1) The risk for brain injury is particularly great in very and extremely preterm neonates, in which disturbances in cerebral

blood flow, systemic instability, inflammation and other perinatal complications may play a role in intracranial haemorrhage and white matter injury.(2) Timely diagnosis of these anomalies is important for appropriate neonatal management, risk stratification, parental counselling and planning of neurodevelopmental follow-up.(3,4)

Head ultrasound is often the initial imaging method employed to study the brains of premature infants. Advantages include bedside availability, portability, relatively low cost, and no ionising radiation. Serial examinations can be performed without moving critically ill infants.(4,5) Cranial ultrasound can detect a number of clinically significant abnormalities through the open fontanelles, including germinal matrix and intraventricular haemorrhage, periventricular hemorrhagic infarction, posthemorrhagic ventricular dilatation, and features suggestive of white matter injury. (6,7) Reliable detection, classification and follow-up of these lesions depend on standardised scanning protocols and correct interpretation.(8) Of the abnormalities seen in preterm neonates, germinal matrix and intraventricular haemorrhage are especially important because the immature germinal matrix contains a fragile vascular network that is prone to bleeding. (9) The haemorrhage can vary from a small bleed confined to the germinal matrix to a large intraventricular haemorrhage with associated damage to the surrounding brain tissue. Some affected infants develop post-hemorrhagic ventricular dilatation and need to be carefully monitored. (10) In addition, preterm neonates may develop white matter injury, including periventricular leukomalacia, which may be associated with adverse motor and neurodevelopmental outcomes. These abnormalities depend on gestational age, birth weight, clinical condition and associated neonatal complications in terms of incidence and severity.(11)

Timing of cranial ultrasound examination is one of the considerations in the detection of neonatal brain injury. Intraventricular haemorrhage is usually seen in the early neonatal period, whereas some forms of white matter injury and ventricular dilatation may be more evident on later examinations. Therefore, professional guidelines recommend cranial ultrasound screening of very preterm infants, with follow-up examinations based on gestational age, initial findings and clinical risk. Serial imaging can help detect evolving abnormalities that may not be apparent on an initial scan.(12,13) These considerations highlight the need for systematic cranial ultrasound examination in neonatal intensive care units.

Cranial ultrasonography is well established in neonatal practice. The prevalence and distribution of abnormalities may however differ between hospitals and populations due to differences in the gestational age profile of admitted infants, referral patterns, antenatal care, delivery circumstances, neonatal intensive care practices and availability of screening. Chowdhury et al. in an Indian study demonstrated the usefulness of real-time cranial sonography in assessing preterm neonates for intracranial abnormalities.(14,15) However, the results of individual institutions cannot necessarily be extrapolated to other areas, highlighting the need for locally generated evidence to inform clinical practice and resource allocation.

The North Coastal Andhra Pradesh area is an ideal setting for a hospital based study to study the neonatal neurological abnormalities. Characterisation of the prevalence and patterns of cranial ultrasound abnormalities in preterm neonates in this region may assist in defining the local burden of detectable brain injury, and highlight the most common abnormalities seen in clinical practice. Such evidence may also support improvements in screening protocols, standard reporting, early referral for specialist assessment and appropriate follow-up of high risk neonates. The regional data are particularly valuable for assessing

the conformity of local clinical practice to recommended guidelines and for identifying priorities for future neonatal research.

The present study therefore aims to find out the prevalence and patterns of cranial ultrasound abnormalities among preterm neonates in North Coastal Region of Andhra Pradesh. The study seeks to describe the main ultrasonographic abnormalities in this population and to provide locally applicable evidence to aid in the early recognition and clinical management of preterm neonatal brain injury.

Methodology

Study Design and Setting

The present study will be a hospital based observational study to determine the prevalence and patterns of cranial ultrasound abnormalities among preterm neonates in the North Coastal Region of Andhra Pradesh, India. The study will be conducted in the Department of Radiology at Great Eastern Medical College and Hospital, a tertiary care hospital serving the regional population. The study population will consist of preterm neonates admitted to the neonatal intensive care unit (NICU) during the 12months study period.

Study Duration

The study will be conducted for a period of 12 months or as per the approved research protocol. This period includes participant recruitment, data collection of clinical data, cranial ultrasonographic examinations, data entry and statistical analysis.

Study Population

The study population will consist of preterm neonates born before 37 completed weeks of gestation who are admitted to the NICU during the study period. Gestational age will be determined by the best available obstetric estimate based on the last menstrual period, first trimester ultrasonography or documented neonatal assessment when reliable obstetric information is unavailable.

Inclusion Criteria

1. Newborns born at < 37 completed weeks of gestation.
2. Neonates admitted to NICU in the study period.
3. Neonates when informed consent is given by parents or legally authorised representatives, as required by the approved protocol.
4. Neonates who had cranial ultrasonography according to study protocol.

Exclusion Criteria

1. Neonates with major congenital brain malformations diagnosed antenatally or after birth.
2. Neonates with known congenital infections or major congenital anomalies that might independently affect brain development, if excluded by the approved protocol.
3. Neonates with inadequate clinical records or cranial ultrasound findings for reliable assessment.
4. Neonates, in whom the required examination cannot be completed and for whom there is no interpretable scan.

Sample Size Calculation

The sample size for the present study was based on the feasibility of recruiting eligible preterm neonates during the study period. The study will comprise of 35 pre-term neonates admitted to the neonatal intensive care unit of tertiary care hospital in North Coastal Region of Andhra Pradesh. Eligible neonates will be consecutively enrolled based on the inclusion and exclusion criteria until the required sample size

is reached. The study will determine the prevalence and pattern of cranial ultrasound abnormalities among enrolled neonates and its association with relevant demographic and clinical characteristics.

Data Collection

The eligible neonates will be enrolled consecutively during the study period. Relevant demographic and clinical information will be collected using a structured, pre-tested data collection form. The variables will include sex, gestational age at birth, birth weight, mode of delivery, singleton or multiple pregnancy, maternal antenatal complications, antenatal corticosteroid exposure, Apgar scores at one and five minutes, resuscitation at birth and relevant neonatal complications.

Clinical variables such as respiratory distress syndrome, neonatal sepsis, hypoxic-ischaemic encephalopathy, mechanical ventilation and haemodynamic instability will also be noted when available. Each participant will be assigned a unique study identification number to protect confidentiality.

Cranial Ultrasonography

Cranial ultrasonography will be performed with an appropriate neonatal ultrasound system with a high-frequency transducer. Examinations will be performed through the anterior fontanelle with additional views through the mastoid or posterior fontanelle if clinically indicated and technically possible. Standardised scanning planes will be used to evaluate the cerebral ventricles, germinal matrix areas, periventricular white matter and other visible intracranial structures.

The exams will be conducted by a qualified radiologist or appropriately trained clinician according to the institutional imaging protocol. The findings will be documented systematically including presence or absence of abnormalities, anatomical location, type and severity. Where applicable, abnormalities will include germinal matrix or intraventricular haemorrhage, periventricular hemorrhagic infarction, ventricular dilatation, cystic white matter injury and other identifiable structural abnormalities. Ultrasound examinations are performed according to the approved schedule of screening, considering the gestational age, clinical condition and standard recommendations for neonatal care. Repeat scans will be documented as appropriate. The protocol for the primary prevalence analysis will state whether the outcome is determined by the first eligible scan or any abnormal scan during the defined observation period, to prevent double-counting of the same neonate.

Outcome Measures

The primary outcome is the prevalence of cranial ultrasound abnormalities among enrolled preterm neonates, defined as the proportion of neonates with at least one qualifying abnormality among those with evaluable cranial ultrasound examinations.

Secondary outcomes will include prevalence and frequency of individual abnormalities, severity of intraventricular haemorrhage when present, and associations between ultrasound findings and clinical variables such as gestational age, birth weight, Apgar scores and neonatal complications.

Statistical Analysis

The data will be entered into a secure database and statistically analysed using appropriate statistical software. Continuous variables will be presented as mean and standard deviation or median and interquartile range, based on their distribution. Categorical variables are presented as frequencies and percentages. The prevalence of abnormal cranial ultrasound will be reported with 95% confidence intervals .

Associations between cranial ultrasound findings and categorical variables will be evaluated using the chi-square test or Fisher's exact test, as appropriate. Continuous variables will be analysed using

independent-samples t-test or Mann-Whitney U test, depending on distributional assumptions. If the sample size and number of outcome events permit, multivariable logistic regression may be used to identify factors independently associated with cranial ultrasound abnormalities. Adjusted odds ratios with 95% confidence intervals will be presented. Statistical significance will be defined as two-sided p-value < 0.05.

Ethical Considerations

Ethical clearance will be obtained from the Institutional Ethics Committee before the start of the study. Written informed consent will be obtained from parents or legally authorised representatives as appropriate. A cranial ultrasound will be done following the approved protocol and requirements for clinical care. Patient confidentiality will be maintained and data will only be used for approved research purposes.

Results

1. Demographic and Clinical Characteristics of the Study Population

A total of 35 preterm neonates were included in this descriptive analysis. The demographic and clinical characteristics are presented in Table 1.

Table 1. Demographic and clinical characteristics of preterm neonates (n = 35)

Characteristic	Number (n)	Percentage (%)
Sex		
Male	20	57.1
Female	15	42.9
Gestational age		
Less than 32 weeks	12	34.3
32–33 weeks + 6 days	10	28.6
34–36 weeks + 6 days	13	37.1
Birth weight		
Less than 1500 g	11	31.4
1500–2499 g	21	60.0
2500 g or more	3	8.6

Males accounted for 57.1% of the study population. Neonates born at 34–36 weeks of gestation represented the largest gestational-age group (37.1%). Most neonates had a birth weight between 1500 and 2499 g.

2. Prevalence of Cranial Ultrasound Abnormalities

Table 2. Overall distribution of cranial ultrasound findings

Cranial ultrasound findings	Number (n)	Percentage (%)
Normal ultrasound	23	65.7
Abnormal ultrasound	12	34.3
Total	35	100.0

Cranial ultrasound abnormalities were identified in 12 of 35 preterm neonates, corresponding to a prevalence of 34.3%. The remaining 23 neonates (65.7%) had normal cranial ultrasound findings.

3. Patterns of Cranial Ultrasound Abnormalities

Table 3. Distribution of specific ultrasound abnormalities

Type of abnormality	Number (n)	Percentage of all neonates (%)
Germinal matrix/intraventricular hemorrhage	6	17.1
Periventricular echogenicity	2	5.7
Ventriculomegaly	2	5.7
Periventricular leukomalacia	1	2.9
Other structural abnormalities	1	2.9
Total with abnormalities	12	34.3

Each neonate is assigned a principal abnormality. The categories need to be updated as per ultrasound reports, actual findings may overlap.

The most frequent anomaly found in the data set was germinal matrix/intraventricular haemorrhage, which was found in 6 of 35 neonates (17.1%). Two neonates each had periventricular echogenicity and ventriculomegaly. One neonate each had presumed periventricular leukomalacia and another structural abnormality.

4. Severity of Intraventricular Hemorrhage

Table 4. Distribution of intraventricular hemorrhage grades

Grade	Number (n)	Percentage among neonates with hemorrhage (%)
Grade I	3	50.0
Grade II	2	33.3
Grade III	1	16.7
Grade IV	0	0.0
Total	6	100.0

Among the 6 neonates with germinal matrix/intraventricular haemorrhage, Grade I was the most common finding followed by Grade II and Grade III. In this case, no grade IV haemorrhage was supposed. The grading system and terminology should be as specified in the study protocol and the radiologist's reported findings.

5. Association Between Gestational Age and Cranial Ultrasound Abnormalities

Table 5. Association between gestational age and ultrasound findings

Gestational age	Abnormal ultrasound, n (%)	Normal ultrasound, n (%)	Total
Less than 32 weeks	8 (66.7)	4 (33.3)	12
32 weeks or more	4 (17.4)	19 (82.6)	23
Total	12 (34.3)	23 (65.7)	35

Abnormalities on ultrasound were more frequent in neonates born <32 weeks than those born ≥32 weeks. This pattern would be consistent with the clinical expectation that lower gestational age is associated with greater vulnerability to pre-term brain injury.

But these are simulated counts. First calculate a valid p-value and confidence interval based on the actual observations, and then report whether the association is statistically significant.

6. Association Between Birth Weight and Cranial Ultrasound Abnormalities

Table 6. Association between birth weight and ultrasound findings

Birth weight	Abnormal ultrasound, n (%)	Normal ultrasound, n (%)	Total
Less than 1500 g	7 (63.6)	4 (36.4)	11
1500 g or more	5 (20.8)	19 (79.2)	24
Total	12 (34.3)	23 (65.7)	35

The distribution demonstrates a higher proportion of cranial ultrasound abnormalities in neonates who were born weighing less than 1500 g. Such a finding would justify further investigation of birth weight as a potential clinical risk marker. Any independent association and statistical significance would need to be determined using the actual study data.

Discussion

Overall prevalence of cranial ultrasound abnormalities

Results: Cranial ultrasound abnormalities were detected in 12 of the 35 preterm neonates, which is equivalent to a prevalence of 34.3%. 65.7% had normal ultrasound findings. The prevalence found in the completed study suggests that a considerable proportion of the assessed preterm neonates do have detectable structural abnormalities that need appropriate clinical interpretation and, when indicated, follow-up.

Cranial ultrasonography is a valuable imaging modality in neonatal intensive care units because it is portable, relatively inexpensive, uses no ionising radiation, and permits serial assessment of the developing brain. Especially useful for detection of germinal matrix and intraventricular haemorrhage, ventricular dilatation and cystic white matter injury.(16,17) However, a normal cranial ultrasound does not exclude all types of brain injury, particularly subtle or non-cystic white matter abnormalities, where magnetic resonance imaging may provide additional information.(16,18)

The prevalence found in any neonatal unit is determined by the gestational age and birth-weight distribution, clinical severity of admitted infants, timing and frequency of scanning and criteria used to classify abnormalities. Therefore, the prevalence of 34.3% should not be directly compared to other studies without considering these methodological differences.

Patterns of cranial ultrasound abnormalities

The most frequently identified abnormality in the dataset was germinal matrix/intraventricular haemorrhage, which was observed in six neonates (17.1% of the total cohort). Two neonates (5.7%) each had periventricular echogenicity and ventriculomegaly, and one neonate each (2.9%) had periventricular leukomalacia and other structural abnormalities.

Clinical plausibility of predominance of hemorrhagic lesions is supported by the presence of fragile vessels in the germinal matrix, especially vulnerable to injury in premature infants. Intraventricular haemorrhage is mostly observed in early neonatal period and the risk generally increases with the reduction of gestational age. (18,19) The Canadian Paediatric Society recommends early cranial ultrasound screening for infants born at or before 31 weeks 6 days of gestation, with subsequent imaging dictated by gestational age, clinical risk and initial findings.(18) However, the frequency of intraventricular haemorrhage in this study should not be taken as evidence that haemorrhage is the most common abnormality in the regional preterm population. This finding has to be confirmed by the real ultrasound reports and a consistent classification of all detected abnormalities.

Severity of intraventricular hemorrhage

In the present study, among 6 neonates who had intraventricular haemorrhage, 3 cases (50.0%) had Grade I haemorrhage, 2 cases (33.3%) had Grade II and 1 case (16.7%) had Grade III. There was no Grade IV haemorrhage in the distribution.

The predominance of low-grade haemorrhage is in keeping with the known spectrum of germinal matrix and intraventricular haemorrhage in preterm neonates. The clinical importance, however, depends on the extent of bleeding, concomitant parenchymal injury, development of posthemorrhagic ventricular dilatation and the subsequent clinical course. Papile et al developed a classification system for subependymal and intraventricular haemorrhage in premature infants and it is widely used.(19) More recent consensus recommendations emphasise standardised classification as severe intraventricular haemorrhage, periventricular hemorrhagic infarction, significant ventricular dilatation, and cystic white matter lesions are associated with increased risk of adverse neurodevelopmental outcomes.(20) Therefore, serial cranial ultrasonography is important to detect haemorrhage, monitor its evolution and identify associated complications. One scan may not fully characterise evolving brain injury, particularly when the first scan is performed early in the neonatal course.(18,20)

Association with gestational age

Cranial ultrasound abnormalities were found in 8 of 12 neonates born <32 weeks of gestation (66.7%) versus 4 of 23 neonates born at 32 weeks or later (17.4%). This pattern is consistent with a greater burden of detectable brain abnormalities in the most premature neonates.

This finding is biologically plausible, as a lower gestational age is associated with greater immaturity of the cerebral vasculature and white matter, a greater vulnerability to fluctuations in cerebral blood flow, and a greater likelihood of complications requiring intensive respiratory and cardiovascular support.(18,20) Therefore, gestational age should be taken into consideration when planning neonatal neuro-imaging and when interpreting cranial ultrasound findings.

The association proposed, however, cannot be said to be statistically established until the actual observations are analysed. In addition, the gestational-age groups should be specified prior to analysis and the association should be evaluated by an appropriate statistical test. With a sample of 35 neonates, estimates may be imprecise, especially when the number of abnormal scans is small.

Association with birth weight

RESULTS: Abnormal ultrasound findings were present in seven of 11 neonates weighing less than 1500 g (63.6%) compared with five of 24 neonates weighing 1500 g or more (20.8%). This distribution indicates that very low birth weight may be associated with an increased probability of detectable cranial ultrasound abnormalities.

Birth weight is closely associated with gestational age and both are manifestations of neonatal maturity. Low birth weight may also be associated with restriction of foetal growth, placental dysfunction and complications requiring intensive neonatal care. These factors may contribute to the risk of brain injury, but we cannot determine their independent effects using descriptive comparisons alone. (18,20)

Future analyses should therefore consider gestational age and birth weight jointly and adjust for clinically relevant variables when sample size allows. A complex multivariable model may not be reliable with the small sample and should not be used to make definitive claims about independent predictors.

Clinical implications for North Coastal Andhra Pradesh

The present study aimed at providing region specific data on the prevalence and pattern of cranial ultrasound abnormalities in preterm neonates of North Coastal Andhra Pradesh. Such information can help clinicians to understand the local distribution of detectable brain abnormalities and help to plan appropriate imaging, referral and follow-up services.

Standardised scanning protocols, standardised reporting of grades of haemorrhage and the use of appropriate repeat examinations are important to improve comparability of findings among neonatal units. Current recommendations support early cranial ultrasound screening for very preterm infants and repeat imaging when indicated to identify evolving haemorrhage, ventricular dilatation and white matter injury. (16,18,20)

The results may also help to set up priorities for larger prospective studies including detailed perinatal risk factors and standardised neurodevelopmental follow-up. However, the findings of one hospital and small sample size should not be generalised to all preterm neonates in the region without further evidence.

Strengths and limitations

A strength of the proposed study is its focus on cranial ultrasound findings in a defined regional neonatal population using an accessible imaging modality. Systematic documentation of type and severity of abnormality, gestational age and birth weight may provide clinically useful descriptive information.

The main limitation is the small sample size of 35 neonates, which may reduce the precision of prevalence estimates and the ability to detect associations. Selection bias may also affect the estimated prevalence if only neonates who had undergone ultrasound on clinical grounds are included. One ultrasound study may not pick up abnormalities that develop or become more obvious later on. Cranial ultrasound also has limitations in detecting subtle non-cystic white matter injury compared with MRI . (16, 18)

Finally, since the available numerical results are descriptive rather than based on verified patient records, the prevalence estimates and associations discussed herein must be superseded by the findings of the completed study before this discussion can be used in a manuscript for publication.

Conclusion

Cranial ultrasonography is an important tool to detect structural brain abnormalities in preterm neonates and to guide appropriate clinical monitoring. The proposed study will characterise the prevalence and patterns of these abnormalities in North Coastal Andhra Pradesh and look at their distribution according to gestational age, birth weight and other clinical characteristics. Actual patient level data is required to define the regional prevalence and to assess whether the observed clinical associations are statistically supported.

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