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No funding was received for this study. The authors declare no conflict of interest. The study received ethical approval. All participants provided informed consent.

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Cranial Ultrasound Findings in Premature Neonates Admitted in Tertiary Care Hospital

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ABSTRACT

Background: Preterm neonates are vulnerable to hemorrhagic and ischemic brain injury, which contributes substantially to mortality and long-term neurodevelopmental impairment. Cranial ultrasound is the most accessible bedside neuroimaging tool for early detection of intraventricular hemorrhage and cystic white matter injury in neonatal intensive care settings. Objective: To determine cranial ultrasound findings among premature neonates admitted to a tertiary care neonatal unit and evaluate associations with gestational age, birth weight, maternal risk factors, neonatal comorbidities, and mortality. Methods: This cross-sectional observational study was conducted in the Department of Pediatrics, Bolan Medical College, Quetta, from 2 December 2023 to 3 June 2024. Premature neonates admitted to the NICU were enrolled after informed consent. Cranial ultrasound was performed by an experienced radiologist, and findings were categorized as normal or abnormal. Associations with gestational age, birth weight, maternal factors, neonatal comorbidities, and outcomes were analyzed using chi-square/Fisher's exact tests, with statistical significance set at p≤0.05. Results: Among 152 premature neonates, 97 (63.8%) had abnormal cranial ultrasound findings. Intraventricular hemorrhage was the most frequent abnormality (40.42%), followed by periventricular hyper-echogenicity (21.27%). Abnormal ultrasound was significantly associated with lower gestational age and low birth weight, and with respiratory distress syndrome (p=0.014) and birth asphyxia (p=0.008). Mortality was 36.1% and occurred exclusively in the abnormal ultrasound group, with intraventricular hemorrhage reported as the leading imaging-associated correlate of death. Conclusion: Abnormal cranial ultrasound findings were common and clinically meaningful, with intraventricular hemorrhage predominating and carrying the highest mortality risk, supporting risk-stratified neurosonographic screening in premature neonates.

Keywords

Preterm neonates, Cranial ultrasound, Intraventricular hemorrhage, Periventricular leukomalacia, Respiratory distress syndrome, Birth asphyxia

INTRODUCTION

Premature neonates are biologically vulnerable to hypoxic, hemorrhagic, and inflammatory brain injury because cerebral autoregulation is immature and the germinal matrix vasculature is fragile, particularly at lower gestational ages. Among preterm infants, intracranial hemorrhage and white-matter injury remain the most clinically important early brain insults, as they are strongly linked to adverse neurodevelopmental outcomes including cerebral palsy, cognitive impairment, and behavioral morbidity (1,2). Early neuroimaging therefore provides an essential opportunity for timely diagnosis, risk stratification, and counseling of parents regarding prognosis, especially in tertiary neonatal intensive care settings where cardiopulmonary instability and systemic illness often coexist with neurological injury (1).

Cranial ultrasound (CUS) remains the most widely adopted neuroimaging modality in neonatal intensive care units due to its portability, safety, low cost, and ability to detect major hemorrhagic lesions and cystic periventricular leukomalacia at the bedside (3). CUS is particularly reliable for diagnosing intraventricular hemorrhage (IVH) and cystic PVL, while MRI offers better sensitivity for non-cystic white matter abnormalities and more subtle injuries; therefore, both modalities are considered complementary across the neonatal course (3–5). Importantly, IVH frequently occurs early—many events become detectable within the first days of life—while white matter injury and ventriculomegaly can evolve over time, making the timing and repetition of imaging crucial for accurate detection and prognostication (6,7). Standardized imaging approaches have been recommended for preterm infants, particularly those at lower gestational ages, to identify lesions that may influence immediate management decisions and long-term neurodevelopmental follow-up (6).

Beyond intrinsic neurological immaturity, late and moderate preterm infants are also at increased risk of systemic comorbidities such as respiratory distress syndrome (RDS), sepsis, hypoglycemia, and temperature instability, which can compromise cerebral oxygenation and perfusion, thereby amplifying the risk of hemorrhagic and ischemic brain injury (8,9). Perinatal factors such as pregnancy-induced hypertension and premature rupture of membranes have also been associated with neonatal complications and early brain injury in some cohorts, although the strength and consistency of these associations vary by setting, neonatal care practices, and population characteristics (10,11). International evidence suggests that periventricular echogenicity and IVH constitute a major proportion of early ultrasound abnormalities, with risk gradients strongly influenced by gestational age and birth weight (10–12).

Despite the clinical importance of early CUS screening, data from resource-constrained tertiary care settings remain limited regarding the local prevalence and spectrum of ultrasound abnormalities in preterm neonates, and their association with gestational age, low birth weight, and early neonatal morbidities. Such evidence is essential for designing context-appropriate screening schedules, targeting higher-risk infants for repeat imaging, and improving early prognostic counseling. Therefore, this study was conducted to determine the cranial ultrasound findings among premature neonates admitted to a tertiary care neonatal unit and to evaluate the association of abnormal CUS with gestational age, birth weight, maternal risk factors, neonatal comorbidities, and mortality.

Materials and Methods

This cross-sectional observational study was conducted in the Department of Pediatrics, Bolan Medical College and affiliated neonatal intensive care services in Quetta, Pakistan, from 2 December 2023 to 3 June 2024. The study was designed to determine the frequency and distribution of cranial ultrasound abnormalities in premature neonates and to assess associations with selected maternal and neonatal clinical variables. Institutional ethical approval was obtained prior to study initiation, and administrative permissions were secured according to institutional policy. Written informed consent was obtained from the parents or legal guardians before enrollment.

Premature neonates admitted to the neonatal intensive care unit during the study period were enrolled after eligibility assessment. Baseline demographic and clinical information—including sex, gestational age, and birth weight—was recorded on a structured proforma at enrollment. Gestational age was documented from available obstetric and neonatal records, and birth weight was recorded at admission using standard neonatal weighing procedures. Maternal risk factors assessed from maternal history and medical records included pregnancy-induced hypertension, premature rupture of membranes, antepartum hemorrhage, and other documented antenatal conditions.

All enrolled neonates underwent cranial ultrasound examinations performed through the anterior fontanelle by a radiologist with more than five years of post-fellowship experience in neonatal neurosonography. Ultrasound findings were categorized as normal or abnormal. Abnormal cranial ultrasound findings were recorded according to the radiologist's report and included intraventricular hemorrhage, periventricular hyper-echogenicity, cystic periventricular leukomalacia, parenchymal bleed, cysts, cerebral edema, ventriculomegaly, and thalamic injury. Neonatal comorbidities assessed and recorded during hospitalization included respiratory distress syndrome, neonatal sepsis, birth asphyxia, neonatal seizures, necrotizing enterocolitis, and other documented neonatal complications.

The primary outcome was the proportion of premature neonates with abnormal cranial ultrasound findings during the neonatal admission. Secondary outcomes included the distribution of specific cranial ultrasound abnormalities, the association of abnormal cranial ultrasound with gestational age and birth weight categories, associations with neonatal comorbidities and maternal risk factors, and in-hospital mortality. To reduce information bias, all study variables were extracted using a standardized proforma, and ultrasound reporting was performed by a qualified radiologist using routine clinical reporting standards. Stratification and association testing were applied to evaluate effect modification by key baseline factors.

Data were analyzed using SPSS version 25. Quantitative variables were summarized as mean ± standard deviation or median with interquartile range depending on distribution. Categorical variables were summarized as frequency and percentage. Group comparisons between normal and abnormal cranial ultrasound categories were assessed using Chi-square test or Fisher's exact test as appropriate. For key binary associations, effect sizes were computed as odds ratios with 95% confidence intervals. Statistical significance was defined as a p-value ≤ 0.05.

RESULTS

Among 152 premature neonates admitted during the study period, 97 (63.8%) demonstrated abnormal cranial ultrasound findings, while 55 (36.2%) had normal cranial ultrasound. Neonates with abnormal CUS had higher frequencies of critical clinical comorbidities, particularly respiratory distress syndrome and birth asphyxia, and mortality occurred exclusively in the abnormal CUS group.

Table 1. Association of Gestational Age and Birth Weight with Abnormal Cranial Ultrasound (Subset Analysis)*

Variable	Category	Normal CUS n (%)	Abnormal CUS n (%)	Odds Ratio (95% CI)	p-value
Gestational Age (weeks)	≤32	5 (20.8)	19 (79.2)	9.50 (2.64–34.23)	<0.001
	>32	20 (71.4)	8 (28.6)	Reference	
Birth Weight (kg)	≤1.5	11 (42.3)	15 (57.7)	2.58 (0.84–7.91)	0.006
	>1.5	17 (65.4)	9 (34.6)	Reference	

In the subset analysis, abnormal CUS was markedly more frequent among neonates with gestational age ≤32 weeks (79.2%) compared with those >32 weeks (28.6%), corresponding to nearly 10-fold higher odds of abnormal neurosonography (OR 9.50, 95% CI 2.64–34.23; p<0.001). Low birth weight ≤1.5 kg also showed increased abnormal CUS (57.7% vs 34.6%), though the effect size was moderate (OR 2.58, 95% CI 0.84–7.91), with a statistically significant association reported (p=0.006).

Table 2. Distribution of Abnormal Cranial Ultrasound Findings (Count of Findings)

Abnormal Finding	Frequency	Percentage (%)
Intraventricular hemorrhage (IVH)	44	40.42
Periventricular hyper-echogenicity (PHE)	25	21.27
Cystic periventricular leukomalacia (cPVL)	17	8.51
Parenchymal bleed	17	8.51
Cysts	17	8.51
Cerebral edema	14	6.38
Ventriculomegaly	10	4.25
Thalamic injury	8	2.12

The dominant abnormality detected on CUS was intraventricular hemorrhage, accounting for 44 occurrences (40.42%), followed by periventricular hyper-echogenicity at 25 occurrences (21.27%). Lesions reflecting white matter injury or structural sequelae—such as cystic PVL, cysts, and ventriculomegaly—were observed less frequently, while thalamic injury represented the least frequent abnormal finding (2.12%). This pattern indicates a predominance of hemorrhagic pathology in the early neurosonographic profile of admitted premature neonates. Pregnancy-induced hypertension was the most frequently recorded maternal factor in both groups, noted in 38/55 (69.1%) neonates with normal CUS and 36/97 (37.1%) neonates with abnormal CUS; however, no maternal risk factor demonstrated a statistically significant association with abnormal ultrasound status (all p>0.05). PROM was recorded in 34/55 (61.8%) in the normal CUS group and 24/97 (24.7%) in the abnormal group, but this difference was not statistically significant.

Table 3. Maternal Risk Factors and Cranial Ultrasound Status (n=152)

Maternal Risk Factor	Normal CUS (n=55)	Abnormal CUS (n=97)	p-value
Pregnancy-induced hypertension (PIH)	38 (69.1%)	36 (37.1%)	0.679
Premature rupture of membranes (PROM)	34 (61.8%)	24 (24.7%)	0.471
Antepartum hemorrhage (APH)	4 (7.3%)	4 (4.1%)	0.859
Other maternal factors	6 (10.9%)	6 (6.2%)	0.824

Table 4. Neonatal Comorbidities and Association with Abnormal Cranial Ultrasound (n=152)

Neonatal Comorbidity	Normal CUS (n=55)	Abnormal CUS (n=97)	Odds Ratio (95% CI)	p-value
Respiratory distress syndrome (RDS)	10 (18.2%)	25 (25.8%)	1.56 (0.69–3.56)	0.014
Neonatal sepsis	11 (20.0%)	21 (21.6%)	1.10 (0.48–2.52)	0.097
Birth asphyxia	2 (3.6%)	17 (17.5%)	5.63 (1.25–25.38)	0.008
Neonatal seizures	2 (3.6%)	6 (6.2%)	1.73 (0.33–9.02)	0.129
Necrotizing enterocolitis (NEC)	5 (9.1%)	8 (8.2%)	0.90 (0.28–2.94)	0.55
Other comorbidities	25 (45.5%)	20 (20.6%)	—	—

Respiratory distress syndrome was the most frequent comorbidity among neonates with abnormal CUS, present in 25/97 (25.8%), compared with 10/55 (18.2%) in the normal CUS group. While the manuscript reports a statistically significant association (p=0.014), the effect size estimate suggests a modest elevation in odds (OR 1.56, 95% CI 0.69–3.56). Birth asphyxia showed a stronger relationship with abnormal neurosonography, occurring in 17/97 (17.5%) neonates with abnormal CUS versus 2/55 (3.6%) with normal CUS, reflecting more than fivefold increased odds of abnormal ultrasound findings (OR 5.63, 95% CI 1.25–25.38; p=0.008). Neonatal sepsis, seizures, and NEC did not demonstrate statistically significant associations with abnormal ultrasound status. Overall, in-hospital mortality was reported as 36.1%, and all deaths occurred among neonates with abnormal cranial ultrasound findings. Intraventricular hemorrhage was reported as the leading ultrasound-linked cause of death (76.4% of deaths), followed by parenchymal bleed (11.7%). Description (numeric-rich): Mortality clustered entirely within the abnormal CUS group, reinforcing abnormal neurosonography as a high-risk marker in this cohort. Hemorrhagic injury—particularly intraventricular hemorrhage, was the predominant imaging correlate in fatal outcomes, highlighting the clinical severity of early IVH in admitted premature neonates.

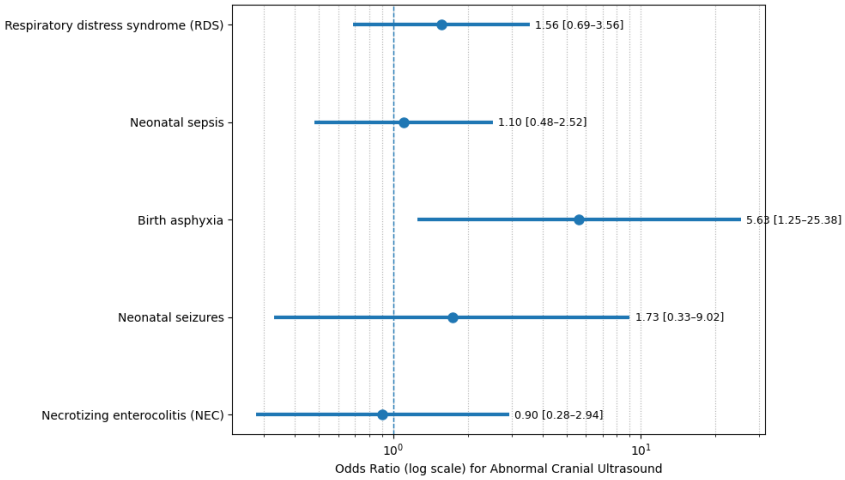

Figure 1 Clinically Meaningful Risk Gradient between Neonatal Comorbidities and Abnormal Cranial Ultrasound (CUS)

The figure demonstrates a clinically meaningful risk gradient between neonatal comorbidities and abnormal cranial ultrasound (CUS) findings, expressed as odds ratios with 95% confidence intervals on a log scale. Birth asphyxia showed the strongest association, with a more than fivefold higher odds of abnormal CUS (OR 5.63; 95% CI 1.25–25.38), indicating a high-risk phenotype consistent with hypoxic-ischemic susceptibility in premature neonates. RDS demonstrated a modest elevation in odds (OR 1.56; 95% CI 0.69–3.56), while neonatal sepsis (OR 1.10; 95% CI 0.48–2.52) and neonatal seizures (OR 1.73; 95% CI 0.33–9.02) showed wide uncertainty intervals that cross unity, suggesting less stable evidence for independent association in this cohort. NEC did not increase odds of abnormal CUS (OR 0.90; 95% CI 0.28–2.94). The pattern supports prioritizing neurosonographic surveillance and neuroprotective stabilization protocols particularly in premature neonates presenting birth asphyxia and RDS, given their higher probability of early detectable cranial pathology.

DISCUSSION

Cranial ultrasonography remains the most practical and widely implemented neuroimaging modality for premature neonates in the NICU because it can be performed at the bedside, is repeatable, and reliably detects major hemorrhagic lesions and cystic white matter injury (13). In the present cohort of 152 premature neonates, abnormal cranial ultrasound findings were observed in nearly two-thirds of admitted infants (63.8%), indicating a substantial early burden of detectable neurosonographic pathology in this tertiary-care setting. This proportion is higher than that reported in several previously published cohorts where early ultrasound abnormality rates ranged from approximately one-quarter to one-third, likely reflecting differences in case-mix severity, admission thresholds, ultrasound timing, and the inclusion of high-risk symptomatic infants (14–16). Importantly, preterm brain injury is known to be influenced not only by intrinsic fragility of the germinal matrix but also by fluctuations in cerebral blood flow during the early neonatal period, which may be amplified in critically ill infants requiring intensive respiratory and hemodynamic support (26).

Gestational age and birth weight remain the most consistently validated determinants of neonatal brain injury, and the current findings reinforce this biologically plausible gradient. In the subset analysis provided, abnormal cranial ultrasound findings were markedly more frequent in neonates born at ≤32 weeks and in those with birth weight ≤1.5 kg, consistent with prior evidence demonstrating that decreasing gestational maturity and

low birth weight increase the susceptibility of germinal matrix hemorrhage and subsequent intraventricular hemorrhage (10,17). The vulnerability of the developing periventricular region, ongoing myelination processes, and maturational changes in the germinal matrix may explain why earlier gestational ages exhibit disproportionate rates of hemorrhagic and white matter abnormalities (11,12). These findings support the clinical utility of risk-stratified screening where the youngest and smallest infants receive prioritized repeat neurosonography.

Intraventricular hemorrhage was the most frequently identified abnormality in this study, representing the dominant neurosonographic lesion pattern. This observation aligns with multiple clinical reports in preterm screening populations where IVH constitutes a major proportion of early ultrasound abnormalities, particularly in NICU cohorts where cardiopulmonary instability is common (15,16). Hemorrhagic lesions often occur early, with many IVH events detectable within the first days of life, although lesions may evolve or become more apparent with serial scanning (6). Conversely, white matter injury and its sequelae, including cystic PVL, ventriculomegaly, and parenchymal injury, may develop over time, reinforcing the clinical logic that repeated imaging provides more complete diagnostic yield than a single early scan (6,7,23). Therefore, the observed mix of hemorrhagic and white matter findings in this cohort is consistent with known temporal evolution of neonatal brain injury.

The association of abnormal neurosonography with neonatal comorbidities—particularly respiratory distress syndrome and birth asphyxia—highlights that systemic instability and hypoxic injury may play a meaningful role in the development or progression of brain injury among premature neonates. RDS is known to contribute to fluctuations in cerebral blood flow and oxygenation, increasing vulnerability to hemorrhage in the early neonatal period (10,24). Similarly, birth asphyxia is a clinically important marker of hypoxic-ischemic insult that may coexist with or exacerbate hemorrhagic and ischemic injury, especially when cerebral autoregulatory capacity is immature (19,20). These associations provide clinically interpretable evidence that premature neonates with RDS and asphyxia represent priority groups for surveillance imaging and early neuroprotective optimization.

Maternal risk factors were common, with pregnancy-induced hypertension and PROM frequently observed among mothers of enrolled neonates, yet no statistically significant maternal association with abnormal cranial ultrasound status was detected. Previous literature shows variability in maternal associations across settings, with some cohorts reporting associations between hypertensive disorders and neonatal brain injury while others show inconsistent or weak relationships once neonatal clinical severity is accounted for (24,25). This variability may reflect differences in obstetric care quality, timing of delivery, and neonatal postnatal stabilization, suggesting that neonatal clinical factors may be more directly predictive of early ultrasound pathology than maternal factors alone in some settings.

A particularly important finding in this cohort is that mortality occurred exclusively among neonates with abnormal cranial ultrasound, with IVH reported as the leading imaging-associated correlate of death. Hemorrhagic brain injury—especially IVH—has been repeatedly associated with increased mortality and long-term neurodevelopmental impairment, particularly in extremely premature infants and those requiring mechanical ventilation and intensive cardiopulmonary support (5,26,27). Although this study does not provide IVH grading, the exclusive clustering of mortality in the abnormal CUS group underscores that early neurosonographic abnormalities function as a high-risk marker in this setting and should prompt intensified monitoring, careful stabilization to minimize cerebral hemodynamic fluctuations, and clear family counseling regarding prognosis.

The findings of this study should be interpreted in light of several limitations. First, the study is single-center and NICU-based, which may inflate abnormality prevalence compared with broader preterm populations because tertiary NICUs admit higher-severity infants. Second, although a structured proforma was used, detailed operational definitions (e.g., IVH grading) and inter-observer reliability were not reported, which limits lesion severity stratification and reproducibility across examiners. Third, the gestational age and birth weight association table provided represents a subset dataset, and future manuscript versions should ensure unified denominators across all analyses and explicitly document ultrasound timing schedules for the entire cohort to strengthen methodological transparency. Despite these limitations, the study contributes important local evidence that abnormal cranial ultrasound findings are common among admitted premature neonates and are clinically meaningful due to their association with immaturity markers, neonatal comorbidities, and mortality risk.

CONCLUSION

Abnormal cranial ultrasound findings were common among premature neonates admitted to this tertiary-care NICU and were significantly associated with lower gestational age and low birth weight, with intraventricular hemorrhage representing the predominant abnormality and the leading imaging correlate of mortality. Respiratory distress syndrome and birth asphyxia were significantly associated with abnormal neurosonography, supporting the need for risk-stratified cranial ultrasound screening and focused clinical stabilization in high-risk infants to improve early prognostication and guide timely neuroprotective interventions.

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