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CLINICAL FEATURES AND OUTCOME OF NEONATAL ENCEPHALOPATHY

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Abstract

Background: Neonatal encephalopathy (NE) is a leading cause of neonatal morbidity and mortality especially in low and middle-income countries. It is defined as a defect of neurological function, which occurs in the first days of life, and is frequently linked to perinatal hypoxic-ischemic brain injury. Only few local studies exist about its clinical spectrum and short term outcomes in Pakistan. **Objective:** To determine the clinical features and outcome of neonatal encephalopathy presenting at Lady Reading Hospital / Medical Teaching Institute. Peshawar. **Methods:** This was a Cross-sectional study that was carried out at Department of pediatrics (Lady Reading Hospital) Peshawar. from December 2024 to May 2025. 120 neonates with NE born at more than 35 weeks gestation. A structured proforma was used to obtain the demographic details, clinical presentation, and immediate outcomes in the hospital, which were recorded in a prospective manner. Data analysis was done with SPSS version 25. Demographic variables were correlated with outcomes and a p-value of < 0.05 was regarded as statistically significant. **Results:** The most common clinical presentation was seizures in 58 (48.3%) neonates, respiratory distress in 39 (32.5%), lethargy in 14 (11.7%) and feeding difficulties in 9 (7.5%). In total, 103 (85.8%) neonates had an uneventful discharge while 17 (14.2%) died in the hospital. Low birth weight (<2.5 kg) and lower

gestational age ($p<0.05$) were significant factors in mortality. **Conclusion:** The major clinical features of NE are seizures and respiratory difficulties. Although deaths were rare in most neonates, the overall mortality rate indicates the need for early diagnosis, timely treatment, and better neonatal care to minimize the negative effects of this condition.

1. INTRODUCTION

Neonatal encephalopathy (NE) is an umbrella term for a clinically recognizable syndrome of altered neurological function that develops in term and late preterm infants (35+ weeks of gestation) during the first days of life. It is marked by a lack of consciousness, trouble starting and keeping up breathing, abnormal muscle tone and reflexes, and in many cases, seizures. Neonatal encephalopathy is a clinical picture not a diagnosis as it covers a wide spectrum of underlying causes that need careful evaluation in order to manage and provide a prognosis [1,2].

Neonatal encephalopathy may have multiple causes, such as hypoxic–ischemic brain injury, neonatal infections, abnormalities of the placenta and umbilical cord, intracranial hemorrhage, metabolic and genetic disorders, vascular insults or coagulation abnormalities. Hypoxic–ischemic encephalopathy (HIE) is the most common cause of encephalopathy but many affected neonates have multifactorial or non-hypoxic causes, emphasizing the need for thorough clinical evaluation and diagnostic workup [3–5].

NE continues to be a significant cause of neonatal mortality and long-term neurodevelopmental disability in the world today. It is estimated that the incidence in high-income countries is around 1.5–2.5 cases per 1000 live births, and is significant in low and middle income countries due to poor obstetric and neonatal resources. Brain injury can occur during the antenatal period, at birth or following birth, and it can be difficult in many clinical situations to determine the exact cause of the injury [1,4,6].

Clinical signs and symptoms of NE depend on the severity of brain injury and its cause. Symptoms vary and include changes in consciousness, hypotonia or hypertonia, decreased or absent primitive reflexes, decreased respiration, feeding problems, irritability, lethargy and convulsions. Because the clinical symptoms and signs are similar in many infections, metabolic, vascular, genetic, and toxic diseases, a systematic diagnostic approach is essential to help make the diagnosis and take action in time [6-8].

While a significant proportion of cases of neonatal encephalopathy is caused by hypoxic–ischemic encephalopathy, a wide differential diagnosis should be considered as early recognition of other causes may have a significant effect on treatment and prognosis. In a recent hospital-based study, seizures were the most common presenting symptom (45.1%) followed by respiratory distress (30.4%), lethargy (15.8%) and feeding difficulties (8.5%). The study also showed that the majority of neonates were discharged successfully (87.8%) while there was still a significant mortality rate (12.1%), highlighting the clinical burden in this condition [8,9].

Although neonatal intensive care (NICU) has improved over the years, there are few published reports on the clinical spectrum and short-term outcomes of neonatal encephalopathy (NE) in many developing countries, including Pakistan. In addition, the proportion of patients that present with each of these clinical scenarios to achieve patient outcomes has not been thoroughly studied in local healthcare contexts. So, the present study was undertaken to find out the clinical picture and prognosis of neonatal encephalopathy in the tertiary care hospital. The results will yield locally relevant evidence for better early recognition, optimizing clinical management, prognostication and ultimately better results of affected infants [10].

2. OBJECTIVE:

To determine the clinical features and outcome of neonatal encephalopathy presenting at Lady Reading Hospital / Medical Teaching Institute. Peshawar

3. METHODOLOGY

This was a Cross-sectional study that was carried out at Department of pediatrics (Lady Reading Hospital) Peshawar. from December 2024 to May 2025. A consecutive non-probability sampling was done and the total sample was 120 neonates who were admitted with clinically diagnosed neonatal encephalopathy (NE). Altered level of consciousness, abnormal muscle tone, reduced reflexes and any seizure, respiratory difficulty and/or feeding problems were indications of inclusion in the neonate group while large congenital abnormalities or metabolic disorders were indications of exclusion. Written informed consent was given by the parents/guardians before enrollment. The clinical status was evaluated in the presence of consultant pediatrician by using a structured data collection form. Demographic and clinical data and outcomes were recorded immediately after hospitalization. The data have been analyzed using SPSS 25.0. A p value < 0.05 was deemed as a statistically significant difference.

3.1 INCLUSION CRITERIA

The neonate those who met the operational definition of neonatal encephalopathy, and were born at a gestation age >35 weeks were included.

3.2 EXCLUSION CRITERIA

Neonates with structural brain malformations, IEM and metabolic derangements (severe hypoglycemia, hyperammonemia) were excluded.

3.3 DATA COLLECTION PROCEDURE

Parents/legal guardians of eligible neonates gave ethical approval and informed consent (written) and neonates were admitted in order. A detailed proforma was employed to collect data regarding demographic details of the newborns including age, sex, gestational age, birth weight and relevant maternal and perinatal history. All neonates were thoroughly checked for symptoms and signs of neonatal encephalopathy (neurodevelopmental dysfunction) such as seizures, breathing problems, lethargy, abnormal muscle tone and feeding problems. Standardized approach was taken to diagnosis with all the clinical assessments performed with the help of a consultant paediatrician. Immediate outcomes within the hospital including mortality and discharge in stable condition were documented. The data collected were checked for completeness and accuracy, and then entered into the study database for statistical analysis.

3.4 DATA ANALYSIS PROCEDURE

These data were fed into a computer by SPSS software version 25.0 and processed through this software. Mean ± standard deviation was used for all continuous variables (birth weight and gestational age) and frequency and percentages were used for all categorical variables (gender, place of residence, socioeconomic status, clinical features, and outcomes). Stratification was used to adjust for possible effect modifiers: birth weight, gestation age, gender and socioeconomic status. To determine the association of categorical variables with the clinical outcome as appropriate, Chi-square test or Fisher's exact test were used. All analysis used a p-value of < 0.05 as statistically significant.

4. RESULTS

In this study, 120 neonates with clinical criteria for inclusion were studied to assess clinical characteristics and immediate outcomes of neonatal encephalopathy. The average birth weight was 2.84 ± 0.45 kg and the average gestation age was 38.2 ± 1.4 weeks. According to the baseline demographic data, 74 (61.7%) and 46 (38.3%) neonates were male and female, respectively. The majority of participants were rural residents and from lower economic status groups (65.0% and 67.5% respectively).

Table 1: Baseline Characteristics

Parameter	Total (N = 120)
Mean Birth Weight (kg)	2.84 ± 0.45
Mean Gestational Age (weeks)	38.2 ± 1.4
Male	74 (61.7%)
Female	46 (38.3%)
Rural Residence	78 (65.0%)
Urban Residence	42 (35.0%)
Lower Socioeconomic Status	81 (67.5%)
Middle Socioeconomic Status	31 (25.8%)
Upper Socioeconomic Status	8 (6.7%)

There was a high proportion of male neonatal babies from rural, low socioeconomic backgrounds.

Table 2: Specifically, the clinical features of N.E. are presented.

Clinical Feature	Frequency	Percentage
Aggression/violence	45	50%
Seizures	58	48.3%
Respiratory Distress	39	32.5%
Lethargy	14	11.7%
Feeding Difficulties	9	7.5%

Seizures (48.3%) and respiratory distress (32.5%) were the two most common clinical features. Feeding problems and lethargy were less common.

Table 3: Immediate Clinical Outcomes

Outcome	Frequency	Percentage
Discharged Stable	103	85.8%
Expired	17	14.2%

A total of 85.8% of the neonates were discharged in stable condition and 14.2% died in hospital.

Table 4: Stratified Clinical Outcome by BW

Birth Weight	Discharged	Expired	p-value
<2.5 kg	22	9	
≥2.5 kg	81	8	0.012

The mortality rate was significantly greater for neonates weighing <2.5 kg as compared to ≥2.5 kg (p = 0.012).

Table 5: Stratification by Gestational Age of Clinical Outcome

Gestational Age	Discharged	Expired	p-value
36–37 weeks	29	10	
>37 weeks	74	7	**0.007**

Lower gestational age was significantly associated with adverse clinical outcomes. The neonates born from 36–37 weeks had significantly higher mortality rate than those born after 37 weeks ($p = 0.007$).

Interpretation

The results show that neonatal encephalopathy is mainly characterised by seizures and respiratory distress. Most of the affected neonates were discharged in stable condition, but there is still a significant mortality in hospital, 14.2%. In addition, low birth weight (<2.5 kg) and lower gestational age (36–37 weeks) were found to be important predictors of mortality, which indicates these factors as important determinants of poor short-term outcomes. The findings are of immense importance and highlight the need for early identification of high-risk neonates and prompt intensive management of neonates, which would help to improve the survival and reduce the morbidity of the neonates.

5. DISCUSSION

Neonatal encephalopathy (NE) is a heterogeneous clinical syndrome with disturbed neurological function in the first days of life, and is a significant cause of neonatal mortality and long-term neurodevelopmental disability worldwide [1]. The most common cause is hypoxic–ischemic encephalopathy (HIE), but recent advances in neonatal medicine have shown that neonatal encephalopathy is a heterogeneous disorder, caused by multiple factors both before and during birth and after birth, necessitating a comprehensive diagnostic evaluation and personalized approach to its management [3]. The diseases are now known to be caused by a variety of factors such as altered placental function, genetic defects, metabolic disorders, and inflammatory conditions, which have enhanced the understanding of the mechanisms of the disease and treatment [4]. In recent genetic studies, however, several pathogenic variants have been identified that play a role in neonatal encephalopathy, thus making it vital to also look at inherited disorders in cases that are not explained [5].

During our investigation it was found that males accounted for 61.7% of the study population. These findings have been observed previously and indicate that male infants are more vulnerable to hypoxic–ischemic brain injury than females, perhaps with a differential in neuronal maturation, inflammatory responses, and endogenous neuroprotective mechanisms [4]. The predilection for male neonates may be partly accounted for by sex-related differences, which are still under investigation in terms of their biological mechanisms.

Respiratory distress was the second most common symptom in our patients (32.5%), with seizures being more common (48.3%). These results are similar to those of Kumari et al. who found seizures in 45.1% and respiratory distress in 30.4% of neonates with encephalopathy [9]. Seizures are one of the earliest signs of cerebral dysfunction and are highly correlated with brain injury in the moderate to severe range of hypoxic–ischemic brain injury [8]. In addition, there is evidence recently that neonatal encephalopathy is not restricted to clinical HIE and that there is a critical need for ongoing electroencephalographic (EEG) monitoring for screening the brain for clinical and electrographic seizures to aid earlier therapeutic intervention and better neurological outcomes [10].

In our study the immediate clinical outcome was that 85.8% of neonates survived (hospital discharge) while 14.2% died during the hospital stay. This mortality rate is similar to what was reported in several developing countries, but is still significantly higher than that reported from developed countries where therapeutic hypothermia and comprehensive neonatal intensive care are routinely provided [3]. Current literature also highlights the importance of early diagnosis of HIE and timely

implementation of evidence-based neuroprotective treatment to enhance survival and neurologic outcomes [11]. The last few years, there have been significant advances in the neuro-imaging of neonatal encephalopathy. Magnetic resonance imaging (MRI), diffusion-weighted imaging (DWI), and magnetic resonance spectroscopy (MRS) can be used to provide important information on timing, severity, and distribution of brain injury as well as help in prognostication and long-term neurodevelopmental counseling [12]. Long-term follow-up studies also show that, although clinically recovered in the neonatal period, the survivors of hypoxic–ischemic encephalopathy continue to suffer from cognitive dysfunction, learning disabilities, behavioral disorders, and executive dysfunction in childhood and adolescence [13]. Neonatal encephalopathy is often associated with damage to multiple organ systems apart from neurological. Coagulation abnormalities have been linked to poor early clinical outcome and this could support early risk stratification and supportive management of the critically ill neonate and make routine coagulation monitoring a useful practice [14]. However, a recent systematic review and meta-analysis found that therapeutic hypothermia can also significantly decrease mortality and improve neurodevelopmental outcomes when used in neonates with moderate to severe HIE and started within the suggested therapeutic window [15]. Early MRI has also been proven to be a useful prognostic tool, as Bach et al. have shown that MRI after therapeutic hypothermia can predict neurodevelopmental outcome at 30 months of age [16]. Nevertheless, the results from the HELIX randomized controlled trial (RCT) in LMICs demonstrated that therapeutic hypothermia did not result in improved survival rates and increased mortality rates [17]. Moreover, Shankaran et al. noted that even conventional MRI is not very useful in predicting death or disability after neonatal HIE, and that neuroimaging findings must always be used in conjunction with clinical and electrophysiologic evaluations [18]. The relatively high rates of death seen in our study might therefore be a result of delayed referral, poor intrapartal fetal monitoring, a lack of neonatal intensive care facilities and socioeconomic constraints to specialized neonatal care.

Our stratified analysis showed that mortality was significantly related to the low birth weight (LBW, < 2.5 kg) and low gestational age groups ($p < 0.05$). Previous studies indicate that immature cerebrovascular autoregulation and decreased antioxidant levels, as well as greater susceptibility to ischemia–reperfusion injury, make premature and low-birth-weight infants more susceptible to neurological injury [4,8]. Early recognition of these high-risk neonates, consequently, is crucial in order to be able to refer as soon as possible and implement timely strategies to prevent neurodevelopmental disability.

Overall, the findings of the present study support that seizures are still the most common clinical symptom of NNE, and low birth weight and gestational age are key factors when considering adverse outcomes. While survival rates are good for most neonates, there is still high mortality rates in resource-limited settings. Increased antenatal surveillance, better intrapartum fetal monitoring, timely referral to tertiary neonatal centers, greater availability of neonatal intensive care, and implementation of evidence-based neonatal neuroprotective strategies are key to improve survival and long-term neurodevelopmental disabilities [1,3–5,8–18].

6. CONCLUSION

The objective of this study is to create awareness among the community about neonatal encephalopathy as a serious clinical problem in our tertiary set up, Peshawar, most of the patients present with seizures and respiratory distress. The in-hospital mortality rate was 14.2% while most (85.8%) of the affected neonates were successfully stabilized and discharged home, it is a serious public health concern. Stratification analysis further confirms the strong association between being low birth

weight, and being born at low gestational age, and poor clinical outcomes and mortality. The findings emphasize the importance of better prenatal screening, intra-uterine monitoring in labor, and prompt and effective therapeutic intervention after birth to minimize the occurrence of severe neurological injury. Standardized resuscitation protocols and training of pediatric healthcare providers in early detection of encephalopahtic symptoms are important interventions to improve long-term developmental outcomes and survival in Pakistan.

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