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**Original Research Article**

# A prospective study to evaluate influence of maternal, obstetric and fetal risk factors on the outcome of asphyxiated neonates born intramurally and extramurally

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## ABSTRACT

**Background:** The present study was planned to determine the influence of maternal, obstetric and fetal risk factors on the outcome of intramurally (born at a tertiary care centre) and extramurally (born at a peripheral centre, home or a private facility) born asphyxiated neonates.
**Methods:** It was an observational clinical research with a prospective design and was conducted in Neonatal Intensive Care Unit (NICU), Paediatric Neurology Clinic attached to Department of Paediatrics and Department of Obstetrics and Gynecology, Dr S N Medical College Jodhpur, Rajasthan. A total of 160 asphyxiated neonates (80 intramural and 80 extramural) were included in the study. A detailed antenatal and perinatal history with obstetrical interventions were recorded. The progress or deterioration in the clinical status of child was noted in hours. Outcome was evaluated in terms of survival, severest Hypoxic Ischaemic Encephalopathy (HIE) stage, time taken to reach non encephalopathic state, requirement of vasopressors and anticonvulsants, ventilator support, hemodynamic stability, time period to attain full enteral feeding, neurological examination at time of discharge and time taken for discharge.
**Results:** Significant difference was observed in the antenatal and perinatal profile, perinatal management and resuscitation, postnatal management, morbidity, mortality and neurodevelopment outcome of extramurally delivered neonates in a peripheral health centre or at home as compared to intramurally delivered neonates in a tertiary institute.
**Conclusions:** It is of paramount importance to have an early referral of asphyxiated neonates to a well equipped NICU using an appropriate well equipped transport unit/ chain so as to improve their outcome.

**Keywords:** Extramural, Hypoxic ischaemic encephalopathy, Intramural, Neonate, Neurodevelopmental outcome, Perinatal asphyxia

## INTRODUCTION

Childhood mortality remains a significant global challenge. Over nine million children die each year during the perinatal and neonatal periods, and nearly all of these deaths occur in developing countries.[1] Perinatal asphyxia remains a major cause of global mortality. Every year approximately four million babies are born

asphyxiated, resulting in one million deaths and an equal number of serious neurological consequences ranging from cerebral palsy and mental retardation to epilepsy.[2]

Ninety eight percent of neonatal deaths occur in low and middle income countries (LMIC) where most births and deaths happen at home. Of the forty countries with the highest NMRs in 2009 India is the country responsible for maximum number of neonatal deaths from 1990-2009.[3] Over half of these deliveries occur at home.

Despite best efforts, the rate of institutional delivery in India is only up to 46.9%. The percentage is still lower in the rural areas. Almost 40% of the deliveries occur at home, either unattended or attended by an untrained personnel.[4] As a national mandate highest levels of efforts are being made to improve number of institutional deliveries to reduce neonatal and maternal morbidity and mortality.

After delivery at a peripheral hospital most of the asphyxiated neonates are referred to a medical college institution or a private hospital equipped with a Neonatal Intensive Care unit (NICU). These neonates on reaching the tertiary care hospital/NICU at a medical college hospital are already critically ill and the definite management in essence starts when the neonate actually arrives at the NICU (long after the asphyxiated neonate is born).

On the contrary, asphyxiated neonates delivered at a tertiary care hospital where facilities for NICU exist are immediately admitted in the NICU for management as per standard protocols and guidelines.

The current study was therefore planned to evaluate the difference in short term and long term outcome of asphyxiated neonates born intramurally where standard management protocol was started immediately after birth and extramurally at home or another hospital from where the asphyxiated neonate was referred and transported to a facility equipped with NICU causing delay in start of standard management protocol. Further influence of maternal, obstetric and fetal risk factors on the outcome of birth asphyxia was also determined.

## METHODS

The present study was an observational clinical research with a prospective design and was conducted in Neonatal Intensive Care Unit and Paediatric Neurology Clinic attached to Department of Paediatrics and Department of Obstetrics and Gynaecology, Dr. S.N. Medical College, Jodhpur, Rajasthan.

### *Inclusion criteria*

All full term appropriate for gestational age (AGA) neonates admitted with history of either slow gasping breathing (moderate asphyxia) or no breathing at 1minute of age (severe asphyxia) were included in the study. Based on place of birth they were divided in two groups intramural (born in Associated Hospitals of Dr. S. N. Medical College) extramural (born outside and were referred to these hospitals).

### *Exclusion criteria*

All the babies who were born preterm, small or large for gestational age, having congenital anomalies, suspected to be having an inborn error of metabolism were excluded from the study.

Personal information of baby, antenatal history, birth history, and clinical details were recorded. Antenatal history was elicited for Pregnancy Induced Hypertension (PIH), Gestational Diabetes Mellitus (GDM), infections of the genitourinary tract, onset of quickening and the perception of foetal movements.

Perinatal history included the onset of labour pains, rupture of membranes and any significant intervention by the handling obstetrician. The mode of delivery, time period between the onset of labour pains and delivery were noted.

All the neonates admitted were managed as per the National Neonatology Forum (NNF) protocol for perinatal asphyxia and HIE. Neurological examination was performed and staging for HIE based on the Sarnat and Sarnat classification was done. The same was repeated at around 6 hours of life and 24hours of life. The changes in the HIE staging in the course was noted at hours of life.

The short-term outcome measures in terms of survival, severest HIE stage, time taken to reach non encephalopathic state, requirement of vasopressors, need for mechanical ventilation, anticonvulsants, oxygen support, time taken to attain for full enteral feeding and neurological status at discharge were compared between two groups. Long term outcome in terms of general wellbeing of child and neurological development was compared between these two groups.

The data were compiled in Microsoft excel and the statistical tests were applied using Windows SPSS version 20. The tests of significance used were the Student t test in the comparison of the mean values of the parameters, the Chi-square test was used in the comparison of short-term outcome between the intramural and extramural neonates.

## RESULTS

During the study period a total of 19,461 neonates were delivered in hospitals attached to Dr. S. N. Medical College, Jodhpur. Out of these 1785 neonates (9.21 %) were admitted in NICU. Out of these 375 (21.01%) were diagnosed as having perinatal asphyxia.

The mean age of the mothers of intramural neonates was 23.51±2.85 years, while that of extramural neonates was 23.45±3.12 years and the difference was not statistically significant. 52.5% of the intramural neonates and 94.75% of the extramural neonates were vaginally delivered with cephalic presentation. The percentage of lower segment Caesarean section (LSCS) deliveries was significantly higher in the intramural neonates (45%) when compared to extramural neonates (5%) (p value <0.01). Two neonates in the intramural group were delivered by forceps due to malpresentation. One of the neonates in the extramural group was delivered by forceps or had a malpresentation.

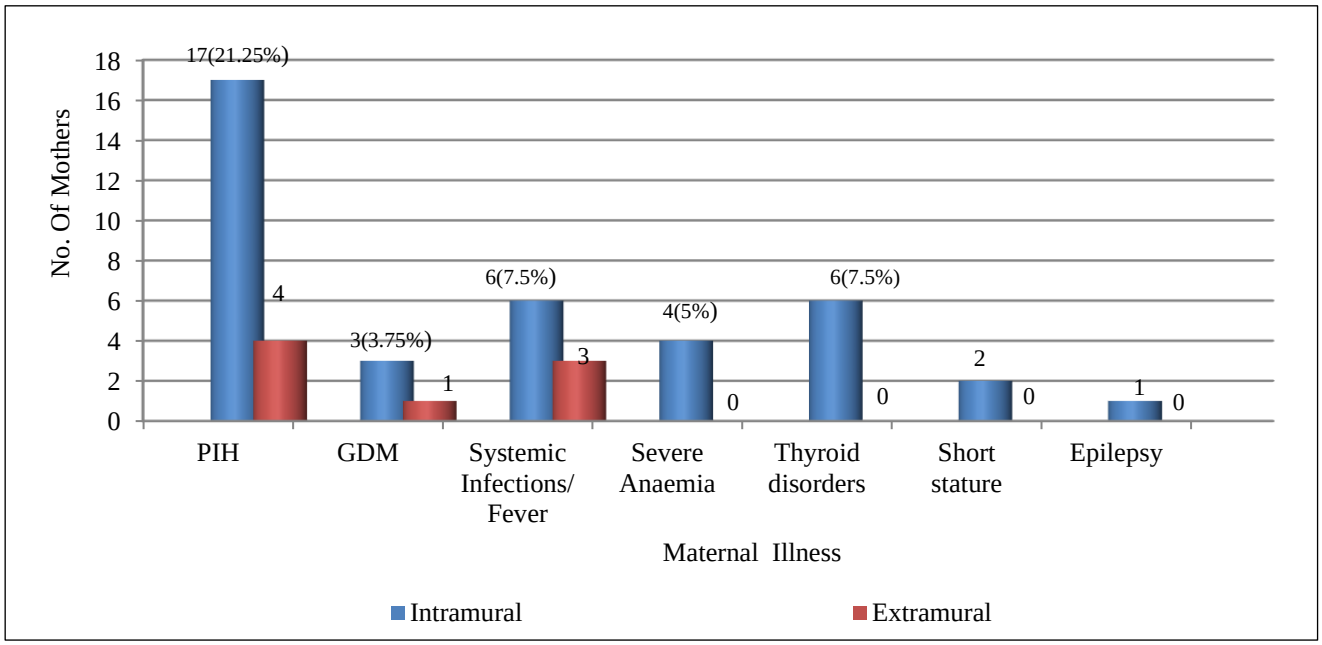


**Figure 1: Maternal characteristics of the cohort.**

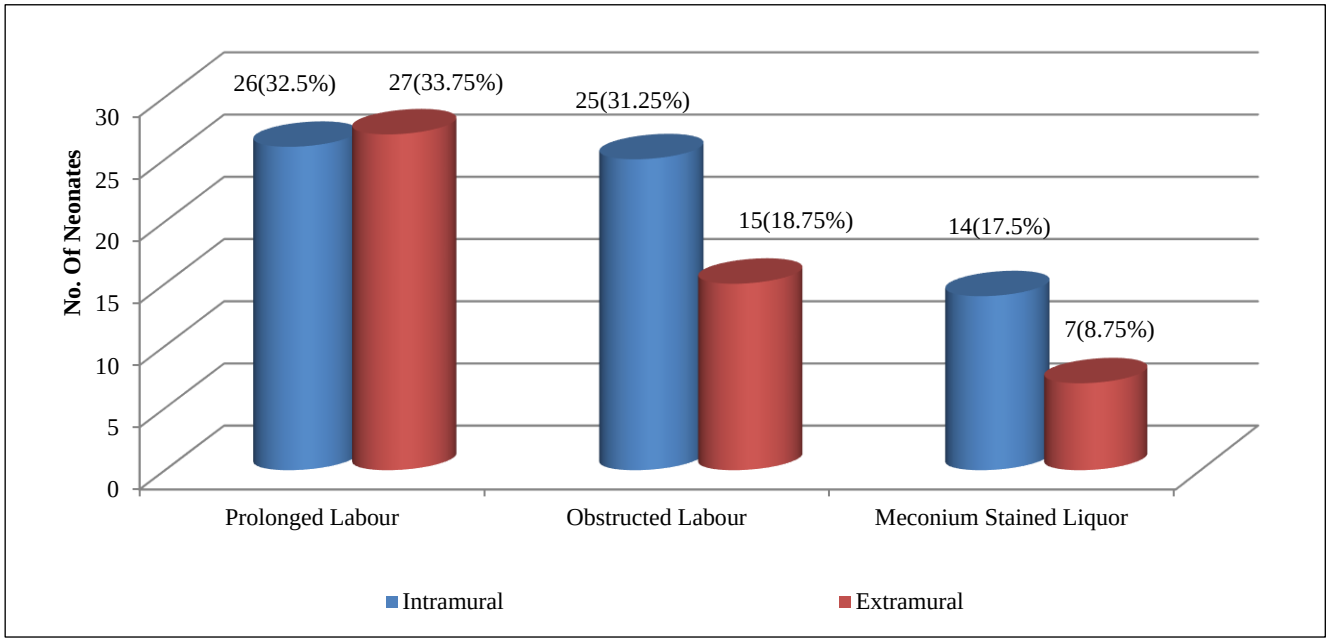


**Figure 2: Comparison of perinatal events between the intramural and extramural group.**

Antenatal complications were higher in the mothers of intramural neonates as compared to the mothers of extramural neonates. PIH in mothers of intramural neonates was statistically higher (p value<0.05) as compared to mothers of extramural neonates (Figure 1).

Prolonged labour was common in both the intramural and extramural group. Mothers of 31.25% of intramural neonates and 18.75% of the extramural neonates had history suggestive of obstructed labour and the difference between the two groups was statistically significant ($p<0.05$). Meconium stained liquor was documented in 17% of the intramural group and 8.5% of the extramural group (Figure 2).

Further the percentage of mothers receiving appropriate antenatal check-ups and visits were also low and most of mothers reached hospital in the last stage of labour with no previous records or investigations. The percentage of mothers who were booked and had at least a minimum of three antenatal check-ups were 25% (n=20) in the intramural group and 17% (n=14) in extramural group. The complications like anemia, poor weight gain, PIH etc. were recognized only at the time of delivery that posed threat to both the life of mother and the foetus.

**TABLE 1: Place of delivery and time of admission to our centre (extramural neonates).**

| Place of Delivery | Number of neonates | Mean time of admission (min) |
|---|---|---|
| Home | 13 (16.25 %) | 493.84±402.84 |
| Sub-centre | 03 (3.75 %) | 620.0±270.55 |
| PHC | 21 (26.25 %) | 825.71±407.65 |
| CHC | 08 (10 %) | 659.65±442 |
| District hospital | 19 (23.75 %) | 786.84±397.65 |
| Private hospital | 16 (20 %) | 457.82±495.43 |

The highest delay in the admission to our centre from the place of birth was seen in neonates who were delivered at a Primary Health Centre and neonates delivered at a Private Hospital were the earliest to reach our centre (Table 1). 47.5% of the extramural neonates were transported through an equipped ambulance with a paramedical staff and 52.5% of the neonates were transported using private vehicles without any trained person accompany.

Of the total 80 extramurally born neonates included in study 38.75% were delivered by Physicians, 25% were delivered by nurses, 22.5% were delivered by ANM/trained dais and unfortunately 13.75% were delivered unattended by any trained health worker/medical personnel (Figure 3). It was also notable in the current study that even when attended by a trained physician, nurse or ANM/trained Dai, the documentation on their referral tickets/discharge tickets was incomplete and there was no mention of basic Perinatal monitoring and resuscitation parameters including fetal heart rate trends or APGAR. Most of the discharge tickets or referral tickets also did not mention the exact resuscitation measures required.

Comparison of short-term outcome between intramural and extramural neonates and outcome of neonates based on time lapse in admission after birth in the extramural group was done (Table 2 and 3). The extramural neonates remained in an encephalopathic state for longer duration as compared to the intramural neonates (Figure 4).

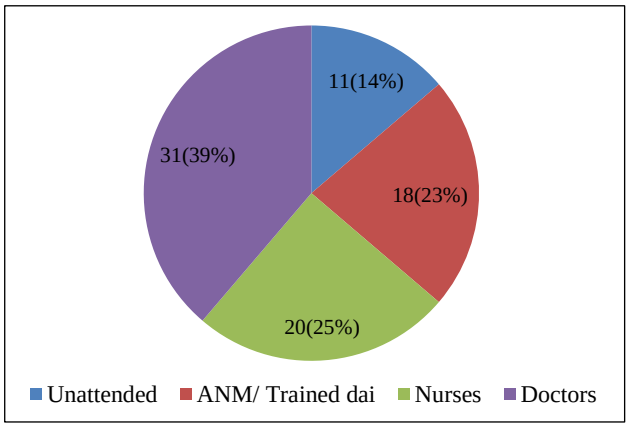


**Figure 3: Attendance of trained/untrained personnel during delivery of extramural neonates.**

**Table 2: Comparison of short term outcome between intramural and extramural neonates.**

| | Intramural | Extramural |
|---|---|---|
| **Mortality** | | |
| Survived | 60(75%) | 57(71.25%) |
| Expired | 20(25%) | 23(28.75%) |
| **HIE staging** | | |
| HIE III | 60(75%) | 48(60%) |
| HIEII | 12(15%) | 29(36.25%) |
| HIE I | 08(10%) | 03(3.75%) |
| **Mean time duration to progress into a less severe HIE stage (hours)** | | |
| Time taken from HIE III to reach HIE II | 21.63±22.92 | 76.53±65.58 |
| Time taken from HIE II to reach HIE I | 58.50±54.50 | 83.29±73.71 |
| Time taken to reach no HIE | 65.65±45.53 | 95.27±51.4 |
| Mean duration of vasopressors (days) | 2.434±2.888 | 3.423±2.912 |
| Mean No. of anticonvulsants | 1.355±0.349 | 1.369±0.412 |
| **Requirement of positive pressure ventilation** | | |
| Number requiring ventilation | 56(70%) | 47(58.75%) |
| Mean duration on ventilator (hours) | 40.08±53.39 | 109.09±98.14 |
| Mean duration of oxygenation (hours) | 99.36±98.32 | 153.86±128.89 |
| **Duration to attain full enteral feed** | | |
| <7days | 49(81.66%) | 32(56.14%) |
| 7-14days | 08(13.33%) | 16(28.07%) |
| >14days | 03(3.75%) | 09(15.79%) |
| **Neurological examination at discharge** | | |
| Normal | 42/60(70%) | 33/57(57.9%) |
| Abnormal | 18/60(30%) | 24/57(42.1%) |

**Table 3: Comparison of outcome of neonates based on time lapse in admission after birth in the extramural group.**

| | <6 hours (n=30) | >6hours (n=50) |
|---|---|---|
| No. of admissions | 30(37.5%) | 50(62.5%) |
| **Maximum stage of HIE** | | |
| HIE III | 21(26.25%) | 27(33.75%) |
| HIE II | 6(7.5%) | 23(28.75) |
| HIE I | 03(3.75%) | 00 |
| **Outcome** | | |
| Live | 20(66.67%) | 37(74%) |
| Expired | 10(23.7%) | 13(26%) |
| Babies requiring mechanical ventilation | 21(24.35%) | 26(51.25%) |
| Mean duration of stay of babies | 14.3±9.23 | 19.86±17.49 |
| Mean time of expiry | 3.3±1.2 | 4.923±2.14 |
| **Neurological examination at discharge** | | |
| Normal | 14(46.67%) | 18(36%) |
| Abnormal | 05(16.67%) | 19(38%) |
| Oral Anticonvulsants | 04(13.33%) | 22(44%) |

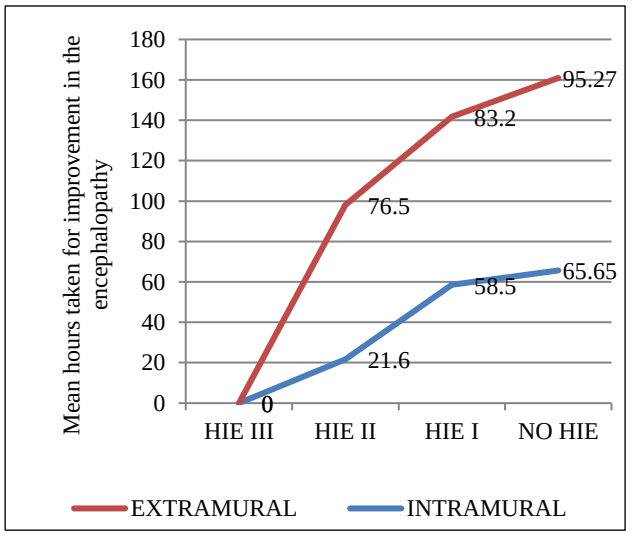


**Figure 4: Comparison of mean duration of improvement of encephalopathy between the intramural and extramural group.**

Extramural neonates also have a higher requirement of vasopressor support in terms of both number and duration. The neurological examination was abnormal in most of the neonates who survived at discharge in the group who were admitted after the first 6hours of life (n=19 out of 37 discharged neonates) in both intramural and extramural neonates. They have a higher chance of going home on an anticonvulsant and also remain on an anticonvulsant at the end of 6 months of age (Table 3). Only 34 intramural neonates and 30 extramural neonates could be followed up until 6 months. 32.35% of the intramural neonates and 60% of the extramural neonates had an abnormal neurological examination at 6 months of age. Developmental delay was observed in 41% of the intramural children and 63% of the extramural children.

## DISCUSSION

Perinatal Asphyxia is a leading cause of neonatal mortality in India and other parts of developing world.[5] It is associated with a very high morbidity during the neonatal period and leads to severe neurodevelopmental disability in survivors.[2]

The maternal characteristics do have a significant role in pathogenesis of asphyxia and include mothers over 35 years of age or less than 20 years of age, presence of preeclampsia/eclampsia, presence of maternal diabetes mellitus, evidence of infection (maternal fever, signs of chorioamnionitis).[6] The study centre serves as the referral centre for Western Rajasthan including six major districts, hence the number of obstetrical emergencies and complications were much higher in the intramural group than the periphery. Higher the maternal complications higher are the chance of foetal compromise manifesting as perinatal asphyxia. This explained the higher number of complicated obstetrical cases in the intramural group.

The number of primiparous mothers were higher in the intramural (53.75%) compared to extramural (48.75%) group. The number of caesarean deliveries were higher in the intramural group as compared to extramural group this may be attributed to the fact that intramural group also had a higher number of maternal complications in primipara women and therefore may have landed into a caesarean delivery, while in the extramural group many deliveries occurred in peripheral hospitals and home, where facilities for caesarean deliveries were not available. Since our centre is a tertiary referral centre and caters to a large percentage of complicated obstetrical cases, the number of modes of delivery other than vaginal delivery was much higher in the intramural group as compared to the extramural group. In general, the percentage of caesarean deliveries was higher in babies who were born asphyxiated. Ilah et al, recorded higher number of emergency caesarean section deliveries (59.6%) in asphyxiated neonates, mainly with indications of prolonged/obstructed labour and eclampsia.[7]

Primigravida deliveries were found to have a higher association with perinatal asphyxia and mortality status as per the reports by Oniyiruka in Benin.[8] In this study, the number of primigravida deliveries were higher both in the intramural and extramural group, however a statistically significant association was not found. The results were similar to that of the reports by Kinoti where a higher number of primigravida deliveries were recorded.[9]

Even with Caesarean section the percentage of delivery of asphyxiated neonate was high in the intramural group. This implies that a much more early intervention was required in these cases. If the extramural neonates who

were born asphyxiated by vaginal delivery, had a chance of an early intervention/termination of labour, had the chance of being born asphyxiated low remains a query. Thus, a vigilant foetal monitoring should be practiced by the obstetrician and the same should be ensured by the birth attendants, midwives and the ANM's who conduct delivery in the periphery. Prolonged labour was common in both the intramural and extramural group. In the study conducted by Oswyn et al, fetal distress was documented in 82% of babies with HIE and 50% had bradycardia.[10] Chandra et al, reported presence of meconium stained liquor in 56% of babies with perinatal asphyxia.[11]

The percentage of mothers receiving appropriate antenatal check-ups and visits were also low and most of mothers reached hospital in the last stage of labour with no previous records or investigations. The complications like anemia, poor weight gain, PIH etc. were recognized only at the time of delivery that posed threat to both the life of mother and the foetus. Amritanshu et al, in their study observed that 272 out of total 370 outborns were home delivered (73.5%) and 98 out of 370 were delivered in a private clinic or maternity home (26.5%).[12] In the study by Sehgal et al, on extramural neonates, the percentage of babies delivered at home unattended by any trained/skilled birth attendant was 15% and asphyxia was the second leading cause of referral next to prematurity.[13] The referral ticket of the extramural neonates did not make a significant difference or contribution in assessing the severity of the neonate's condition at birth, resuscitation and post-natal management.

In the study by Shah et al, the percentage of asphyxiated neonates delivered by health personnel was 33.8%, the trained birth attendants 29.5% and most of the others were not attended.[14] A higher mortality and morbidity was seen in the group of neonates delivered at home without supervision. It was also notable in the current study that even when attended by a trained physician, nurse or ANM/trained dai, the documentation on their referral tickets/discharge tickets was incomplete and there was no mention of basic perinatal monitoring and resuscitation parameters including fetal heart rate trends or APGAR. Most of the discharge tickets or referral tickets also did not mention the exact resuscitation measures required. This also led to delayed or inaccurate identification of the gravity of situation, inaccurate diagnosis and in many cases delayed referral and transport to an appropriate referral centre.

The percentage of HIE stage III was statistically higher in the intramural group when compared to extramural group ($p<0.05$). Amritanshu et al, in their study showed that at admission 81.33% (488) were in Stage I HIE, 14.16% (85) were in Stage II HIE and 4.5% (27) were in Stage III HIE.[12] Mohan et al, in their study showed a maximum number of neonates with features of stage II (54%) while 31% and 14% with stage I and III respectively.[15] Tiwari et al, in their study observed as per Sarnat and Sarnat staging 20% (24) were in stage I, 30% (36) were in stage II and 16.6% (20) were in stage III of hypoxic ischemic encephalopathy.[16]

In our study the extramural neonates remained in an encephalopathic state for longer duration as compared to the intramural neonates (Figure 4). This is probably a reflection of better protocolised neonatal resuscitation, early admission into a specialized well equipped NICU and early initiation of specific treatment in the intramural group as compared to the extramural group. In the study by Memon et al, on neurological evaluation done within 24 hours of admission 180 (30%) babies were in stage I, 210 (35%) in Stage II and 120 (20%) in stage III of HIE.[17] The early outcome was measured after 72 hours of admission in terms of clinically improved, having features of HIE, or expired. Almost all the babies in stage I HIE improved while those in stage III either expired or discharged with disability. This observation mandates the need for an early referral of asphyxiated neonates to a well equipped NICU using an appropriate well equipped transport unit/chain so as to improve their outcome.

The neurological examination at discharge was normal in 70% of the intramural neonates and 58% of the extramural neonates. Abnormal neurological examination was present in 30% of the intramural and 42% of the extramural neonates. Memon et al, showed that the probability of neurological disability due to HIE after birth asphyxia was 4.615 times more in out-born babies.[17] This might be due to fact that inborn babies were admitted earlier (within 6hours) as compared to out-born babies. It means if the asphyxiated neonate had reached the facility early, there were better chances to recover without sequelae. Delayed referral land into poor morbidity or mortality irrelevant to place of delivery. This observation was also confirmed in relation to age at admission. The delay in reaching hospital caused more neurological disability. This was also found to be statistically significant when considering mortality.

## CONCLUSION

This study has demonstrated the significant differences that exist in the antenatal and perinatal profile, perinatal management and resuscitation, postnatal management, morbidity, mortality and long term neurodevelopment outcome of extramurally delivered neonates in a peripheral health centre or at home as compared to intramurally delivered neonates in a tertiary level institute. It is therefore paramount to have an early referral of asphyxiated neonates to a well equipped NICU using an appropriate well equipped transport unit/chain so as to improve their outcome.

Despite significant improvement in the health care delivery system with incentives to institutional deliveries (through Janani Suraksha Yojana) the numbers of home deliveries continue to be high in the rural areas of Western Rajasthan. There continues to be a large gap in the infrastructure and skilled manpower availability in

peripheral health services when compared to well-equipped tertiary health centres leading to a difference in the care and management of asphyxiated neonates.

It is therefore very pertinent and important to understand the factors which determine the difference in outcome of babies born at a tertiary care centre versus babies who are not born in a tertiary care centre. A clear understanding of these factors will help in improving the facilities in peripheral health centres, provide guidelines/ recommendations for early referral and improve transportation of sick neonates so as to reduce morbidity.

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