Morbidity and mortality pattern of intramural and extramural neonate: a prospective observational study

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INTRODUCTION

Though, there has been improvement in perinatal services, neonatal phase of life carries the highest risk of mortality than any other phase during the childhood. In 2019, globally 2.4 million children died in the neonatal period—approximately 6700 neonatal deaths every day and 47% neonatal deaths accounted for under-five mortality. In India, there is slight decline (from 28 in 2013 to 22 in 2019) in neonatal mortality with interstate, rural-urban variation but lags behind that of infant and under-five mortality. While, sepsis (36%), prematurity (28%) and birth asphyxia (23%) are the major causes of neonatal deaths in developing countries, prematurity and malformations are the causes in developed countries. The major causes of newborn deaths in India are preterm births (35%), neonatal infections (33%), birth asphyxia (20%) and congenital malformation (9%).

Morbidity and mortality profile of intramural neonates those who are treated in neonatal intensive care unit is well studied. However accurate data of extramural neonates is scanty. Morbidity and mortality pattern may be different in extramural neonates due to they might be home delivered, long distance travel, poor care or no care during transportation or previous admission to a different...
setting and data on such details are lacking in India and
globally. In developing countries with poor resources
setting, neonatal intensive care units are not available or
of limited capacity, extramural neonates are treated in
general pediatric wards but information’s about such
neonates are limited.12,13

With this background, this study aimed to document the
morbidity and mortality pattern of intramural and
extramural neonates and identify the factors that can
further improve the outcome.

METHODS

This prospective observational study was undertaken on
both intramural (inborn) and extramural (outborn)
neonates over a period of 1 year from January 2018 to
December 2018 at Government medical college and
hospital, Nagpur (Maharashtra), after approval from the
institutional ethical committee and informed valid
consent from parents. Intramural neonates included those
neonates delivered in our hospital and required
hospitalization in our NICU while extramural neonates
are delivered outside the hospital premises (at home,
government facilities, private hospital) and referred to
and admitted through either outpatient or emergency
department in our institute. Neonates whose parents left
the hospital against medical advice and not willing to
participate in the study were excluded. Intramural
neonates were treated in our 20 bedded levels III NICU.
As per the policy of the hospital, extramural neonates are
not admitted in our NICU hence they are kept in the
general pediatric wards where there are separate blocks in
each ward, equipped with central oxygen supply,
phototherapy units and bubble CPAP.

Data were collected following admission, from either the
mother or caregiver in a structured data sheet. Maternal
details included age, gravidity/parity statuses, details of
antenatal care, obstetrics complications and mode of
delivery were recorded. In extramural neonates, in
addition to maternal details, place of delivery, distance
from institute, referral person, mode of transport and
distance travelled by the neonate were recorded.
Socioeconomic status of parents was classified on the
basis of modified Kuppuswammy scale.14 Neonatal data
included gestational age (assessed by menstrual history of
mother, available ultrasound report or by new Ballard
scoring), gender, birth weight/weight on admission, age
at admission, clinical presentation, duration of hospital
stay.15 All neonates were investigated, diagnosed,
managed and monitored as per the standard treatment
protocol till discharge or death using clinical information
and necessary laboratory investigation.

Hypothermia (axillary temperature by digital
thermometer), capillary refill time (>3 sec) was taken as
prolonged), blood sugar (<45 mg/dl was taken as
hypoglycemia) and other life threatening events were
recorded. Birth asphyxia, respiratory distress, meconium
aspiration syndrome and sepsis were defined as per
National Neonatal Perinatal Database.

Statistical analysis

The data were entered into microsoft excel sheet and
analysis was done using software STATA version 14
(Texas USA). The data regarding the numerical variables
were summarized through percentage, average, median,
and deviation pattern. Comparisons of categorical data
were carried out using Pearson’s Chi square of Fisher’s
exact test. P<0.05 was taken as statistically significant.

RESULTS

A total of 7330 patients of 0-12 years were admitted in
general pediatric ward during study period, out of which
1207 (16.47%) were in the neonatal (0-28 days) age
group. Among 1207 neonates, 210 were excluded from
the study because parents left the hospital against medical
advice and/or were not willing to participate in the study.
Hence 997 were included and analyzed. Out of 997
neonates, 287 died, giving a mortality rate of 28.79%.

A total of 11838 live births took place in our hospital and
1770 (14.95%) neonates required admission in NICU, out
of these 394 succumbed, giving a mortality rate of
22.26%.

Characteristics of study participant

Of the intramural neonates, male to female ratio was
1.27:1 while in extramural neonates the ratio was 1.3:1.
Preterm 941 (53.16%) neonates were predominant in the
extramural group and term 548(54.96%) neonates in the
intramural group. 1157 (65.37%) intramural neonates
had birth weight ranging from 1500 gms to 2999 gms
compared to 866 (86.86%) neonates of similar range on
admission but extremely and very low birth weight
neonates were predominant in intramural compared to
extramural group (p<0.001). Vaginally born neonates
(65.60%) were predominant in extramural group while
cesarean delivered predominated in the intramural group
(p<0.001). Most of the mothers were from lower
socioeconomic class of rural areas but mortality was
significantly higher in extramural neonates (p<0.001).
Maternal illness during pregnancy were significantly
more in mothers of extramural neonates compared to
intramural neonates (p<0.001). Anemia was the
commonest maternal condition during pregnancy
followed by systemic hypertension while pregnancy
induced hypertension was the most common obstetrics
complication in both the groups (Table 1).

Antenatal care and transport of extramural neonates

A total 586 (58.78%) mothers received antenatal care by
medical officer either at primary, secondary health care
level or district hospital. 325 (32.6%) neonates were
referred by trained dai/ASHA workers. Mortality was
significantly higher in neonates who received antenatal care by trained dai (p=0.03), ASHA workers (p<0.001) and by medical officers (p=0.004) at primary health care level while mortality was also significantly higher in neonates who were referred by the same personnel (p<0.001). Mean distance travelled by the neonate was 85.92±78.89 kms with a range of 5-368 kms. Those neonates who travelled longer distance (98.52±37.72 kms) had significantly higher mortality than the shorter distance ones (78.53±42.61 kms) (p=0.001). None of the baby was transported in ambulance with medical attendant and no supportive care was given during transportation. There was no prior communication before transport (Table 2).

### Table 1: Neonatal and maternal variables in study population.

| Variables                      | Intramural; all cases (N=1770, %) | Extramural; all cases (N=997, %) | P value |
|--------------------------------|-----------------------------------|----------------------------------|---------|
| **Gender** (male)              | 990 (55.93)                       | 564 (56.57)                      | 0.8     |
| **Gestational age**            |                                   |                                  |         |
| Preterm                        | 941 (53.16)                       | 434 (43.54)                      | <0.001  |
| Term                           | 819 (46.27)                       | 548 (54.96)                      | 0.001   |
| Post-term                      | 10 (0.57)                         | 15 (1.50)                        |         |
| **Weight on admission (in gms)** |                                   |                                  |         |
| <1000                          | 125 (7.06)                        | 15 (1.50)                        | <0.001  |
| 10001-1499                     | 430 (24.29)                       | 54 (5.42)                        | 1       |
| 1500-2499                      | 716 (40.45)                       | 456 (45.74)                      |         |
| 2500-2999                      | 441 (24.92)                       | 410 (41.12)                      |         |
| >3000                          | 58 (3.28)                         | 62 (6.22)                        |         |
| **Mode of delivery**           |                                   |                                  |         |
| Vaginal                        | 887 (50.11)                       | 654 (65.60)                      | <0.001  |
| Cesarean                       | 871 (49.21)                       | 315 (31.59)                      | 1       |
| Assisted                       | 12 (0.68)                         | 28 (2.81)                        |         |
| **Residence (rural)**          | 1256 (70.96)                      | 737 (73.92)                      | 0.1     |
| **Socioeconomic status (lower)** | 1221 (68.98)                     | 698 (70.01)                      | 0.6     |
| **Maternal conditions**        |                                   |                                  |         |
| Anemia                         | 560 (31.64)                       | 447 (44.83)                      | 0<0.01  |
| Hypertension                   | 78 (4.41)                         | 67 (6.72)                        | 0.01    |
| Heart disease                  | 10 (0.56)                         | 6 (0.60)                         |         |
| Diabetes                       | 7 (0.40)                          | 3 (0.30)                         |         |
| Hemoglobinopathy               | 21 (1.19)                         | 24 (2.41)                        |         |
| Liver diseases                 | 5 (0.28)                          | 2 (0.20)                         |         |
| Hypothyroidism                 | 27 (1.53)                         | 8 (0.80)                         |         |
| **Obstetrics complication**    |                                   |                                  |         |
| PIH                            | 255 (14.41)                       | 187 (18.76)                      |         |
| Eclampsia                      | 50 (2.82)                         | 10 (1.00)                        |         |
| Gestational diabetes           | 18 (1.01)                         | 3 (0.30)                         |         |
| APH                            | 50 (2.82)                         | 2 (0.20)                         | 0.003   |
| PROM >24 hours                 | 75 (4.24)                         | 57 (5.72)                        |         |
| Malpresentation                | 42 (2.37)                         | 3 (0.30)                         |         |
| Twining                        | 66 (3.73)                         | 24 (2.41)                        |         |

### Table 2: Antenatal care and transport of extramural neonates.

| Variables               | All cases (N=997, %) | Survival (N=710, %) | Non-survival (N=287, %) | P value |
|-------------------------|----------------------|---------------------|--------------------------|---------|
| **ANC care provider**   |                      |                     |                          |         |
| Trained dai             | 14 (1.4)             | 6 (0.85)            | 8 (2.79)                 | 0.03    |
| ASHA worker             | 89 (8.93)            | 37 (5.21)           | 52 (18.12)               | <0.001  |
| Medical officer         | 586 (58.78)          | 438 (61.69)         | 148 (51.57)              | 0.004   |

Continued.
ASHA worker-accredited social health activist worker.

### Table 3: Clinical details of cases (not exclusive).

| Clinical variables                  | Intramural All cases (N=1770, %) | Extramural All cases (N=997, %) | P value | Intramural Non-survival (N=394, %) | Extramural Non-survival (N=287, %) | P value |
|------------------------------------|----------------------------------|---------------------------------|---------|-----------------------------------|-----------------------------------|---------|
| Lethargy                           | 840 (47.46)                      | 560 (56.17)                     | 0.001   | 154 (39.09)                       | 116 (40.42)                       | 0.78    |
| Hypothermia                        | 245 (13.84)                      | 223 (22.37)                     | <0.001  | 98 (24.87)                        | 54 (18.82)                        | 0.07    |
| Cyanosis                           | 347 (19.60)                      | 57 (5.72)                       | <0.001  | 216 (54.82)                       | 37 (12.89)                        | <0.001  |
| Convulsion                         | 311 (17.57)                      | 34 (3.41)                       | <0.001  | 267 (67.77)                       | 20 (6.97)                         | <0.001  |
| Apnea                              | 456 (25.76)                      | 47 (4.71)                       | <0.001  | 287 (72.84)                       | 14 (4.88)                         | <0.001  |
| Respiratory distress               | 876 (49.49)                      | 446 (44.73)                     | 0.01    | 274 (69.54)                       | 148 (51.57)                       | <0.001  |
| Prolonged CFT                      | 224 (12.66)                      | 146 (14.64)                     | 0.15    | 125 (31.72)                       | 78 (27.18)                        | 0.23    |
| Jaundice                           | 487 (27.51)                      | 112 (11.23)                     | <0.001  | 117 (26.70)                       | 10 (3.48)                         | <0.001  |
| Meconium stain                     | 375 (21.19)                      | 46 (4.61)                       | <0.001  | 137 (34.77)                       | 28 (9.76)                         | <0.001  |
| Bleeding manifestation             | 134 (7.57)                       | 24 (2.41)                       | <0.001  | 89 (22.59)                        | 18 (6.27)                         | <0.001  |

### Table 4: Morbidity profile in study population.

| Clinical diagnosis                               | Intramural All cases (N=1770, %) | Extramural All cases (N=997, %) | P value |
|--------------------------------------------------|----------------------------------|---------------------------------|---------|
| Sepsis/pneumonia/meningitis                       | 371 (20.96)                      | 369 (37.01)                     | <0.001  |
| Prematurity with respiratory distress syndrome    | 560 (31.64)                      | 159 (15.95)                     | <0.001  |
| Respiratory distress (other causes)               | 36 (2.03)                        | 39 (3.91)                       | 0.005   |
| Birth asphyxia                                    | 135 (7.63)                       | 49 (4.91)                       | 0.007   |
| Malformations                                     | 107 (6.05)                       | 61 (6.12)                       | 0.93    |
| Meconium aspiration syndrome                      | 87 (4.92)                        | 47 (4.71)                       | 0.88    |
| Jaundice requiring phototherapy                   | 412 (23.27)                      | 167 (16.75)                     | 0.0006  |
| Hypoglycemia                                      | 10 (0.56)                        | 37 (3.71)                       | <0.001  |
| Other                                             | 52 (2.94)                        | 69 (6.92)                       | <0.001  |

### Table 5: Neonatal and maternal variables in non-survival.

| Variables                     | Intramural non-survival (N=394, %) | Extramural non-survival (N=287, %) | P value |
|-------------------------------|-----------------------------------|-----------------------------------|---------|
| Gender (male)                 | 218 (55.33)                       | 176 (61.32)                       | 0.13    |
| Gestational age               |                                   |                                   |         |
| Preterm                       | 305 (77.41)                       | 118 (41.12)                       | <0.001  |
| Term                          | 88 (22.34)                        | 164 (57.14)                       |         |
| Post-term                     | 1 (0.25)                          | 5 (1.74)                          |         |
| Weight on admission (in gms)  |                                   |                                   |         |
| <1000                         | 107 (27.16)                       | 2 (0.70)                          |         |
| 10001-1499                    | 135 (34.26)                       | 17 (5.92)                         | <0.001  |
| 1500-2499                     | 115 (29.19)                       | 140 (48.78)                       |         |
| 2500-2999                     | 34 (8.63)                         | 113 (39.37)                       |         |
| >3000                         | 3 (0.76)                          | 15 (5.23)                         |         |
| Mode of delivery              |                                   |                                   |         |

Continued.
**Table 6: Mortality profile in study population.**

| Clinical diagnosis                                      | Intramural non-survival (N=394; %) | Extramural non-survival (N=287; %) | P value |
|---------------------------------------------------------|------------------------------------|-----------------------------------|---------|
| Sepsis                                                   | 66 (16.75)                         | 121 (42.16)                       | <0.001  |
| Prematurity with respiratory distress syndrome           | 203 (51.52)                        | 65 (22.64)                        | <0.001  |
| Respiratory distress (other causes)                      | 18 (4.57)                          | 23 (8.01)                         | 0.07    |
| Birth asphyxia                                           | 40 (10.15)                         | 24 (8.36)                         | 0.5     |
| Malformations                                            | 43 (10.91)                         | 41 (14.29)                        | 0.22    |
| Meconium aspiration syndrome                             | 22 (5.58)                          | 5 (1.74)                          | 0.01    |
| Jaundice                                                 | 00                                 | 6 (2.09)                          | 0.005   |
| Unknown                                                  | 2 (0.51)                           | 2 (0.71)                          | 0.74    |

**Clinical presentation of study participant**

Lethargy and respiratory distress was the commonest presentation in both group but lethargy and hypothermia was significantly more in extramural group (p<0.001) while respiratory distress was statistically higher in intramural group (p=0.01). Apnea, jaundice and bleeding manifestations were more common in intramural group (p<0.001) (Table 3).

**Morbidity and mortality profile**

The leading causes of admission in intramural neonates was prematurity with respiratory distress syndrome (31.64%) followed by jaundice (23.27%) while in extramural neonates, it was sepsis (37.01%) followed by jaundice (16.75%) and this difference was statistically significant.
significant. Other morbidities include birth asphyxia, meconium aspiration syndrome and malformation (Table 4). Mortality rate in intramural neonate was 22.26% while in extramural neonate was 28.79% (Figure 1). Mortality was significantly higher in extramural neonates (p=0.0001). Male neonates had significantly higher mortality than female. Preterm and extremely/very low birth weight had higher mortality in intramural group compared to extramural neonates while term and average birth weight had better survival in intramural group as compared to extramural (p<0.001). Mortality was significantly higher in extramural neonates with maternal illness during pregnancy compared to intramural neonates (Table 5). Major causes of death in intramural neonates were preterm birth complication (51.52%) followed by sepsis (42.16%) while in extramural neonates leading cause of death was sepsis (16.75%) while in extramural neonates leading cause of death was sepsis (42.16%) followed by prematurity and its complications (22.65%). Other causes of mortality include asphyxia, meconium aspiration syndrome and malformations in both groups of neonates (Table 6).

**DISCUSSION**

Neonates are the weakest members of the society. Morbidity and mortality pattern of extramural neonates are different because of, mostly they are home delivered or delivered at an inadequate facility, travel a long distance with poor or no care during transport and are older at admission compared to intramural neonates as they are born at well-equipped center with trained personnel. Limited data are available on such extramural neonates treated in general pediatric wards. So, this study was conducted to know the morbidity and mortality of intramural neonates who were treated in NICU and extramural neonates treated in general pediatric wards.

We observed that a total of 14.95% intramural and 16.47% extramural neonates required hospitalization during the study period. Okposio et al reported 18.2% extramural neonates required hospitalization in their study. Similar to other authors, in our study male were predominant in both intramural and extramural group. This might be because of biological vulnerability of male neonates and gender bias in our society. Indian literature suggest that expenditure of health care is around fourfold higher with male neonates compared to cheaper treatment options for females. Preterm, extremely/very low birth weight neonates were predominant in intramural group compared to extramural group (p<0.001) due to high risk mothers being treated in our institute. Around 50% neonates were delivered by cesarean section in intramural group compared to 31.59% in extramural group (p<0.001) and our findings were concomitant with other researchers.

We observed 70.96% in the intramural group and 73.92% in the extramural group mothers to be from rural area and most of them belonged to lower socioeconomic class. 69.11% mothers of extramural neonates received antenatal care by dai, ASHA workers or medical officers of either primary or secondary health care level. Maternal illnesses and obstetrics complications were significantly higher in mothers of extramural group compared to intramural group. Effective antenatal care is very important to detect the high risk mothers for better pregnancy outcome. Inspite of free ambulance services and janani suraksha yojana for mothers and neonates, none of the neonate were transported by ambulance with medical attendant or any prior communication. 67.2% extramural neonates were referred by dai/ASHA workers and medical officers as a similar observation by Rakholia et al and it was observed that mortality was significantly higher in these neonates. Provision of timely transport of mothers and neonates in equipped ambulance is very important to reduce the mortality.

In the present study, lethargy and hypothermia was significantly higher among extramural neonates while cyanosis, convulsion and apnea were the common presentation in intramural neonates (p<0.001) as most of preterm and extremely/very low birth weight neonates belonged to the intramural group. Similar to the finding of Bokade et al mortality was significantly higher in neonates who presented with hypothermia, cyanosis, convulsion and apnea. Identification and intervention of acute life threatening events is important to reduce the mortality.

Sepsis was the commonest cause of admission in extramural neonates compared to intramural group (p<0.001). This might be because of more than 60% extramural neonates being delivered by peripheral health workers by vaginal route probably with inadequate aseptic precaution compared to adequate aseptic methods in intramural neonates. Similar to our findings, high incidence of neonatal sepsis in extramural neonates were reported by Malpani et al, Kumar MK et al and Okposio et al and low incidence in intramural neonates by Sharma et al, Kumar et al and Fahmy et al.

Prematurity and its complication like respiratory distress syndrome (51.52% versus 22.64%), birth asphyxia (10.15% versus 8.36%) and meconium aspiration syndrome (5.58% versus 1.74%) were more prevalent in intramural neonates compared to extramural neonates because high risk mothers were referred and delivered in institute which resulted in preterm birth and extremely/very low birth weight neonates. It is also true that most of the mothers are reported in active labor resulting in more asphyxiated and meconium aspirated neonates. Various authors observed similar findings in their studies. In contrast to the finding in the literatures, other causes of respiratory distress was more predominant in intramural neonate (3.91% versus 2.03%) compared to intramural neonates. This might be due to the fact that extramural neonates were already admitted and also received treatment from other setting before getting admitted to us. Neonatal jaundice requiring phototherapy was more prevalent in intramural neonates...
Mortality rate was significantly higher in extramural neonates (28.79% versus 22.26%) than in intramural neonates. Such high mortality rates in extramural neonates were observed by Sharma et al (33.03% versus 22.03%), Kumar et al (8.87% versus 7.69%) compared to intramural neonates. Preterm, extremely/very low birth weight neonates had higher mortality in intramural group compared to extramural neonates and male neonates had significantly higher mortality in both the groups. In the present study, preterm, low birth weight and male neonates are more prone for mortality and our observations are concomitant with other researchers.\textsuperscript{16,17,21,23}

Sepsis was the most common cause of death in extramural neonates followed by prematurity with respiratory distress syndrome while prematurity with respiratory distress syndrome followed by sepsis in intramural neonates and this difference was statistically significant (p<0.001). Similar types of observations were observed by Malik et al, Kumar et al, Sharma et al and Malpani et al. Other causes of mortality were birth asphyxia, congenital malformations and meconium aspiration syndrome as observed in our study. The limitations of this study was the different level of neonatal care for intramural and extramural neonates that was received.

CONCLUSION

Sepsis is the most common cause of morbidity and mortality in extramural neonates while prematurity and its complication is leading cause of admission and death in intramural neonates. It is important to improve the neonatal and obstetrics services as well as training and practice to implement aseptic precaution at peripheral health centers in the management of immediate neonatal health and to make available good transport service to achieve single digit neonatal mortality by 2030.

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