International Journal of Contemporary Pediatrics
Meshram RM et al. Int J Contemp Pediatr. 2021 Jun;8(6):1006-1013
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: https://dx.doi.org/10.18203/2349-3291.ijcp20212039

Original Research Article

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

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Received: 19 April 2021
Revised: 11 May 2021
Accepted: 12 May 2021

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ABSTRACT

Background: Neonatal period carries higher risk of death inspite of advances in perinatal and neonatal services. The objective of the study was to assess the morbidity/mortality pattern of intramural and extramural neonates.
Methods: Prospective observational study was undertaken on all intramural and extramural neonates who fulfill the inclusion criteria at a tertiary institute for one year. Morbidity and mortality patterns were analyzed.
Results: A total 1770 intramural and 997 extramural neonates required admission during the study period. Mortality rate in intramural neonate was 22.26% while in extramural neonate was 28.79%. The male to female ratio was 1.27:1 in intramural while 1.3:1 in extramural neonates. Preterm neonates with extremely/very low birth weight were predominant in intramural group and term neonates in extramural group ($p<0.001$). Maternal illness during pregnancy were significantly more in mothers of extramural neonates compared to that of intramural neonates ($p<0.001$). Lethargy and hypothermia was significantly more in extramural group ($p<0.001$) while respiratory distress was significantly higher in intramural group ($p=0.01$). The leading causes of admission in intramural neonates was prematurity with respiratory distress syndrome (31.64%) while sepsis (37.01%) in extramural group of neonates. Preterm birth complication (51.52%) was the common cause of mortality in intramural neonates while sepsis (42.16%) in extramural neonates.
Conclusions: Sepsis is the most common cause of morbidity/mortality in extramural neonates while prematurity and its complication in intramural neonates.

Keywords: Extramural, Intramural neonate, Morbidity/mortality pattern

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.[1] 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.[2] 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.[2-6] 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.[7] The major causes of newborn deaths in India are preterm births (35%), neonatal infections (33%), birth asphyxia (20%) and congenital malformation (9%).[8]

Morbidity and mortality profile of intramural neonates those who are treated in neonatal intensive care unit is well studied.[9-11] 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, gravida/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 intramural group and term 548(54.96%) neonates in the extramural 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 refereed 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)	<0.00
Term	819 (46.27)	548 (54.96)	01
Post-term	10 (0.57)	15 (1.50)	
Weight on admission (in gms)			
<1000	125 (7.06)	15 (1.50)	<0.00
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)	<0.00
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<0.0
Hypertension	78 (4.41)	67 (6.72)	01
Heart disease	10 (0.56)	6 (0.60)	
Diabetes	7 (0.40)	3 (0.30)	
Hemoglobinpathy	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.

Variables	All cases (N=997, %)	Survival (N=710, %)	Non-survival (N=287, %)	P value
Obstetrician	308 (30.89)	229 (32.25)	79 (27.52)	0.16
Referral person of neonate				
Trained dai	97 (9.73)	55 (7.75)	42 (14.63)	0.001
ASHA worker	228 (22.87)	130 (18.31)	98 (34.15)	<0.001
Medical officer	345 (34.60)	285 (40.14)	60 (20.91)	<0.001
Private hospital	327 (32.80)	240 (33.80)	87 (30.31)	0.32

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 (N=1770, %)	Extramural (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)	
1500-2499	115 (29.19)	140 (48.78)	<0.001
2500-2999	34 (8.63)	113 (39.37)	
>3000	3 (0.76)	15 (5.23)	
Mode of delivery			

Continued.

Variables	Intramural (non-survival) ((N=394, %)	Extramural (non-survival) ((N=287, %)	P value
Vaginal	223 (56.60)	182 (63.41)	
Cesarean	168 (42.64)	98 (34.15)	0.2
Assisted	3 (0.76)	7 (2.44)	
Average duration of stay (in days)	3.61±2.93	6.61±6.80	
Residence (rural)	216 (54.82)	201 (70.03)	<0.001
Socioeconomic status (lower)	280 (71.07)	223 (77.70)	0.05
Maternal conditions			
Anemia	113 (28.68)	134 (46.69)	
Hypertension	22 (5.58)	15 (5.23)	
Heart disease	1 (0.25)	1 (0.35)	
Diabetes	1 (0.25)	1 (0.35)	<0.01
Hemoglobinpathy	3 (0.76)	2 (0.70)	
Liver diseases	1 (0.25)	0	
Hypothyroidism	5 (1.27)	1 (0.35)	
Obstetrics complication			
PIH	59 (14.97)	42 (14.63)	
Eclampsia	22 (5.58)	4 (1.39)	
Gestational diabetes	1 (0.25)	0	
APH	20 (5.08)	1 (0.35)	0.91
PROM >24 hours	20 (5.08)	18 (6.27)	
Malpresentation	13 (3.30)	1 (0.35)	
Twining	19 (4.82)	11 (3.83)	

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

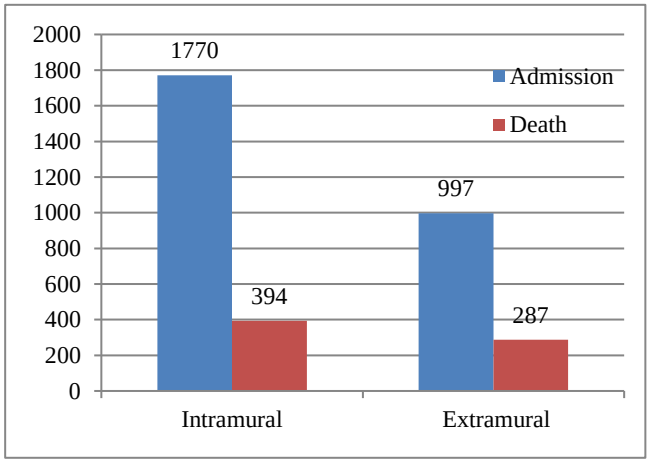

Figure 1: Mortality rate in study population.

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. 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 (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.[12,13,16] 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.[13] Similar to other authors, in our study male were predominant in both intramural and extramural group.[17-19] 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.[20] 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.[21,22]

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.[23] 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.[12]

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.[24-26]

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.[21,22] In contrast to the finding in the literatures, other causes of respiratory distress was more predominant in extramural 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

(23.27% versus 16.75%) compared to extramural neonates and our finding were similar to Sharma et al (12.54% versus 9.09%) but other researchers reported higher incidence of jaundice in extramural neonates.[22,26]

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.[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.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Meshram RM, Jain DL, Apte MU, Denge A. Morbidity and mortality pattern of intramural and extramural neonate: a prospective observational study. Int J Contemp Pediatr 2021;8:1006-13.