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Survival of Extremely Preterm Neonates in a Resource-limited Setting

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ABSTRACT

Background: Preterm birth is a major contributor to neonatal and under-five mortality, and births at lower gestational ages (GA) contribute more to these statistics. Most developed countries have succeeded in improving survival at extremes of GA, while most developing countries like Nigeria still lag behind. The objective of this retrospective study was to document the survival rates among extremely preterm neonates and factors associated with mortality in a tertiary center in Nigeria.

Methods: The labor ward delivery and neonatal unit admission records were reviewed from January 2010 to December 2017. The GA, gender, mode of delivery, birth weight, duration of admission, and outcomes for babies delivered at 24 to 27 weeks + 6 days of gestation were recorded. The survival rates and factors associated with mortality were analyzed.

Results: During this period, there were 11,607 live births with 1,685 (14.5%) preterm deliveries. There were 4,523 admissions to the neonatal unit; overall, 736 (16.3%) cases were preterm neonates out of which 152 (3.4%) subjects were extremely preterm. The overall survival rate was 24.3%, and the survival rate increased with increasing GA and birth weight (BW). Most deaths occurred in the first week of life. The means of BW and GA were significantly lower in babies that died, compared to those who survived. The median duration of admission was also lower for those that died, compared to those that survived. The most common causes of death were respiratory distress, sepsis, and intracranial hemorrhage.

Conclusion: The survival rate of extremely preterm neonates is low in this study. Facilities to improve care, especially for respiratory support should be put in place to reduce mortality.

Keywords: Extremely preterm, Resource-limited settings, Survival rate

Introduction

Preterm birth is a global problem with an estimated 15 million preterm births yearly, and more than 1 million of these babies die shortly after birth (1). More than 60% of these births occur in sub-Saharan Africa and South Asia with Nigeria having the 3rd highest number (773,600) of preterm births annually (2). Preterm birth is currently the highest cause of neonatal mortality globally accounting for 28% of neonatal deaths (3) and 15% of all deaths in children under five years of age (4).

Survival of preterm neonates is largely dependent on the maturity of their organs, which is often a function of their gestational age (GA), birth weight (BW), and the availability of necessary interventions and facilities to help them cope with being born too early. Their survival is also dependent on where they are born; babies born in high-income countries have access to advanced intensive neonatal care, and the mortality rate is lower than 10% in these countries. On the other hand, babies born in low-income countries have little or no access to advanced neonatal care, and more than 90% of these babies die (1).

Survival is directly proportional to GA as those with a higher GA have a better chance of survival than those with lower GA with extremely preterm neonates (delivered below the GA of 28 weeks) having poorer outcomes (5). A study conducted

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on the survival of extremely preterm neonates in England reported the rates of 40% (n=178) at 24, 66% (n=346) at 25, and 77% (n=448) at 26 weeks of gestation (6). However, this is not true for their counterparts delivered in low- and middle-income countries, such as Nigeria, where the age of viability is still officially 28 weeks of gestation.

Therefore, most babies delivered at lower GAs outside tertiary and secondary facilities are frequently not offered any resuscitation as they are not regarded as live births. An earlier study done about 20 years ago in Nigeria (7) reported a mortality rate of 92.6%, while a study performed in Delhi in 2004 reported a mortality rate of 55% in babies delivered at 26-28 weeks of gestation (8).

However, over the years, different low-cost interventions have been shown to improve survival in preterm babies by preventing mortality in estimated three-quarters of the preterm babies. These interventions include the use of antenatal corticosteroids, prompt use of antibiotics to prevent infections, Kangaroo mother care (i.e., prolonged skin to skin contact with the mother for the provision of warmth), and use of continuous positive airway pressure (CPAP) to support ventilation. All these interventions were recently put together in a recommendation by the World Health Organization (9).

In the study center, which is a tertiary referral hospital for high-risk pregnancies, there are facilities for antenatal corticosteroids for mothers with imminent preterm delivery, cesarean section, as well as incubator care, and kangaroo mother care is practiced for stable preterm neonates. Other available facilities include those for oxygen delivery, laboratory support, CPAP for respiratory support, and antibiotic therapy for treating infections. Hence, an improvement of the earlier reported survival rate is expected.

It is important to document the current survival rate of extremely preterm neonates in the hospital to aid obstetricians in decision-making concerning the management of these high-risk pregnancies. It is hoped that the findings will aid advocacy for improved care and counseling of parents of these vulnerable babies. The aim of this study was to document the survival rate of extremely preterm neonates managed in the neonatal unit of the hospital and the factors associated with poor outcomes.

Methods

The admission records of the inborn neonatal unit (where the sick babies who are delivered in the hospital are admitted for special care) and the labor ward records were retrospectively reviewed from January 2010 to December 2017. Babies with major congenital abnormalities not compatible with life and stillbirths were excluded. The mode of delivery, booking status of the mother, multiple gestations, baby's 5th minute Apgar score, gender, BW, and cause of death in those who died was obtained from the records for all babies delivered at GA of 24 to lower than 28 weeks of gestation. The GA was determined by using early antenatal ultrasound scan report, date of onset of mother's last menstrual period, or modified Ballard's score.

The diagnosis recorded was based on a combination of clinical and laboratory findings. Diagnoses of respiratory distress syndrome and necrotizing enterocolitis were confirmed by the chest and abdominal X-ray, respectively, while neonatal sepsis was confirmed with positive blood and cerebrospinal or urine culture. However, neonates with perinatal risk factors for sepsis and clinical signs of sepsis with a complete blood count suggestive of sepsis (at least two of the items, including immature neutrophil/neutrophil ratio>0.2, micro-erythrocyte sedimentation rate>15 mm in the first hour, absolute neutrophil count<1750 or >5400 cells/cmm, and total white blood cell count>21000 or <5000 cells/cmm) or elevated acute phase reactants (procalcitonin or C-reactive protein) were categorized as sepsis cases.

Intracranial hemorrhage was diagnosed by transfontanelle ultrasound. Cause of death was determined from clinical diagnosis and/or autopsy where this was performed after demise. The main outcome measure for the study was survival at the time of discharge from the neonatal unit. All babies who show any signs of life, such as cord pulsation, respiratory effort or audible heart sounds by auscultation at delivery, are resuscitated at birth, and those that respond to resuscitation are admitted in the neonatal unit.

The unit has incubators, facilities for oxygen administration, improvised bubble CPAP ventilation, and parenteral nutrition. There are also facilities for laboratory, blood banking, radiological, as well as theatre and pharmacy services in the hospital. Kangaroo mother care is also practiced in the unit. Ethical approval was obtained from the Health Research and Ethics Committee of the hospital. All the information obtained will be treated as confidential, and all identifiers were excluded from the data.

All obtained data were entered into SPSS software (version 21). Descriptive data were

reported as proportions and percentages for categorical variables, as well as means, standard deviations or medians, and interquartile range (when data was skewed or had outliers) for continuous variables. Test of association between categorical variables was done using the Pearson correlation coefficient, Chi-square test, or Fisher's exact test where applicable. The student t-test was used to test any significant differences between the mean BWs and mean GAs for those that survived and those that died. The Mann-Whitney U non-parametric test was used to compare the median duration of admissions of the two groups as the data was skewed. P-value less than 0.05 was considered significant.

Results

The total number of live births during the study period was 11,607 out of which 1,685 (14.5%) were preterm deliveries. The total admissions to the neonatal unit during the study period was 4,523 out of which 736 (16.3%) and 152 (3.4%) cases were preterm and extremely preterm neonates, respectively, accounting for 3.4% and 20.7% of all admissions and preterm admissions to the unit.

Overall, 73 extremely preterm neonates were male, while 79 were female giving a M:F ratio of 1:1.08. Regarding the delivery type, 86 (56.6%) cases were delivered vaginally, while 66 (43.4%) subjects were delivered by cesarean section. In addition, 105 (69.1%) pregnancies were booked, while the remaining 47 (30.9%) pregnancies were unbooked in the hospital. Moreover, 89 (58.6%) deliveries were singletons, while 63 (41.4%) deliveries were products of multiple gestations.

The overall mean weight of the study population was 909.1±220.7 g, and the mean GA was 26.07±0.97 weeks. The frequency of extremely preterm births in different GA categories increased with increasing GA as shown in Table 1. The survival rate increased with GA as shown in Figure1. Consequently, 37 (24.3%) of the extremely preterm neonates survived and were discharged from the unit, while 115 of them died. These deaths contributed 23.3% to the overall 493 mortalities during the period.

In addition, 88 (76.5 %) deaths occurred in the first week of life, and the most common conditions causing death were respiratory distress (38.3%), sepsis (26.1%), and intracranial hemorrhage (23.5%) as shown in Table 2. Other conditions include apnoea of prematurity, necrotizing enterocolitis, and severe anemia. Figure 1 depicts a gradual increase in survival rate as GA increased with 0% survival at 24 weeks of gestation and 42.2% at 27 weeks of gestation.

The overall survival rate among the extremely

Table 1. Frequency of extreme preterm admission by gestational age

Gestational age (weeks)	Frequency	(%)
24	13	8.6
25	28	18.4
26	47	30.9
27	64	42.1
Total	152	100

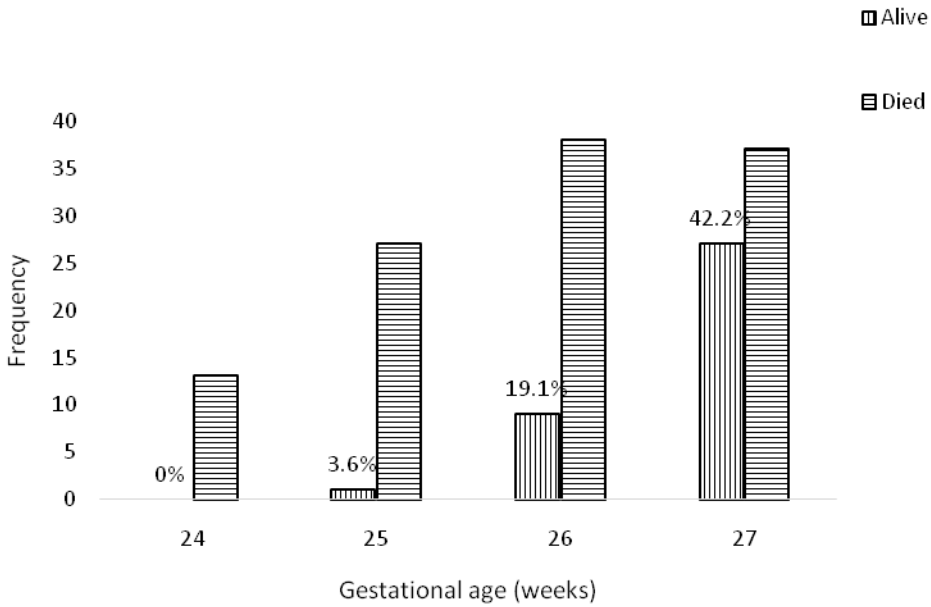

Figure 1. Extreme preterm survival by gestational age

Table 2. Diagnosis at death for extreme preterm neonates

Diagnosis	n (%)
RDS	44 (38.3)
Sepsis	30 (26.1)
ICH (IVH and SAH)	27 (23.5)
Apnoea of prematurity	6 (5.2)
Necrotizing enterocolitis	3 (2.6)
Severe anemia	2 (1.7)
Severe perinatal asphyxia	3 (2.6)

RDS: Respiratory distress syndrome; ICH: Intracranial hemorrhage; IVH: Intraventricular hemorrhage; SAH: Subarachnoid hemorrhage

low-BW preterm neonates was 12.2% (12/98), compared to 46.3% (25/54) in babies weighing≥1000 g. The survival rate for neonates with BW≥700g was 28.4%. No baby with BW lower than 700 g survived. Figure 2 depicts the survival rates of the different BW categories. The median interquartile range duration of admission was significantly shorter in neonates that died, compared to those that survived (i.e., 2.0 days [6.50] versus 53.5 days [45.75]) (P=0.000). When factors associated with poor outcomes were tested for association with mortality only the birth weight, GA, and duration of admission were statistically significant as shown in Table 3.

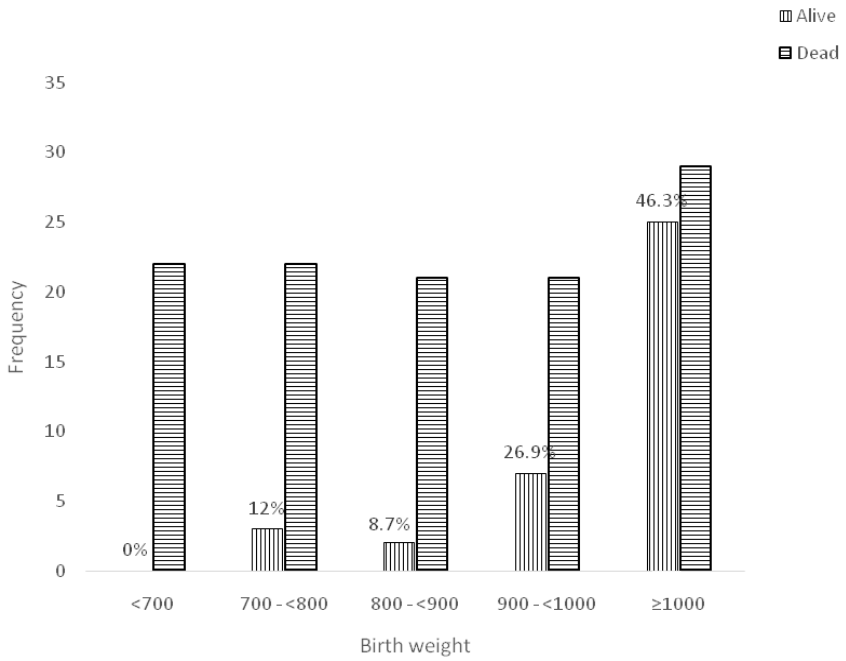

Figure 2. Survival of extreme preterm neonates by birth weight

Table 3. Factors associated with mortality in extreme preterm neonates

Variable	Survived (n-37)	Died (n-115)	P-value
Booking status			
Unbooked status n (%)	12 (25.5)	35 (74.5)	0.840
Booked n (%)	25 (23.8)	80 (76.2)	
Mode of delivery			
Vaginal delivery n (%)	22 (25.0)	64 (75.0)	0.825
Cesarean section n (%)	15 (22.4)	51 (77.6)	
Type of gestation			
Multiple gestation n (%)	11 (17.5)	52 (82.5)	0.125
Singleton n (%)	26 (29.2)	63 (70.8)	
Gender			
Male n (%)	18 (23.1)	55 (74.3)	0.850
Female n (%)	19 (25.7)	60 (76.9)	
Mean gestational age±(s.d)	26.68±0.52	25.86±0.99	0.000*
Mean birth weight±(s.d)	1070.27±192.87	857.23±204.01	0.000*
Median DOA (IQR)	2.00 (6.50)	53.5 (45.75)	0.000*

DOA: Duration of admission; IQR: Interquartile range; s.d: Standard deviation

Discussion

The results of this study showed that 24.3% of extremely preterm babies survived with the present level of neonatal care available in the facility. This rate is lower than those reported in studies from England (6), United States of America (10, 11), and France (12) in which neonatal care is more advanced and available. However, this rate is higher than that reported in an earlier study in Nigeria over two decades ago (7). This difference may be due to the improvement in facilities for neonatal care.

There was an increase in survival rates with increasing GA in this study similar to other studies (6, 10-12), and it was the lowest at 24 and 25 weeks of gestation. This is not surprising as the majority of babies born at ≤25 weeks of gestation were more likely to have respiratory distress requiring mechanical ventilation, which is currently not available in the facility. Respiratory support in the hospital is currently limited to the provision of CPAP and surfactant administration, which is not readily accessible to the majority of patients due to the high cost.

However, the survival rate documented in this study was lower at all GAs, compared to those reported in studies conducted in more developed countries (6, 10-13). Though the overall survival rate in this study was low, it was a starting point to improve upon while strengthening advocacy for the improvement of obstetrics and intensive neonatal care to increase the chances of survival.

Stoll et. al. (14) in a study on "Trends in care practices, morbidity, and mortality in extremely preterm neonates in 1993-2012" in the United States reported an increase in survival rate with changes to maternal and neonatal care practices. This supports the need to improve intensive neonatal care practices in Nigeria to help reduce the contribution of this group of neonates to the overall neonatal mortality rate that was as high as 23.3% in this study.

Extremely low-BW neonates in this study had a 12.2% chance of survival. This is much lower than the survival rate of 26.5% reported by Kalimba *et al.* in South Africa (15). This may be due to the availability of better health care services in South Africa, compared to those in Nigeria. The median duration of admission was significantly shorter for those that died, compared to those that survived (P=0.000) because most of the deaths occurred within 7 days of life. This finding is in agreement with the results of a study by Kalimba et al. (15) reporting that 79% of deaths occurred in the first week of life, a period considered as the most important period of the life of the neonate when considering survival.

Lower BW and lower gestational age were both significantly associated with mortality in this study that is similar to the findings of other studies (10-12). This can be explained by the fact that the lower the GA, the more the immaturity and ineffectiveness in the function of the organs. Thus, the more immature the organs, the more likely the dependence on more support to survive. This explains why some countries set limits of viability to judiciously allocate the limited resources to the babies whose organs are likely to be more mature and require support for shorter periods. This is also linked to the long-term disability associated with survival in these neonates.

A systematic review of 44 guidelines on the resuscitation of extremely preterm neonates from 4 international groups and 23 developed countries reports a 65% agreement to offer active care, while none agreed to comfort care for babies delivered at ≥25 weeks of gestation (16). This report supports the findings in the current study as majority of the 24.3% of cases who survived among the study population would not have had any chance of survival if they were not resuscitated. This would have resulted in an increase in the neonatal and under-five mortality rates.

Conclusion

In conclusion, the survival rate of extremely preterm neonates in this study was low. However, babies born at GA≥25 weeks or BW≥700g had a 27% and 28% chance of survival, respectively. Efforts to improve respiratory support and prevent and promptly treat infections may help in improving the survival of these babies. Future longitudinal studies on the long-term outcomes of extremely preterm babies discharged from the neonatal unit are recommended for adequate family counseling and formulation of national guidelines on the resuscitation of babies at these low GAs.

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Conflicts of interests

The authors declare that there is no conflict of interest.

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