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# Gestational age-related neonatal survival at a tertiary health institution in Nigeria: The age of fetal viability dilemma

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**Abstract***: Background:* Although the official age of fetal viability in Nigeria is 28 weeks, there are pockets of reports some anecdotal, of survival of babies delivered at younger gestational age (GA) from different parts of the country. The routine resuscitation and management of premature infants born before the official age of fetal viability (28 weeks) is likely to generate important ethical and medical concerns that are bound to influence our approach to the management of such infants.
*Aim:* To determine the GA-specific neonatal mortality and survival among preterm deliveries at the National Hospital Abuja.
Subjects and Methods: A retrospective review of relevant data from the National Hospital Neonatal Registry Database based on the Research Electronic Data Capture software (REDCap) was undertaken to determine the mortality rate of preterm babies managed in the neonatal intensive care unit (NICU) from January 2017 to February 2018. Disaggregated GA specific mortality rates were also computed to determine the fetal age at which extra uterine neonatal survival rate was at least 50%. Gestational age estimation was based on mothers' last menstrual period (LMP) in over 96% of cases.
*Results:* Sixty-three (63) of 305 preterm babies admitted died during hospitalization giving a mortality rate of 20.7%. This was significantly higher than the mortality rate among term babies (7.5%, P=0.01) hospitalized over the same period. Antenatal corticosteroid use was low (11.2%), 188 (25.8%) received CPAP for Respiratory Distress Syndrome (RDS), and none of the babies received surfactant or mechanical ventilation. There were no survivors among babies delivered at GA of 22-25 weeks (11, 3.6%). However, the survival rate at 26 weeks gestation was 53.8%, and this subsequently increased, reaching a peak of 96.5% survival at 35 weeks. RDS accounted for 53.9% of all deaths.
*Conclusion:* It is concluded that the survival rate (53.8%) of babies at GA of 26 weeks despite minimal antenatal interventions and limited postnatal respiratory support was reasonably high, and this could serve the basis for discussions for a downward review of the age of fetal viability in Nigeria.

**Key words:** Gestational age. Fetal viability

## Introduction/Study background

The neonatal mortality rate in Nigeria (NMR) (36/1000) is among the top 10 highest in the world[1]. Over the last decade, neonatal sepsis, perinatal asphyxia and, prematurity have consistently remained the leading causes of neonatal deaths in the country.[2,3] Global interventions targeted at these significant neonatal morbidities in Nigeria have not impacted significantly on neonatal mortality rate in the country. For instance, the reported consistent reduction in NMR from 2003, through 2008 to 2013 (52/1000, 41/1000 and 39/1000)fell short of expectations of the Millennium Development Goals, with neonatal deaths accounting for an increasing proportion of under 5 mortality; 25%, 31% and 36.3% in 2003, 2008 and 2013 respectively.[4]

Of the 3 major neonatal morbidities responsible for neonatal mortality in Nigeria, prematurity is of particular concern because it is also a risk factor for perinatal asphyxia and neonatal sepsis. The incidence of preterm

delivery in Nigeria varies from 5.7% to 16.8%.[5,6,7,8] Nigeria was ranked 3rd among the 10 countries with the highest number of preterm births in the world in 2010, behind China and India.[9]

Survival of premature infants is a function of multiple factors, the most important of which is the degree of prematurity, as illustrated by Stoll et al [9] who reported a 6% survival for preterm babies at 22weeks and 92% at 28weeks gestation respectively. Although extreme prematurity constitutes a small proportion of preterm babies, it is associated with the highest rate of mortality.[10] Other important determinants of survival include the use of antenatal corticosteroid (ACS), respiratory support systems, postnatal surfactant administration, as well as medical expertise to manage the preterm infant,[11] some of which are not uniformly available in lower level NICUs. This disparity accounts for between-hospital variations in the outcome of periviable babies.[11, 12]

Age of fetal viability is defined as the gestational age (GA) at which the probability of extra-uterine survival equals the risk of death, i.e. a survival rate of 50%. [13, 14, 15.] The official age of fetal viability in Nigeria is 28 weeks [16]. Babies delivered before 27 completed weeks of gestations in Nigeria would then be classified in the 'grey zone' described as the threshold of viability or periviability. This is in sharp contrast to the Royal College of Obstetricians and Gynaecologists' definition which includes babies delivered at $23^{+0}$ weeks to $24^{+6}$ weeks gestation, reflecting the high survival rates for babies born at 25 weeks and beyond in developed nations.[17] There are medical and ethical considerations in the care of babies delivered at the threshold of viability. As a result of the associated substantial risk of death despite intensive care, such babies may not be actively resuscitated without parental informed consent.[18]

Extra-uterine survival at the threshold of viability is grossly limited. The physiologic basis of this limitation includes; gross deficiency of alveolar-capillary interphase, inadequacy of surfactant production, poorly developed respiratory neuromuscular control and maturation limitations in renal function.[19] Although exogenous surfactant and mechanical ventilation may provide solutions to surfactant deficiency and poorly developed respiratory neuromuscular control respectively, poorly developed alveolar-capillary interface remains a significant postnatal challenge. Beyond survival, long term neurologic sequelae in babies at the threshold of viability, is a function of poor neuronal connections for cognitive development coupled with increased susceptibility to cerebrovascular events.

Antenatal corticosteroid for inevitable preterm delivery results in improved neonatal outcome essentially as a result of its effect on surfactant synthesis. Although it is recommended for pregnancies at 24 to $33^{+6}$ weeks when delivery is anticipated within seven days, the benefit of this recommendation is yet to be validated in low-income countries as studies are underway to fill this knowledge gap.[20]

At the National Hospital Abuja (NHA), pregnant mothers with GA between $27^{+0}$ and $33^{+6}$ weeks are selectively offered ACS when delivery is anticipated within seven days and there are no contraindications to the use of steroids. Our approach to the management of births occurring before the official GA of viability is dictated by ethical and medical concerns. For instance, an infertile couple with a strong desire for a child may request for aggressive resuscitation of a low gestation, in-vitro-fertilization (IVF) conceived baby even when the prognosis for this baby is clearly bleak.

While in technologically advanced countries, extra-uterine survival of a 23 weeks fetus has been reported, there are limited, mainly anecdotal reports from different parts of Nigeria on the survival of babies delivered before 28 weeks of gestation. Ikechebelu et al [16] had reported the survival of a 27 weeks GA baby with a birth weight of 1.03kg from the Southern part of Nigeria in 2012 and suggested a downward review of the age of fetal viability in Nigeria. They however realized the limitation of their recommendation, which was based on an isolated report. On the other hand, Iyoke et al[21] lamented the high rate of stillbirth and early neonatal deaths among products of very early gestations (<28weeks) in the Eastern part of Nigeria, attributed this partly to inadequate care and attention given to this category of babies presumably as a result of the official age of viability in Nigeria. They therefore advocated a downward review of the Nigeria's official age of fetal viability as a legal support for the care of very low gestation babies

Wide disparities in expertise and available infrastructure/technology for newborn care exist across Nigerian hospitals and this may result in variations in the survivability of preterm babies from one hospital to another with better results expectedly emanating from tertiary hospitals, a large number of which are University-affiliated hospitals. It is important to begin the discussion on a possible review of our current age of fetal viability, albeit mindful of this inter-hospital variability. This study was, therefore, conducted to determine the gestational age-specific neonatal survival rates among preterm babies managed at the National Hospital Abuja and to document the GA of fetal viability for our setting. It was hypothesized that this GA would be lower than 28 weeks currently designated age of fetal viability in Nigeria.

## Subjects and method

Study site: National hospital is a 500-bed tertiary hospital located at the Central District area of the Federal Capital Territory, providing care for residents of the city and patients from six neighboring states. The newborn unit of the hospital is a level 2 neonatal intensive care unit with an admission capacity of 45 (incubators/baby cots) and an admission rate of 1500-2000 babies per annum. About 55% of neonatal admissions are out born referred from other hospitals or self-referred if born at home. There are facilities for non-invasive respiratory

support [bubble continuous airway pressure (BCPAP)], and all inborn very preterm babies are commenced on BCPAP as soon as they are stabilized in the labour room but surfactant use is limited by parental affordability. Caffeine citrate or aminophylline is used in very low birth weight babies to prevent apnea of prematurity.

Beginning from January 2017, an electronic Neonatal Registry database using Research Electronic Data Capture (REDCap) software was introduced in our neonatal intensive care unit (NICU) in partnership with 2 other NICUs of tertiary institutions; University of Benin Teaching Hospital (UBTH and Lagos University Teaching Hospital (LUTH) in Nigeria, funded by Indiana University, USA for the systematic collection of Patient and Centre level Clinical and Outcome Data. This was to provide high quality data to support clinical research, quality improvement efforts and stimulate collaborative efforts. (REDCap) gave rise to a substantial improvement in clinical documentation and eliminated the problems associated with the retrieval of patient records prior to its introduction. Electronic Data entry for each baby in NICU is commenced at admission and concluded at discharge from hospital or death. This is a preliminary analysis of NICU admissions following the introduction of the Neonatal Registry at the National Hospital Abuja. For the purpose of this study, we retrospectively reviewed data collected on all preterm neonates admitted in NICU at the NHA over a period of 13 months (January 2017 to February 2018). We needed a sample size of 260 preterm babies to detect a difference of 10% in the survival rates between babies delivered at GA<28 weeks and those 28 weeks and above, at 5% level of significance with a study power of 90%.

Relevant demographic and clinical data were extracted from the Neonatal Registry database. These included gestational age, birth weight, antenatal care including use of antenatal corticosteroids (ACS), admission diagnosis, postnatal (hospital) care including use of Surfactant and any form of respiratory support. Respiratory distress syndrome was diagnosed when the preterm baby presented with signs of respiratory distress; (chest retractions, grunting, nasal flaring, tachypnea), cyanosis and hypoxia (SPO2 <85%) and Chest XR signs of homogenous opacities with air bronchogram. [22]

Data were entered into and analysed using Statistical Package for Social Sciences (SPSS) version 20 (IBM-SPSS, Armonk, NY). Descriptive statistic was used to summarise the general characteristics and types of morbidities encountered in the neonates. Disaggregated gestational age specific mortality rates were computed to determine the fetal age at which extra uterine neonatal survival rate was at least 50% and values were tabulated and graphically illustrated as appropriate. Babies were grouped according to gestational age as follows: Extreme preterm (<28 weeks), Earlypreterm (28-32 weeks) Moderate to Late preterm (33-36$^{+6}$). [23]

### Ethical Approval

The ethics committee of the National Hospital Abuja reviewed and approved the neonatal registry before data entry was commenced.

## Results
### General Characteristics

As shown in table 1, a total of 305 preterm babies with clinical evidence of life at birth with an almost equal number of males and females admitted into our NICU and captured in the Neonatal Registry were analysed for this study. This constituted 41.8% (305/730) of all neonatal admissions during the period under review. Gestational age assessment was done by LMP in 94.6%, while only 0.4% of the babies had first-trimester ultrasound assessment and inborn babies were also clinically assessed. Moderate to Late preterm made up 45.5%, followed by Very preterm 43.9%, while Extreme preterm accounted for 10.5%. The majority of the preterm babies (72.8%) were inborn while out born babies accounted for 22.9% of admissions. Mothers of 82 (22.9%) babies received antenatal corticosteroids while 94 (30.8%) babies were treated with CPAP for respiratory distress syndrome. None of the babies received mechanical ventilatory support or Surfactant.

### Outcome of hospitalization in relation to gestational age group

Two hundred and thirty-nine (78.4%) of the preterm babies survived and were discharged from hospital. The survival rates were 45.5%, 66.7% and 92.5 % for extreme, moderate and late preterm babies, respectively. The difference in gestational age-related survival rates was statistically significant ($X^2$ = 51.07, P = 0.00001) (Table 2).

**Table 1:** General Characteristics

| Characteristics | frequency | Percentage |
|---|---|---|
| Total number | 305 | 100 |
| *Gender distribution* | | |
| Male | 151 | 49.5 |
| Female | 153 | 50.2 |
| Missing | 1 | 0.3 |
| *Gestational age group* | | |
| Extreme preterm | 32 | 10.6 |
| Very preterm | 132 | 43.9 |
| Moderate to Late preterm | 137 | 45.5 |
| *Place of birth* | | |
| Inborn | 222 | 72.8 |
| Out born | 82 | 26.9 |
| Missing | 1 | 0.3 |
| Mortality | 63 | 20.3 |
| *ACS use* | | |
| Yes | 82 | 26.9 |
| No | 223 | 73.9 |
| *CPAP* | | |
| Yes | 94 | 30.8 |
| No | 211 | 62.9 |
| Surfactant | Nil | 0 |
| Mechanical ventilation | Nil | 0 |

CPAP: Continuous positive airway pressure.
ACS: antenatal corticosteroid

*Cause of death among preterm babies.*

Respiratory distress syndrome was responsible for 54% of deaths followed by neonatal sepsis 24.8% and congenital malformations 11.3% (Table 3). Twenty-six of the 34 (76.5%) deaths resulting from RDS occurred in babies delivered at the gestational age of <28 weeks.

*Survival to discharge in relation to gestational age*

None of the ten babies with gestational age between 22-25 weeks (all in-born) survived while the survival rate at 26 weeks of gestation was 53.8%. The survival rate subsequently increased with increasing gestation, albeit with intermittent dips, with a peak of 96.5 % at 35 weeks gestation (Table 4 and Figure 1).

**Table 2:** Outcome of management of preterm babies according to gestational age group

| Gestational age group | | Outcome of hospitalization | |
|---|---|---|---|
| | Died (%) | Discharged home (%) | Total (%) |
| <28 weeks | 19 (59.4) | 13 (40.6) | 32 (100) |
| 28-32 weeks | 37 (28.0) | 95 (72.0) | 132 (100) |
| 33-36 weeks | 7 (5.3) | 126 (94.7) | 133 (100) |
| Total | 63 (20.6) | 234 (79.4) | 297 (100) |
| $X^2 = 51.8008$, P =00001. | | | |

Parents of two late preterm babies requested for discharge against medical advice while two moderate preterm babies were transferred after stabilization to other hospitals at the request of their parents.

**Table 3:** Morbidity among preterm babies who died during hospitalization

| Morbidity | Frequency (%) |
|---|---|
| Respiratory Distress Syndrome | 34 (54.0) |
| Neonatal Sepsis | 15 (24.8) |
| Congenital malformations | 7 (11.3) |
| Perinatal Asphyxia | 3 (4.8) |
| Neonatal hyperbilirubinaemia | 2 (3.2) |
| Intra uterine growth restriction | 1 (1.6) |
| Blood transfusion reaction | 1 (1.6) |
| Total | 63 (100) |

**Table 4:** Gestational age Vs Survival to discharge

| Gestation (weeks) | Died n (%) | Survived n (%) | Total n (%) |
|---|---|---|---|
| 22 | 1 (100) | 0 (0) | 1 (100) |
| 23 | 2 (100) | 0 (0) | 2 (100) |
| 24 | 1 (100) | 0 (0) | 1 (100) |
| 25 | 6 (100) | 0 (0) | 6 (100) |
| 26 | 6 (46.2) | 7 (53.8) | 13 (100) |
| 27 | 3 (33.3) | 6 (66.7) | 9 (100) |
| 28 | 15 (42.9) | 20 (57.1) | 35 (100) |
| 29 | 7 (35.0) | 13 (65.0) | 20 (100) |
| 30 | 6 (24.0) | 19 (76.0) | 25 (100) |
| 31 | 5 (21.8) | 18 (78.2) | 23 (100) |
| 32 | 4 (13.8) | 25 (86.2) | 29 (100) |
| 33 | 2 (5.4) | 35 (94.6) | 37 (100) |
| 34 | 2 (5.3) | 36 (94.7) | 38 (100) |
| 35 | 1 (3.6) | 27 (96.4) | 28 (100) |
| 36 | 2 (6.7) | 28 (93.3) | 30 (100) |

**Fig 1:** Gestational age specific survival rates at the National Hospital Abuja
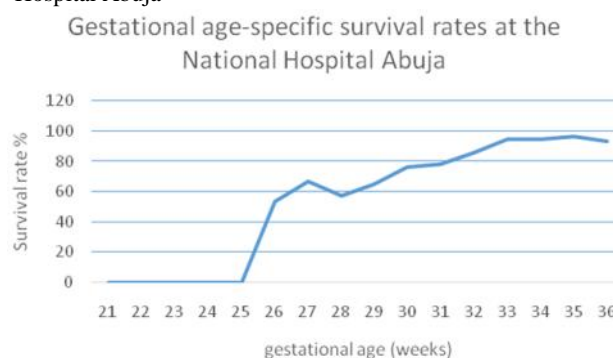


**Discussion**

Three hundred and one preterm babies of gestational age between 22 and $36^{+6/7}$ weeks were admitted during the 13 months period of review, majority (45,6%) of whom were moderate to late preterm while 43.9% were early preterm and 10.6% were extreme preterm. The gestational age distribution of preterm babies in this study is similar to the generally documented proportional distribution of preterm infants, the moderate to late preterm being predominant and extreme preterm the least prevalent. [24] Azeez Butali *et al*[8] however reported a much higher proportion of early preterm babies from Lagos (28%) presumably because the study was limited to babies with GA from 22-31 weeks.

The overall survival rate was 78.5% among the preterm babies managed in our NICU and further analysis based on gestational age segregation showed a significantly lower survival among the earlier gestations; 40.6% for extreme preterm babies compared to 94.7% for moderate to late preterm babies. Although a similar pattern of gestational age related mortality rate was reported by Bello et al [25] from Maiduguri the figures should be cautiously compared, because the gestational age grouping used in their study, (25 to <32 as early preterm and 35 to <37as late preterm) differs from that used in our study. Afjeh S.A *et al*[26] also reported higher mortality rates with lower gestations in a level III NICU in Tehran.

In 1997 Larrogue et al [27] reported an overall NICU survival rate of 89% for preterm deliveries with GA 22-32 weeks in a population based prospective study in France. The corresponding survival rate for this gestational age cohort in our study was 65.9%. The obvious disparity between the survival rate from France and that from our study is further magnified if the time interval between these studies (20years) is built into the comparative analysis. Similarly, the preponderance of RDS as a cause of mortality in our study in contrast to the findings from France, is not unconnected with the limited support for fetal pulmonary maturation (ACS) and postnatal respiratory management (Surfactant and Mechanical ventilation) in our center. Preterm infants below 26 weeks of gestation may not respond satisfactorily to non-invasive ventilation, especially when such infants

had not benefitted from antenatal steroid-induced pulmonary maturation.

None of the babies delivered at the threshold of fetal viability (GA 22-25 weeks) survived and this accounted for the dismal low survival rate of 40.6% for all babies born before 28 weeks gestation. However, an earlier study from a secondary level hospital in the Southern part of Nigeria had reported a much lower survival rate of 14.3% in preterm babies born before 28 weeks of gestation. [28] While babies delivered at 22-24 weeks with evidence of life would not be ignored, aggressive labour room resuscitation is often avoided because of limited facilities for post resuscitation NICU management in our center. Patel et al[29] in the US observed improved survival of very preterm babies (24-28 weeks gestation) between the periods 2000-2003 and 2008-2011 and attributed this to a decrease in RDS related mortality which resulted from increased use of antenatal corticosteroids (ACS) and aggressive postnatal respiratory management. Surviving extremely low gestation babies, however, often present with significant neonatal morbidities such as Surgical Necrotizing Enterocolitis (NEC) and grades 3-4 Intraventricular hemorrhage (IVH),[30] the majority of which would pose a significant management challenge in most neonatal centers in Nigeria.

The most common cause of death among preterm babies was respiratory distress syndrome (53.9%), followed by sepsis (22.2%) and congenital malformations (11.1%). This is in contrast to the findings of Schindler et al[31] from New South Wales and Australian Capital Territory which showed that higher grade IVH was the most common cause of death (22%) in preterm babies of GA less than 32 weeks and this was closely followed by acute respiratory illness.[26] The difference in the pattern of cause-specific mortality may be partly attributed to the higher utilization rate of antenatal corticosteroids (90%) and mechanical ventilation in the Australian study. The contribution of IVH and other possible causes of mortality in our study may have been underestimated due to the fact that relevant diagnostic facilities are not sufficiently available and sometimes the babies may be too ill to be moved for such investigations. An earlier study from Maiduguri, in Northern Nigeria had reported a significant impact of ACS on neonatal survival of preterm deliveries.[32]

The survival of preterm babies at 26 weeks of gestation in our study was over 50% despite minimal use of antenatal corticosteroids, postnatal surfactant and mechanical ventilatory support. Kunle-Olowu et al [24] in a previous study in 2014 had reported much lower survival rates of 25% and 33% for preterm babies at 26 and 28, respectively, in a tertiary health institution from the southern part of Nigeria. It was not clear from the study to what extent antenatal corticosteroid, surfactant, and ventilator support were used. Oluwafemi et al [33] in a recent study from the western part of Nigeria, documented a survival rate of 29.4% for extremely low birth weight babies. The study however did not analyse for gestational age-specific survival rate and therefore cannot be compared with our findings. The current practice in most tertiary hospitals in Nigeria is to administer corticosteroid when a delivery is anticipated at 28-33 weeks to accelerate lung maturation and reduce the risk of respiratory distress. Antenatal corticosteroid for lower gestations (26-27 weeks) is at the discretion of the Obstetrician in collaboration with the Neonatologist. The uniform fatality documented for babies in the 24-25 gestation in our study could easily be explained by the limited use of antenatal corticosteroid and surfactant in addition to the virtual absence of mechanical ventilator support. The survival of preterm babies at 26 weeks of gestation was over 50% despite minimal use of antenatal corticosteroids, postnatal surfactant and mechanical ventilator support. This subsequently increased with increasing gestation with a peak of 94.7% for babies at 36 weeks gestation.

## Conclusion

The survival rate of extremely preterm babies is low in our center but the survival rate at 26 weeks of gestation was over 50%. We, therefore, speculate a fetal viability age of 26 weeks for our center. It is our belief that our study will stimulate interest in multicenter collaborative studies across the country to generate a larger data set to kick-start the discussions on a review of the official age of fetal viability for Nigeria.

*Study limitations*

This is a single-center study; a multicenter study generating a much larger sample for analysis will, therefore, be necessary to validate this report.

Gestational age was estimated largely from LMP and clinical examination at birth, while first-trimester abdominal ultrasound estimation was available in a negligible proportion of babies. This may affect the reliability of the information on gestational age assessment.

The inclusion of preterm babies with major congenital malformations may increase the risk of death in these babies.

The study did not include the long-term outcome of the babies who survived. This is, however, a preliminary report and follow up of the survivors will form the subject of a subsequent report.

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