Causes of and Modifiable Factors Contributing to Neonatal Deaths at Dora Nginza Hospital in the Eastern Cape, South Africa

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Abstract
Dora Nginza Hospital (DNH) has a neonatal mortality rate higher than global and national averages. In 2015 to 2016 the neonatal mortality rate in South Africa was 18.1/1000 live births compared with 31.3/1000 live births at DNH. A retrospective study was conducted including neonates less than 28 days of life with a birth weight ≥500 g that demised in DNH neonatal unit. The NMR for the study period was 17.7/1000 live births. There were 101 (70.6%) early and 42 (29.4%) late neonatal deaths. Causes of death included infection (n=47; 32.9%), immaturity-related (n=42; 29.4%), congenital abnormalities (n=26; 18.2%), hypoxia (n=24; 16.8%) and other (n=4; 2.8%). There were significant associations between cause of death and administrative-related factors (P<.01), health-personnel related factors (P<.001) and patient-related factors (P=.01). Key strategies to be implemented include improving infection prevention and control, appropriate resource allocation, improved attendance and quality of antenatal care, ongoing skills training, and interventions to maintain normothermia.

Keywords
deaths, neonatal, neonatal mortality rate, causes

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Background
Neonatal mortality rates (NMR) remain high worldwide with a global NMR in 2020 of 17/1000 live births.1 However, NMR varies by region and is highest in low- and middle-income countries and lowest in high-income countries. For example, in 2020 the NMR in Australia was reported as 2.4/1000 live births whereas as that in Sub-Saharan Africa was 27/1000 live births.2 It is estimated that a child born in Sub-Saharan Africa is 10 times more likely to die in the first month of life than a child born in a high-income country.1

The NMR at Dora Nginza Hospital (DNH) in South Africa is similarly high and has historically been higher than global and national averages (31.1/1000 vs 18.6 and 18.1/1000 live births respectively).3,4 The NMR at the neonatal unit at DNH declined from 31.3/1000 live births in 2016 to 19.4/1000 live births in 2019.5 Despite this relative success, the high NMR at DNH remains a concern.

The main causes of neonatal deaths globally are prematurity (28%), sepsis (26%) and asphyxia/birth related hypoxia (23%).6 In South Africa, prematurity (36%), intrapartum hypoxia (20%) and infection (14%) are the main causes of neonatal deaths.7 At DNH specifically, the most common causes of death between 2016 and 2019 were infection (n = 47; 32.9%), immaturity-related (n = 42; 29.4%), congenital abnormalities (n = 26; 18.2%), hypoxia (n = 24; 16.8%) and other (n = 4; 2.8%).

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specific for each setting. Studies conducted in low- and middle-income countries have shown that the most common modifiable factors are accessibility to health care facilities, antenatal care, postnatal care and early initiation of breastfeeding.\(^8\)

Although strategies employed to reduce NMR at DNH have been studied,\(^5\) the specific causes and modifiable factors associated with neonatal deaths in the unit have not been formally audited. We therefore aimed to determine the current NMR at DNH, identify causes of neonatal deaths and determine avoidable or modifiable factors associated with these deaths in order to improve outcome.

**Methods**

A retrospective study was conducted from 1 January 2020 to 31 December 2020. Quantitative research approaches were used to gather, describe, quantify and analyze the data. Live born neonates with birth weight \(\geq 500\) g who died in the neonatal unit at DNH during the study period, and who were less than 28 completed days of life at the time of death, were included in the study. Babies who were stillborn, those with incomplete records and deaths that occurred outside the neonatal unit were excluded. Neonatal deaths occurring in the general pediatric wards of the hospital were not included in the study as they are covered by a separate clinical and administrative team and could not be accurately accounted for by the neonatal team.

All neonatal deaths in the unit were audited by the neonatology team weekly and a death audit tool, based on data collected by the perinatal problem identification program (PPIP), was completed. Data collected included maternal and neonatal characteristics, classification of the death as an early (<7 days) or a late (>7 days) neonatal death, cause of death and possible modifiable factors classified as patient-related, health worker-related or administration-related.

Congenital infections were defined as infections transmitted from mother to baby transplacentally (during pregnancy) or peripartum (during delivery).\(^9\) Early onset sepsis refers to clinical manifestation of infection within the first 72 hours of life with late onset sepsis occurring after 72 hours of life.\(^10\) Proven sepsis was defined as the presence of laboratory and clinical findings with a positive culture taken from a normally sterile site.\(^10\) Presumed sepsis was defined as the presence of clinical symptoms such as lethargy, respiratory distress, hypotension, prolonged capillary refill as well as suggestive laboratory findings including leucocytosis, leucopenia, thrombocytopenia, raised C-reactive protein and/or raised procalcitonin.\(^11\)

The audit tool was validated by requesting neonatal experts (neonatologists, pediatricians, midwives and other nursing staff) to provide inputs before it was used. It was also consistent with data required to complete PPIP forms for submission to the South African Department of Health (DoH). No pilot study was conducted.

Data was analyzed using version 26 of the Statistical Package for Social Sciences, IBM SPSS Statistics 26. Frequency tables, figures and graphs were used. Categorical variables such as sex, birth weight categories and modifiable factors were expressed using frequencies and percentages. The Chi-square test was used to analyze associations between categorical variables such as cause of death and birth weight category. Ethical clearance and permissions were obtained from the Walter Sisulu University Ethics and Human Research Committee (096/2021), the Eastern Cape Department of Health and DNH management. Informed consent was waived due to the retrospective study design and beneficent nature of the study. Privacy and anonymity were strictly maintained.

**Results**

There were 8101 live births and 167 deaths for the study period with 24 deaths being excluded: 6 had a birth weight less than 500 g and 18 were infants over 28 days of life. Therefore 143 neonatal deaths were included, resulting in a NMR of 17.7/1000 live births. Details of maternal and neonatal characteristics are presented in Table 1.

There were 101 (70.6%) early neonatal deaths resulting in an early neonatal mortality rate of 12.5/1000 live births. The neonatal causes of deaths are presented in Figure 1.

Infection was the most common cause of death identified (47 deaths). Congenital infection was identified in 4 (8.5%) with 3 (6.4%) being congenital syphilis and 1 (2.1%) congenital cytomegalovirus. Early onset sepsis or infection was identified in 5 (10.6%) and late onset sepsis (LOS) in 38 (80.9%) with 26 (55.3%) of these neonates being culture positive and the remaining 21 (44.7%) with presumed infection. The 42 immaturity-related deaths were due to apnea in 16 (38.1%), extreme multi-organ immaturity in 12 (28.6%), pulmonary hemorrhage in 10 (23.8%), hyaline membrane disease (HMD) in 3 (7.1%) and intra-ventricular hemorrhage (IVH) in 1 (2.4%). The hypoxia-related deaths (n=24) were mostly due to perinatal asphyxia (n=16; 66.7%) with meconium aspiration syndrome (MAS) in 4 (16.7%) and persistent pulmonary hypertension of the newborn (PPHN) in 4 (16.7%) of the neonates.
Of the 26 congenital abnormalities, 12 (46.2%) were suspected or confirmed syndromes, 9 (34.6%) had cardiac abnormalities, neurological abnormalities in 4 (15.4%) and a suspected sequence in 1 (3.8%). Four patients (2.8%) demised under the category of other of which one patient died of hemorrhagic disease of the newborn following maternal warfarin use, one due to aspiration, one due to severe congenital anemia and one following an accidental ingestion of alcohol cleaning solution.

There were 111 inborn neonates among the 143 deaths, resulting in an inborn mortality rate of 13.7/1000 live births. From the 32 outborn neonates, 21 (65.6%) were early neonatal deaths. The causes of death for the outborn neonates were infection in 13 (40.6%), hypoxia in 7 (21.9%), immaturity-related in 7 (21.9%), congenital abnormalities in 4 (12.5%) and other in 1 (3.1%). In the infection group, 7 were LOS.

### Table 1. Neonatal (n = 143) and Maternal (n = 141) Characteristics of the Study Population.

| Characteristics                  | Frequency (n) | Percentage (%) |
|----------------------------------|--------------|---------------|
| Sex                              |              |               |
| Male                             | 86           | 60.1          |
| Female                           | 56           | 39.2          |
| Disorder of sexual development   | 1            | 0.7           |
| Mode of delivery                 |              |               |
| Cesarean section                 | 67           | 46.9          |
| Normal vertex delivery           | 76           | 53.1          |
| Birth type                       |              |               |
| Singleton                        | 134          | 93.7          |
| Twins                            | 6            | 4.2           |
| Triplets                         | 3            | 2.1           |
| Place of delivery                |              |               |
| Inborn                           | 111          | 77.6          |
| Outborn                          | 32           | 22.4          |
| Birth weight category (g)        |              |               |
| < 800                            | 23           | 16.1          |
| 800-999                          | 28           | 19.6          |
| 1000-1499                        | 22           | 15.4          |
| 1500-1999                        | 20           | 14            |
| 2000-2499                        | 17           | 11.9          |
| ≥2500                            | 33           | 23.1          |
| Gestational age (weeks)          |              |               |
| < 28                             | 25           | 17.5          |
| 28-34                            | 58           | 40.6          |
| 35-37                            | 13           | 9.1           |
| > 37                             | 43           | 30.1          |
| Unknown                          | 4            | 2.8           |
| 5-min Apgar                      |              |               |
| < 7                              | 59           | 41.3          |
| ≥ 7                              | 76           | 53.1          |
| Unknown                          | 8            | 5.6           |
| Maternal age (years)             |              |               |
| < 20                             | 18           | 12.8          |
| 20-34                            | 97           | 68.8          |
| ≥35                              | 26           | 18.4          |
| Received antenatal care          |              |               |
| Yes                              | 115          | 81.6          |
| No                               | 26           | 18.4          |
| Parity                           |              |               |
| Primiparous                      | 49           | 34.8          |
| Multiparous                      | 81           | 57.4          |
| Grand multiparous                | 11           | 7.8           |
| Alcohol, smoking, or drug use    |              |               |
| No                               | 76           | 53.9          |
| Yes                              | 15           | 10.6          |
| Unknown                          | 50           | 35.5          |

### Table 1. (continued)

| Maternal illnesses                | Frequency (n) | Percentage (%) |
|-----------------------------------|--------------|---------------|
| Pregnancy-associated hypertensive conditions | 38 | 27 |
| Medical conditions                | 14           | 9.9           |
| None                              | 89           | 63.1          |

*: Number of mothers differs from number of neonatal deaths due to multiple pregnancies. Inborn*: Neonates born at DNH; Outborn*: Neonates born at referring facilities and transferred to DNH after birth.

Figure 1. Neonatal causes of death (n = 143). Of the 26 congenital abnormalities, 12 (46.2%) were suspected or confirmed syndromes, 9 (34.6%) had cardiac abnormalities, neurological abnormalities in 4 (15.4%) and a suspected sequence in 1 (3.8%). Four patients (2.8%) demised under the category of other of which one patient died of hemorrhagic disease of the newborn following maternal warfarin use, one due to aspiration, one due to severe congenital anemia and one following an accidental ingestion of alcohol cleaning solution.

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The most common obstetric cause of death was spontaneous preterm labor in 32 (22.4%), followed by neonatal congenital abnormalities in 29 (20.3%), pre-eclampsia in 24 (16.8%), intrapartum asphyxia in 15 (10.5%), maternal infection in 13 (9.1%), antepartum hemorrhage in 10 (7.0%) and other causes in 7 (4.9%) of the neonatal deaths. In 13 (9.1%) cases no obstetric cause of death was identified.

The mean birth weight of the study population was 1681 g (n = 143; SD 941 g). There was no difference in the mean birth weight when comparing early with late neonatal deaths. The low-birth-weight rate (LBWR) was 13.6/1000 live births for the study period. There was also no difference in mean gestational age between neonates who succumbed to early neonatal deaths and those who suffered late neonatal deaths; 33 weeks (n = 97; SD 5.7) and 34 weeks (n = 42; SD 4.9) respectively (P-value .41).

There were 51 patient-related, 65 administrative-related and 165 health personnel-related modifiable factors identified. Most of the deaths had multiple factors identified. Modifiable factors are presented in Table 2.

The associations of modifiable factors with the timing, cause of death and birth weight category are presented in Table 3.

Immaturity-related conditions resulted mainly in early neonatal deaths (P-value < .01) and infection in late neonatal deaths (P-value < .01). Deaths in neonates with lower birth weight were mostly due to immaturity-related conditions (P-value < .01) and those with higher birth weight were predominantly due to hypoxia (P-value < .01) and congenital abnormalities (P-value < .01).

There was a significant association between health-personnel related factors and time of death (P-value .012). The most common health-personnel related modifiable factors associated with early neonatal deaths were antenatal steroids not given, congenital abnormality not detected antenatally, delay in referring to tertiary facility, hypothermia, inadequate neonatal resuscitation, and missed maternal diagnosis. The only modifiable factor identified that correlated with late neonatal deaths was hospital acquired infection.

There was a significant association between patient-related factors and neonatal cause of death (P-value .01). A high proportion of deaths due to immaturity-related conditions and infection had a mother who received minimal or no antenatal care. Pregnancies with minimal/no antenatal care were also more likely to be associated with early neonatal deaths (P-value .02). There was also a significant association between cause of death and administrative-related factors (P-value < .01) and health personnel-related factors (P-value < .001). Deaths due to immaturity-related conditions, infections and hypoxia had a significant association with inadequate facilities and equipment. Hypothermia was mostly associated with deaths due to immaturity-related conditions and infection. Deaths due to infection were predominantly due to the modifiable factor of hospital acquired infection.

There was a significant association between administrative-related modifiable factors and birth weight category (P-value .003). The majority of deaths in the category of ≥2500 g were associated with inadequate facilities and equipment. Health-personnel related

| Table 2. Modifiable factors (n=281*). |
|-------------------------------------|
| **Modifiable factors** | **Frequency (n)** | **Percentage (%)** |
|-------------------------------------|
| **Patient related (n = 51)** | | |
| Unbooked or booked late for antenatal care | 30 | 21 |
| Smoking, alcohol and drugs | 19 | 13.3 |
| Attempted termination of pregnancy | 2 | 1.4 |
| None | 106 | 74.1 |
| **Administrative (n = 65)** | | |
| Inadequate facilities/equipment | 43 | 30.1 |
| Insufficient nurses on duty | 12 | 8.4 |
| Lack of adequate neonatal transport | 10 | 7 |
| None | 98 | 68.5 |
| **Health personnel (n = 165)** | | |
| Hypothermia | 62 | 43.4 |
| Hospital-acquired infection | 38 | 26.6 |
| Congenital abnormality not detected antenatally | 20 | 14 |
| Other | 45 | 31.4 |
| None | 25 | 17.5 |

*Most deaths had multiple modifiable factors identified.
modifiable factors were also significantly associated with birth weight category (P-value .04). Deaths in neonates with a birth weight <1500 g had a significant association with hypothermia on admission.

**Discussion**

The NMR of 17.7/1000 live births in our study is considerably higher than the institutional NMR in South Africa in 2020 which was 12/1000 live births but considerably lower than the NMR of 27/1000 live births for Sub-Saharan Africa. There was a predominance of early neonatal deaths. The most common cause of neonatal death was infection followed by immaturity-related, congenital abnormalities and hypoxia-related deaths. Multiple modifiable factors were identified in most cases. The most common modifiable factors were related to healthcare workers and included, in descending order of frequency, hypothermia, congenital abnormality not detected antenatally and hospital-acquired infections. This was followed by administrative factors, predominantly inadequate resources and facilities, and patient factors, specifically failure to attend antenatal care and substance abuse.

The high neonatal mortality rate in our study may be the result of DNH being a tertiary hospital that receives referrals from several surrounding facilities. This includes high-risk pregnancies and deliveries as well as neonates that require higher levels of care after delivery. A more accurate approach would be to include all neonatal deaths in the catchment area and calculate NMR based on all live births for the same area. However, we did not have this additional information. It is likely that the high mortality rate observed at DNH is not representative of the overall NMR in the Western region of the Eastern Cape. Despite this, the key factors driving the NMR at DNH should not be disregarded.

The predominance of early neonatal deaths in our study is not uncommon and, although higher than the ENMR of 10.2/1000 live births in SA in 2016, is similar to several other low- and middle-income countries. Importantly, early neonatal mortality has been associated with prematurity, poor neonatal resuscitation practices and hypothermia. These risk factors are largely avoidable and can be easily improved and prevented with cost-effective strategies.

Hypoxia-related causes remain a significant contributor to neonatal deaths at DNH. The South African “Saving Babies Report” for 2014 to 2016 showed that in

| Time of death  | Patient related factors (n = 51) | Administrative factors (n = 65) | Health personnel factors (n = 165) |
|----------------|-------------------------------|-------------------------------|----------------------------------|
| Early          | 38                            | 45                            | 105                              |
| Late           | 13                            | 20                            | 60                               |
| P-value        | .75                           | .51                           | .012                             |
| Cause of death |                               |                               |                                  |
| Congenital abnormality | 4                             | 6                             | 24                               |
| Hypoxia        | 2                             | 22                            | 22                               |
| Immaturity     | 30                            | 17                            | 43                               |
| Infection      | 15                            | 20                            | 76                               |
| P-value        | .01                           | <.01                          | <.001                            |
| Birth weight category (g) |                   |                               |                                  |
| <800           | 13                            | 5                             | 26                               |
| 800-999        | 11                            | 9                             | 33                               |
| 1000-1499      | 10                            | 10                            | 32                               |
| 1500-1999      | 8                             | 8                             | 21                               |
| 2000-2499      | 3                             | 5                             | 19                               |
| ≥2500          | 6                             | 28                            | 34                               |
| P-value        | .21                           | .003                          | .04                              |
72% of neonatal deaths due to perinatal asphyxia there was no maternal obstetric condition that contributed to the neonatal death. This suggests that poor intra-partum care is a significant contributor. Intrapartum and immediate postpartum care are important determinants of neonatal mortality related to hypoxia/ischemia and ongoing education in this regard is crucial.

Several modifiable factors were identified in this study. The most common factors were health worker-related, key of which was hypothermia on admission to the neonatal unit. The significant association between hypothermia and neonatal mortality, specifically in premature infants, is well-described and easily avoidable. Simple interventions such as covering VLBW neonates in plastic wrapping after delivery, maintaining an adequate room temperature, supplying head caps, skin-to-skin contact with mom and using functional incubators can prevent hypothermia in settings where other interventions are not available. Maintaining normothermia is a simple, low-cost, high-impact intervention that can significantly improve neonatal outcomes.

Administrative factors were the second most common modifiable factors in our study. These included inadequate facilities/equipment (including NICU beds), insufficient nurses on duty and lack of adequate neonatal transport. The Saving Babies Report for 2014 to 2016 similarly identified the most common administrative factors as inadequate facilities/equipment (14.7%), lack of transport from home to facility (11.9%) and no NICU bed available (8.9%). Reliable, cost-effective, and proven resources, such as monitoring devices, CPAP units and incubators, need to be sourced and appropriately allocated to improve neonatal facilities at the study site as well as elsewhere in SA. This requires coordinated, site-specific needs-analysis, funding support at facility as well as regional levels and efficient procurement of necessary equipment.

The lack of adequate neonatal transport, which was identified in almost a quarter of patients born outside the study center, is also concerning. Delays in emergency transport of patients to appropriate facilities has been identified as a significant contributor to neonatal mortality across SA. Furthermore, a study conducted in SA showed that adverse events occur in 75% of neonatal transfers. In various regions globally there are dedicated neonatal retrieval teams that effectively and safely transfer neonates from peripheral areas to central facilities able to provide the level of care that they require. These dedicated neonatal emergency transport services are currently being used in countries such as Australia, France, USA, Japan and Italy. Similar resources are not currently available in SA and carry a significant financial cost. However, current resources and services should as a minimum be improved and optimized with the ultimate goal of developing a dedicated neonatal transport service tailored to the available resources and patient needs in SA.

Finally, several patient-related factors were identified as contributing to neonatal deaths in the study. The most important of these was the lack of antenatal care in 18.9% of patients. Multiple studies have shown the importance of attending antenatal care which is provided free of charge in SA. Although the COVID pandemic may have impacted accessibility and attendance at antenatal care, barriers to attendance need to be actively investigated and strategies developed to support pregnant women in this regard. In addition, it is vital to educate women on the availability and benefits of attending antenatal care in order to reduce neonatal mortality.

The study had several limitations. Due to the retrospective study design, data was dependent on what was recorded in the neonatal mortality audit tool. The study only included neonates who died while admitted in the neonatal unit, thus excluding neonates who were readmitted to the general pediatric wards following discharge. Extremely premature neonates, that were older than 28 days at the time of death, were also excluded but should ideally be reviewed in this type of audit. The study was also done at a regional hospital in the Eastern Cape and the findings may not be generalizable to other settings. Despite these limitations, the study identified multiple areas for improvement in order to impact neonatal outcomes in the study center which could also be of potential benefit to those in similar settings. Targeted protocols and guidelines can be implemented based on the findings.

**Conclusion**

The NMR in our study remains higher than global and national averages. The neonatal causes of death were slightly different to those found in other studies across South Africa, highlighting the importance of center-based audit and review. Key strategies, with a focus on low-cost, high-impact interventions, need to be implemented in order to reduce neonatal mortality.

**Author’s note**

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