# Pediatric perioperative mortality in Southeastern Nigeria—a multicenter, prospective study

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# Abstract

## Background

The perioperative mortality rate is a key indicator of the quality of surgical services in low and middle-income countries. (LMIC).

## Objective

To determine the perioperative mortality rate of pediatric surgical conditions and the predictive factors in Southeastern Nigeria.

## Methodology

A prospective, multicenter study of peri-operative mortalities occurring in children under 18 years in five tertiary hospitals in Southeastern Nigeria over nine months was conducted. All-cause and case-specific in-hospital peri-operative mortality rates, and predictive factors were identified. The mortality rate was expressed as percentages with a 95% confidence interval. The data were analyzed using SPSS 26.

## Results

A total of 775 patients underwent anesthesia or surgery, with 28 deaths. The perioperative mortality rates within 24 hours and 30 days after the procedure were 1.94% (95% CI = 1.09–3.17) and 1.17% (95% CI = 0.91–2.91) respectively. The mortality rates was 100% for Gastroschisis and ruptured omphalocele with overwhelming sepsis being the major cause of death (53.6%). Significant determinants of mortality were a higher ASA status (AOR) = 13.944, 95% CI = 1.509-128.851, p = 0.020], sedation without ventilatory support (AOR) = 15.295, 95% CI = 3.304–70.800, p = 0.001] and associated comorbidities (AOR) = 65.448, 95% CI = 11.244-380.962, p = 0.001].

## Conclusion

The pediatric peri-operative mortality rate in Southeastern Nigeria is high for Gastroschisis. Associated comorbidities, higher ASA status, and sedation without ventilatory support were significant predictors of mortality.


# Introduction

The demand for surgeries differs across the world, with western sub-Saharan Africa requiring an estimated 6495 operations per 100,000 people.[1] Based on available information, it appears that between 6% and 12% of pediatric hospitalizations in sub-Saharan Africa are due to surgical procedures. However, it is possible that the percentage is higher in certain urban locations.[2] in Uganda, about a third of pediatric deaths result from surgical conditions.[3] The Lancet Commission on Global Surgery recommended the national peri-operative mortality rate (POMR) as one of six key indicators to measure the strength of a country's surgical system.[4]

Despite the usefulness of hospital mortality data in the monitoring and evaluation of health care services, there is a dearth of information on the availability, accessibility, and quality of hospital mortality data in most of sub-Saharan Africa.[5] There is limited information about the risk of specific subgroups of patients and about the incidence of the contribution of anesthesia and surgical factors to short and long-term mortality.[6]

The POMR is defined as death following surgery and anesthesia within two time periods: on the day of surgery (including death in the operating theatre) and before discharge from hospital or within 30 days of surgery divided by the number of procedures performed, has been championed as a useful indicator to measure surgical safety at an institutional and national level.[7, 8] Perioperative mortality may not reflect poor performance but could be attributable to complications from the operation or pre-existing medical conditions.[9]

Pediatric peri-operative mortality is low, but it is underreported in peer-reviewed journals, making it difficult to understand the magnitude of the problem.[10] The low peri-operative mortality rate in pediatric surgery precludes effective analysis of mortality at individual institutions. Therefore, analysis of multi-institutional data is essential to determine any patterns of peri-operative death in children.[11] This is Southeastern Nigeria's first multi-institutional, prospective study of pediatric peri-operative mortality.

The study aims to provide multi-institutional benchmark data on pediatric peri-operative mortality in Southeastern Nigeria.

The objectives are:

1. To determine all-cause and case-specific pediatric peri-operative mortality rates in Southeastern Nigeria
2. Identify the possible predictive factors.
3. Determine any relationship between facility factors viz: dedicated theatres, pediatric anesthesiologists and pediatric nurses, and pediatric peri-operative mortality.

## Methodology

# Study design

A prospective, multicenter study of peri-operative mortalities in children under 18 years in five tertiary hospitals, in the five states in Southeastern Nigeria, between May 2021 and January 2022 was performed. The all-cause and the case-specific peri-operative mortality rate was determined, and predictive factors were identified.

# Study Area

Hospitals involved in the study were: University of Nigeria Teaching Hospital Enugu (UNTH), Nnamdi Azikiwe University Teaching Hospital Nnewi, Anambra (NAUTH), Alex Ekwueme Federal University Teaching Hospital, Abakaliki (AEFUTHA), Federal Medical Center, Umuahia, Abia (FMC, Umuahia) and Federal Medical Center Owerri, Imo (FMC, Owerri) and receive the majority of referrals in pediatric surgery in Southeastern Nigeria. There is no pediatric or neonatal intensive care unit (NICU) in any of the hospitals and pediatric total parenteral nutrition (TPN) is not available in any of the hospitals involved in the study. Other features of the participating hospitals are shown in Table I

**Table I. Hospitals participating in the study**.

| Hospital | Capacity | Pediatric nurses | Pediatric anesthesiologists | Pediatric surgeons | Pediatric ORs |
|---|---|---|---|---|---|
| UNTH | 530 | 2 | 0 | 6 | 0 |
| NAUTH | 430 | 0 | 0 | 4 | 0 |
| AEFETHA | 740 | 0 | 0 | 3 | 0 |
| FMC, Umuahia | 405 | 0 | 0 | 2 | 0 |
| FMC, Owerri | 523 | 2 | 0 | 2 | 0 |

# Data collection

The study recruited patients from clinics, children emergency room (CHER) and special care baby units (SCBU). Inclusion criteria included children with a surgical problem for which anesthesia may/ may not be required and those whose parents consented to be part of the study. Exclusion criteria included children undergoing cardiac, plastic, orthopedic and ophthalmic surgeries, (these surgeries are not performed by pediatric surgeons) and those whose parents did not give consent.

The data collection tool was adapted to Ademola et al., [12] and patients' biodata, weight at presentation, symptoms duration, diagnosis, associated anomalies, ASA grade, urgency of the procedure, time to intervention, the cadre of attending surgeon and anesthesiologist, surgical procedure and number of surgeries within 30 days, anesthetic technique, mortalities, time of death, cause of death and duration of hospital stay were entered into a register opened for this purpose. Where a 30-day follow-up record was unavailable, the condition at discharge from the hospital was used. A pediatric surgeon from each of the participating hospitals ensured data was verified and correct before being documented in the register.

**Ethical considerations**. The nature and motives of the planned study were explained to parents, guardians, and caregivers including older patients. Those who wished to participate gave verbal consent as written consent was not possible in most cases. Patients and caregivers were free to withdraw from the study anytime they wanted. Ethical clearance for the study was obtained from the Health Research Ethics Committee (HREC) of each of the participating institutions.

Children were grouped as follows: preterm, neonates, infants, preschool (1–3 years), young children (4–10 years) and older children (11–18 years). Each mortality was discussed by a team of surgeons and anesthesiologists involved in the management to determine the cause of death.

The primary causes of death were classified according to a study by de Bruin L et al. [6] attributable to preoperative child condition or disease (when comorbidities were the only or the major contributory factor)

1. attributable to a preoperative trauma event (with subsequent surgery)
2. anesthesia either fully or partially contributed to the death (when the child's disease or condition was the primary factor, but anesthesia-related problems represented an additional factor)
3. the surgical procedure either fully or partially contributed to the death (when the child's disease or condition was the primary factor, but surgery-related problems represented an additional factor)

Categories 1 and 2 include all deaths in which the panel agreed that neither surgery nor the aesthetic procedure contributed to death. Deaths, where anesthesia contributed, were defined as described by Bonasso et al. [11] using the definition by Griend and colleagues: patients for which the panel agreed that anesthesia or factors under the responsibility of the anesthetist contributed to death. The same panel-based assessment was applied to the category ‘surgery-related death’. This protocol was replicated in all the participating hospitals.

# Statistical analysis

The mortality rate was calculated in percentages with a 95% confidence interval using the Clopper-Pearson exact method. Risk per procedure was reported. Variables were described using frequencies and proportions. Univariate and multivariate Logistic regression analyses were done to identify risk factors for peri-operative mortality. SPSS Version 26.0 was used with a $P < 0.05$ significance level.

# Results

A total of 789 surgical procedures, 477 being major surgeries, were conducted on 775 patients with 28 mortalities (all from major surgeries). Peri-operative mortality rates within 24 hours and 30 days after the procedure were 1.94% (95% CI = 1.09–3.17) and 1.17% (95% CI = 0.91–2.91) respectively. [Table II]

**Table II: Patient’s demographic characteristics and mortality rates**

| | Cases (n) | Death ≤ 30days (%) | Percentage mortality (95% CI) | $\chi^2$ | P-value |
|---|---|---|---|---|---|
| Gender | | | | 3.05 | 0.081 |
| Male | 493 | 14(50.0) | 2.84 (1.56-4.72) | | |
| Female | 254 | 14(50.0) | 5.51 (3.05-9.07) | | |
| Age | | | | 108.71 | < 0.001 |
| Preterm | 1 | 1(3.6) | - | | |
| Neonate | 81 | 17(60.7) | 20.99 (12.73-31.46) | | |
| Infant | 182 | 6(21.4) | 3.30 (1.22-7.04) | | |
| Preschool | 239 | 2(7.1) | 0.84 (0.10-2.99) | | |
| Young children | 149 | 1(3.6) | 0.67 (0.02-3.68) | | |
| Older children | 123 | 1(3.6) | 0.81 (0.02-4.45) | | |
| Nature of Surgery | | | | 29.91 | < 0.001 |
| Elective | 458 | 2(7.1) | 0.44 (0.05-1.57) | | |
| Emergency | 315 | 24(85.7) | 7.62 (4.94-11.12) | | |
| ASA Status | | | | 52.03 | < 0.001 |
| I&II | 528 | 1(3.6) | 0.19 (0.00-1.05) | | |
| III | 136 | 13(46.4) | 9.56 (5.19-15.79) | | |
| IV&V | 109 | 12(42.9) | 11.01 (5.82-18.44) | | |
| Time of Death | | | | | |
| ≤24 hours | | 15(53.6) | 1.94 (1.09-3.17) | | |
| 24 hours to 30d | | 13(46.4) | 1.17 (0.91-2.91) | | |
| Total | 775 | 28 | 3.61 (2.41-5.18) | | |

CI, Confidence intervals are for the proportion of the deaths relative to the specific group.

The case-specific mortality rates ranged from 100% for Gastroschisis [5/5] and ruptured omphalocele [1/1] to 3.4% for Hirschsprung's disease [1/29]. [Table III]

Table III: Case-specific mortality rates

| Diagnosis | No. of Cases | No. of Deaths | Percentage Mortality (%) | Percentage of Total (%) |
|---|---|---|---|---|
| Gastric outlet obstruction | 7 | 1 | 14.3 | 3.6 |
| Ruptured Omphalocele | 1 | 1 | 100 | 3.6 |
| Duodenal atresia | 6 | 2 | 33.3 | 7.1 |
| EA- TEF | 5 | 3 | 60.0 | 10.7 |
| Hirschsprung's disease | 29 | 1 | 3.4 | 3.6 |
| Bowel perforations | 44 | 3 | 6.8 | 10.7 |
| Tumors | 34 | 2 | 5.9 | 7.1 |
| Gastroschisis | 5 | 5 | 100 | 17.6 |
| Intussusception | 79 | 6 | 7.6 | 21.4 |
| Malrotation | 21 | 1 | 4.7 | 3.6 |
| Anorectal malformation | 45 | 2 | 4.4 | 7.1 |
| Jejuno-ileal atresia | 18 | 1 | 5.6 | 3.6 |

Most mortalities were attributed to the disease process, [Figure I] resulting commonly from overwhelming sepsis. (53.6%) [Table IV].

**Figure I: Classification of primary cause of death.**

**Table IV: Main clinical causes of death and mortality rate**

| Cause of death | Number (%)28) | Mortality (95% CI) |
|---|---|---|
| Overwhelming sepsis | 15(53.6) | 1.94 (1.09-3.17) |
| Cardio-respiratory failure | 4(14.3) | 0.51 (0.14-1.30) |
| Metabolic failure | 1(3.6) | 0.13 (0.00-0.72) |
| Aspiration pneumonitis | 5(17.9) | 0.65 (0.21-1.50) |
| Renal failure | 2(7.1) | 0.26 (0.03-0.93) |
| Advanced malignancy with metastasis | 1(3.6) | 0.13 (0.00-0.72) |

CI, Confidence intervals are for the proportion of the deaths relative to the total number of cases

Univariate logistic regression identified neonatal age group, higher ASA status, emergency surgery, and presence of associated congenital abnormalities related to increased mortality. On multivariate regression analysis, the significant determinants of mortality were a higher ASA status (AOR)=13.944, 95% CI=1.509-128.851, p=0.020], sedation (with midazolam or diazepam) alone or with local anesthesia (with lignocaine) (AOR)=15.295, 95% CI=3.304-70.800, p=0.001] and associated comorbidities (AOR)=65.448, 95% CI=11.244-380.962, p=0.001]. [Table V]

**Table V: Univariate and multivariate logistic regression analyses of variables that predict mortality.**

| Variable | Univariate analysis | | | Multivariate analysis | | |
|---|---|---|---|---|---|---|
| | **OR** | **95%CI** | **p-value** | **AOR** | **95%CI** | **p-value** |
| **Age of patients**<br>Neonates<br>1-216 months (ref) | 16.49 | 7.41–36.72 | < 0.001 | 1.810 | 0.397–8.258 | 0.444 |
| **ASA Grade**<br>I&II (ref)<br>III, IV&V | 59.89 | 8.06–444.70 | < 0.001 | 13.944 | 1.509-128.851 | 0.020 |
| **Surgeon Cadre**<br>Consultant (ref)<br>Resident | 0.330 | 0.113–0.968 | 0.043 | 0.270 | 0.052–1.417 | 0.122 |
| **Anesthetic Cadre**<br>Consultant (ref)<br>Resident | 0.913 | 0.376–2.220 | 0.841 | 1.570 | 0.230-10.738 | 0.646 |
| **Nature of Surgery**<br>Elective (ref)<br>Emergency | 19.72 | 4.64–83.90 | < 0.001 | 5.337 | 0.556–51.193 | 0.147 |
| **Congenital abnormality**<br>Present<br>Absent (ref) | 313.29 | 95.86-1023.91 | < 0.001 | 65.448 | 11.244-380.962 | < 0.001 |
| **Type of Anesthesia**<br>GA + ETI (ref)<br>Other | 15.529 | 6.762–35.664 | < 0.001 | 15.295 | 3.304–70.800 | < 0.001 |
| ref = reference | | | | | | |

# Discussion

The POMRs on within 24 hours and 30 days after the procedure were 1.94% (95% CI = 11.09–3.17) and 1.17% (95% CI = 0.91–2.91), respectively and compares with a similar study conducted in a single center in Southwest Nigeria by Ademola et al.[12] A Kenyan multicenter study reported 24-hour and 7-day mortality rates of 0.8% and 1.7%, respectively[13] in contrast to middle-income countries (MICs) and high-income countries (HICs) with 0.7% and 0.3%, respectively[14] and represents more than 2-fold and 6-fold increased mortality in LMICs in comparison with MICs and HICs respectively.

The highest perioperative mortalities occurred in patients with gastroschisis and esophageal atresia, 100% and 60.0% mortality rates, respectively. Four patients with gastroschisis presented in very poor clinical condition and died before any form of intervention and were excluded from this study. Three had improvised silo application and two had laparotomies and primary surgical closure. In Kano, Northern Nigeria, Anyanwu et al. (2020) reported 87.2% mortality rate for gastroschisis, and later, observed a significant improvement in outcome (p = 0.035) when they reverted to sutureless application of improvised silo. [15] As with the present study, most mortalities were due to starvation and late presentation with sepsis. A Global PedSurg prospective study (2021), reported 90.0% POMRs for gastroschisis, in LICs, 31.9% in MICs and 1.4% in HICs.[14] Lack of prenatal diagnosis and immediate postnatal interventions might be responsible for the dismal outcome in LMICs. [12, 15, 16] Two mortalities in EA-TOF had thoracotomy with primary repair, and one had laparotomy in addition, for associated duodenal atresia. Others had gastrostomies with gastric banding due to late presentation with aspiration pneumonitis. All required prolonged ventilatory support, like the report by Puri et al. (2019) [17] though this could not be sustained owing to the unavailability of NICU and requisite expertise, especially for the nursing care of such patients. The need for prolonged oxygen or ventilatory support has been linked to higher neonatal perioperative mortality. [18]

Neonates accounted for the majority (60.7% ) of deaths, mirroring Ademola et al.'s finding of 58.8% [12] Neonates encounter distinct challenges as they transit from intrauterine life to postnatal life, and going through surgery can disrupt this delicate balance, making them more vulnerable to sepsis, nutritional deficiencies, and respiratory problems. [19]The neonatal surgical mortality (NSM) rate was 19.8%, lower than reports from India (33.33%),[17] Bangladesh (14.6%),[20] and Tunisia[21] but higher than those from HICs. [14, 22–24] The lower neonatal mortality rates in HICs have been linked to advanced perioperative support systems, prenatal diagnosis, improved perinatal care, availability of NICUs, and TPN. [12, 14, 25–27]

Most (72%) mortalities were attributed to preoperative child conditions and overwhelming sepsis was the leading cause of death (53.6%), consistent with other reports on pediatric perioperative mortality rates. [12, 14, 17] Late presentation, often with complications and sepsis, is common in the subregion.[28,29] In the present study, all the patients who died from intussusception presented more than 24 hours of the onset of symptoms in poor clinical conditions, and some required multiple surgeries. Limitations in theatre space availability created further delays in intervention contributing to the observed mortality.

Presentation after 24 hours is known to increase the risk of perioperative mortality in children with intussusception. [28]

Factors related to anesthesia were responsible for or confounded the pre-existing condition in 20% of deaths, which is a significant contrast to de Bruin L et al.'s report of less than 0.02%.[6] The absence of pediatric anesthesiologists and the lack of suitable equipment for pediatric anesthesia in the participating hospitals may account for this difference. Emergency surgeries had significantly more mortalities than elective surgical cases, while the surgical procedure accounted for 16% of mortalities and this may be due to technical errors and suboptimal theatre conditions for pediatric surgeries. Consultant surgeons performed most of the more delicate surgeries and this might explain why more mortalities were seen when the consultant and not the Resident was the surgeon.

We found no significant difference in perioperative mortalities in surgeries for congenital and acquired cases contrary to Ademola[12] and this might be due to the exclusion of cardiac cases in the present study.

Multivariable logistic regression showed that higher ASA status and associated comorbidities were significant predictors of perioperative mortality, supporting earlier findings on the subject. [12, 14, 15] Associated comorbidities identified were associated congenital malformations, low birth weight, and immunosuppression had increased odds of 30-day mortality. Patients with ASA status III or greater represented 89.3% of deaths. Other forms of anesthesia aside from general anesthesia with or without ETT were significantly related to increased mortality. These forms of anesthesia were mostly sedation (with midazolam or diazepam) or sedation in combination with local infiltration with lignocaine. Although sedation using these agents is commonly used in pediatric surgery,[30] we believe that the provision of adequate ventilatory support could have made a significant difference for the patients in this study. It is possible that the lack of proper equipment or expertise, or both, may have contributed to the fatalities observed with this type of anesthesia. Inadequate or inappropriate use of anesthetic medication, limited ventilatory support, unavailability of airway devices, and the required skills are linked to increased pediatric perioperative mortality.[31] We hope to explore this in a follow-up study further. More mortalities were recorded when the anesthesiologist was a trainee. This was not surprising as most emergencies were undertaken by the trainees. While the results were not statistically significant, it might be necessary to provide additional oversight for trainees in anesthesiology undertaking major pediatric surgeries.

# Limitations of the study

Despite the reported high POMRs reported in this study, the actual figure could be higher because data collection was at tertiary centers where there is access to expert pediatric surgical services. Pediatric surgeries performed outside these centers were not captured. The exclusion of cardiac, orthopedic, and plastic surgeries in the pediatric age group may affect the overall POMR for pediatric surgeries and this needs to be considered when interpreting the results.

## Recommendations /Future Study

A follow-up study to explore the impact of a combination of sedation and ventilatory support on pediatric perioperative mortality is necessary. Research that includes all pediatric surgical procedures (cardiac, orthopedic plastic, and thoracic) performed in all hospitals including tertiary, private, and mission hospitals is necessary to capture the actual POMR in Nigeria. A shift towards sutureless silo application in gastroschisis and improved supervision of anesthesiologist Residents during major pediatric surgeries should be encouraged. It is crucial to maintain efforts towards training and retaining pediatric anesthesiologists, and pediatric surgery nurses in the subregion, as well as providing essential resources such as TPN and NICU facilities. Furthermore, it is important to focus on establishing these resources at tertiary centers in Southeastern Nigeria to effectively manage at-risk neonates.

## Conclusion

The risk of death in children undergoing major surgeries, particularly gastroschisis and esophageal atresia in Southeast Nigeria is unacceptably high. Emergency surgeries, neonatal age, late presentation with overwhelming sepsis, and unsupervised anesthesiologist trainees contribute to increased perioperative mortality. Higher ASA status, associated comorbidities, and sedation alone or in combination with local anesthesia without ventilatory support significantly increase the perioperative mortality rate.

## Declarations

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Data Availability: The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Author contribution:

Conceptualization, writing original draft, review, and editing: Nwankwo EP

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# Figures

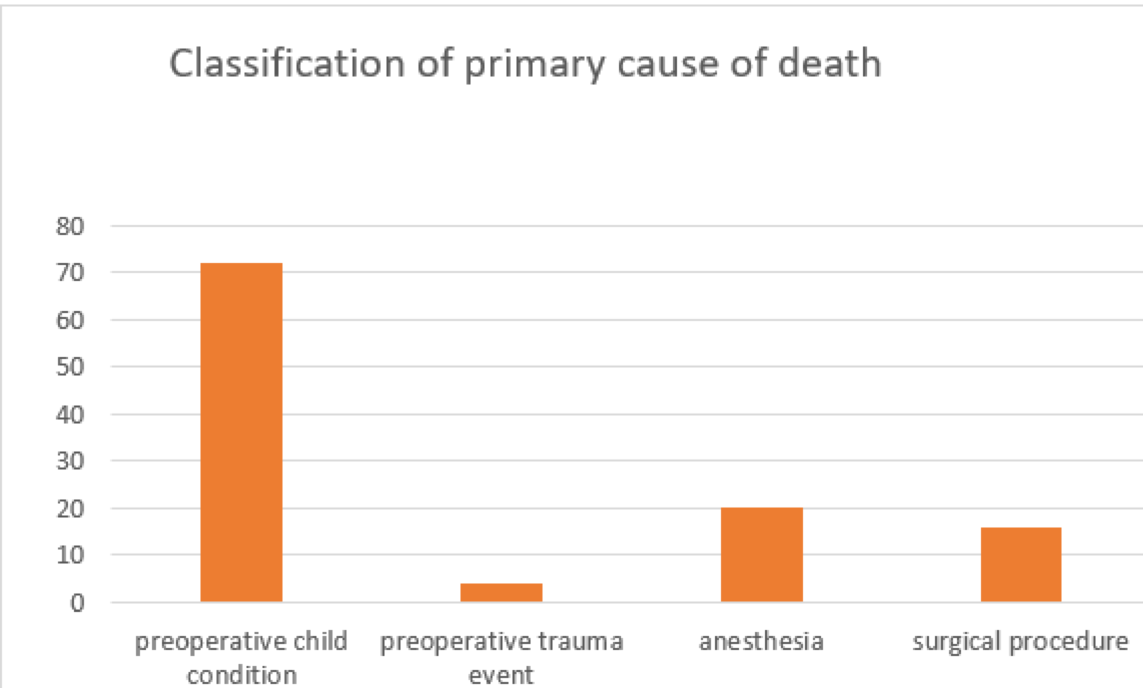


**Figure 1**

**Classification of primary cause of death.**