African Surgical Outcomes Study in Paediatric patients (ASOS-Paeds)

An African, international multi-centre fourteen-day evaluation of patient care and clinical outcomes for paediatric patients undergoing surgery

STATISTICAL ANALYSIS PLAN
VERSION 1.0

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Working Title:

An evaluation of intra-operative severe critical events in ASOS-Paeds (African Surgical Outcomes Study in Paediatric patients): a 14-day prospective, observational cohort study of paediatric surgical patients

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Table of Contents

Introduction and rationale for the "severe critical events" analysis

Universal Health Coverage aims to guarantee access to needed health care services for all people without financial burden, which includes surgical service delivery. (1) The World Health Assembly resolution EB152(3), stated "integrated Emergency Critical Operative Care for universal health care (ECO-UHC) and protection from health emergencies" should be part of global health improvement interventions. It advocates for the delivery of quality health care for acutely ill people. This includes early access and intervention for general acute childcare including operative care. This is particularly important in low and middle income countries because the proportion of child population is estimated to be half of the total population. (2)

Paediatric mortality after surgical procedures continues to be high. One study reported a mortality of 12%, with oesophageal atresia accounting for 72% and jejunoileal atresia for 35%. (3) The human resources available for paediatric surgery are limited, with a low number of paediatric surgeons and paediatric anaesthesiologists compared to the burden of the paediatric surgical population. The result is that in many places non-specialists and even other non-physician professionals might be solely responsible for peri-operative care. (4,) (5) This can result in excess intra-operative critical events. Critical events are however, inadequately investigated in Africa. The existing data are derived from registries which are often incomplete and may not target critical events.

Intraoperative critical events can have multiple risk factors and contribute to anaesthesia related complications. The incidence ranges from 2.32% to 11.7% and shows significant variability among different settings. The largest intraoperative critical event study in Europe showed a high number of intraoperative severe critical events (5.2%) with significant variability between hospitals. Respiratory critical events were the most common (3.1%) followed by cardiovascular instability (1.9%). The immediate poor outcome was 5.4%. (6)

There are specific considerations that should be sought in Paediatric population aesthesia related critical events. These may include the choice of drug and their response. Additionally, the anaesthesia related adverse effects may have long term sequelae for children. As a result, studying those critical events will help to identify the factors related and final outcomes which will help in standardizing the care. It will also be a base to advocate for intraoperative care.

Reported incidences from high income countries

Studies from Europe reported incidences ranging from 0.14% for serious adverse events to 3.4% for critical incidents. (7) Similarly a study done by Cohen et al showed a severe anaesthesia critical event rate of 1.4 per 1000. The commonest events were respiratory followed by cardiac. (8) A large international multicentric cohort study covering North America, Oceania and Europe reported an incidence of 24 % for intraoperative adverse events. (9)

Reported incidences from low- and middle-income countries

The reported incidences for critical events vary across low and middle-income countries (LMICs). A South Korean study reported a 0.4% incidence of paediatric anaesthesia related critical incidents, with respiratory events been the commonest (55% of the cases), (10) compared to an Indian study which reported a 12% incidence, predominated by respiratory complications. (11) Generally, LMICs may carry at least double the burden of intraoperative critical events to high-income countries, although the risk should be similar to that of HICs. These excess events should be preventable. (12)

Types of complications

Respiratory related complications are most commonly reported, followed by cardiovascular events.

Risks associated with complications

The following patient and surgical risk factors have been shown to contribute to intraoperative critical events: age <1 year, ASA physical status III and IV, urgency of the surgical procedure, and preexisting comorbidities. The level of training of the anaesthesia providers and the number of years of experience, as well as the type of anaesthesia and surgery done are potentially important risk factors. (13)

Study rationale

African Surgical Outcomes Study in Paediatric patients (ASOS-Paeds) determined the incidence of in-hospital postoperative complications up to 30 days after surgery in paediatric surgical patients across different hospitals in Africa. This study will evaluate the intra-operative critical incidents reported in ASOS-Paeds. It is hoped that these findings will contribute to improving perioperative care for paediatric surgical patients in Africa.

Aims and objectives of the "severe critical incidents" analysis

Aims

The aims of this study are to describe the incidence of intraoperative severe critical events, the types of severe critical events, and risk factors independently associated with severe critical events.

Objectives of the study

Primary objective

1. To describe the incidence of intra-operative severe critical events in paediatric surgical patients in Africa

Secondary objectives

1. To describe the categories and types of severe critical events
2. To identify risk factors independently associated with severe critical events

Sensitivity analyses

1. Two sensitivity analyses will be conducted:
    a. The sensitivity analyses of elective surgical patients, and emergency surgical patients, and
    b. A sensitivity analysis excluding the two countries providing more than 10% of the patients to the dataset (Egypt and South Africa)

Statistical Analysis Plan

A) Data Validation

- Report on the number of incomplete data points
- Report on primary outcome data
    - % missing data for incidence of severe critical events
- Provide STROBE diagram of recruited patients

B) Statistical tests

- Categorical variables will be described as number and proportions (percentage) and will be compared using appropriate Chi-squared or Fisher's exact tests.
- Continuous variables will be calculated and reported as mean and standard deviation (SD) if normally distributed, or median and inter-quartile range (IQR) if not normally distributed.
- Comparisons of continuous variables between groups will be performed using t-tests, one-way ANOVA or equivalent non-parametric tests as appropriate.
- If < 5% of data are missing for the primary outcomes, a complete case analysis will be conducted
- A p-value of less than 0.05 will be considered statistically significant for all analyses
- Generalized mixed effects model analysis will be performed for exploration of candidate variables for prediction of risks for the primary outcome i.e. incidence of severe critical events
    - Further description to follow in the section discussing risk prediction
- Sensitivity analyses will be conducted.

C) Primary objective

1. To describe the incidence of intra-operative severe critical events in paediatric surgical patients in Africa

This will be presented as number (n/N), percentage (%)

The cohort will be described according to the variables (Table 1)

- Age, ASA PS, sex
- Comorbidities
- Describe the Hospital, Surgery and Anaesthesia information
    - Hospital level
    - Urgency of surgery (elective, emergency)
    - Severity of surgery (minor, intermediate, severe),
    - Indication for surgery
    - Type of surgery
    - Intraoperative factors
    - Most senior anaesthetist
    - Most senior surgeon

- Time of induction

D) Secondary objectives

1. To describe the categories and type of intra-operative severe critical events

- Outcome definitions are defined in the study protocol
    - The categories of severe critical events will be presented as airway, respiratory, cardiovascular, metabolic, and other severe critical events categories (Table 2) using % to indicate the incidence (number of patients with severe critical events divided by the number of patients) and 95% confidence intervals.
    - To describe the types of severe critical events within each category
    - The categories and types of severe critical events will also be presented by the level of facility, and the level of the anesthesia providers (Table S1)

2. To identify risk factors independently associated with severe critical events

- All variables will be entered into the model, unless there are less than 10 events per variable. If this is the case, risk factors with a p value ≤ 0.05 for severe critical events identified by univariate analysis will be entered into the model. (Table 3) The reference category for the surgical discipline will be decided by the surgical discipline with the lowest incidence of severe critical events

    - Results will be presented as unadjusted and adjusted odds ratios (ORs) with 95% confidence intervals (CI's).

Analyses will be conducted using Statistical Package for the Social Sciences (SPSS) version 30 (SPSS Inc., Chicago, IL, USA) and R: A language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing (2024) using Studio: Integrated Development Environment for R. Boston, MA: RStudio, Inc. (2024).

Tables

Table 1. Description of cohort including patient, surgical, anaesthesia and facility characteristics

		All patients (n=)	**Patients with severe critical events (n=)**	**Patients without severe critical events (n=)**
		n/N (%)	n/N (%)	n/N (%)
Age	Mean (SD) Median (IQR)			
Sex				
Male				
Female				
Age categories				
0-28 days				
29 days to < 1 yr				
1 to < 4 yr				
4 to < 13 yr				
13 to <18 yr				
ASA PS				
I				
II				
III				
IV-V				
Urgency of surgery				
Routine				
Emergency				
Severity of surgery				
Minor				
Intermediate				
Major				
Primary indication for surgery				
Non-communicable disease				
Infective				
Trauma				
Congenital				
Hospital level				
First				
Second				
Third				
Most senior anaesthetist				

Specialist			
Non-specialist physician			
Nurse			
Non-physician			
Most senior surgeon			
Specialist			
Non-specialist physician			
Nurse			
Non-physician			
Type of surgery			
Orthopaedic			
Cardiac			
ENT			
Gynaecological			
Hepatobiliary			
Kidney/urological			
Gastrointestinal			
Thoracic			
Ophthalmology			
Maxillo-facial/ dental			
Plastic/cutaneous			
Neurosurgery			
Burns			
Comorbidities			
Cardiac disease			
Chronic respiratory disease			
Neurological disorder			
HIV/AIDS			
Cancer			
Current respiratory tract infection			
Intraoperative factors			
Duration			
Surgical checklist used			
Time			
Daytime			
After hours			

Table 2: The categories and types of intra-operative severe critical events

	Overall	**Incidence**
	n/N (%)	**% (95% CI)**
Categories of anaesthetic severe critical incidents		
Any		
Any Airway/respiratory		
Any CVS		
Any Other		
Types of severe critical events by category		
Airway/respiratory		
Difficult BMV		
Difficult Intubation		
Failed Intubation		
Laryngospasm		
Bronchospasm		
Aspiration		
Severe Hypoxia		
CVS		
Bradycardia		
Cardiovascular instability		
Cardiac Arrest		
Metabolic		
Temp < 36		
Low Glucose		
Other		
Anaphylaxis		
Drug error		
Death		
Yes		
No		

Table 3. Univariable and multivariable analysis of preoperative factors associated with intra-operative severe critical events

	Univariable		Multivariable	
	OR (95% CI)	**p-value**	**OR (95% CI)**	**p-value**
Age (per 1 year)				
Sex				
Male				
Female	Reference			
ASA PS				
I	Reference			
II				
III				
IV-V				
Urgency of surgery				
Routine	Reference			
Emergency				
Severity of surgery				
Minor	Reference			
Intermediate				
Major				
Primary indication for surgery				
Non-communicable disease	Reference			
Infective				
Trauma				
Congenital				
Hospital level				
First				
Second				
Third	Reference			
Most senior surgeon				
Specialist	Reference			
Non-specialist physician				
Nurse				
Non-physician				
Most senior anaesthetist				
Specialist	Reference			

Non-specialist physician				
Nurse				
Non-physician				
Type of surgery				
Orthopaedic				
Cardiac				
ENT				
Gynaecological				
Hepatobiliary				
Kidney/urological				
Gastrointestinal				
Thoracic				
Ophthalmology				
Maxillo-facial/ dental				
Plastic/cutaneous				
Neurosurgery				
Burns				
Comorbidities				
Cardiac disease				
Chronic respiratory disease				
Neurological disorder				
HIV/AIDS				
Cancer				
Current respiratory tract infection				
Intraoperative factors				
Duration				
Surgical checklist used	Reference			
Surgical checklist not used				
Time				
Daytime	Reference			
After hours				

Table S1: Intra-operative severe critical events by facility and anaesthesia provider

	Hospital level			Most senior anaesthetist			
	District	**Regional**	**Tertiary**	**Specialist**	**Non-specialist physician**	**Nurse**	**Non-physician**
Categories of anaesthetic severe critical incidents							
Any							
Any Airway/respiratory							
Any CVS							
Any Other							
Types of severe critical events by category							
Airway/respiratory							
Difficult BMV							
Difficult Intubation							
Failed Intubation							
Laryngospasm							
Bronchospasm							
Aspiration							
Severe Hypoxia							
CVS							
Bradycardia							
Cardiovascular instability							

Cardiac Arrest							
Metabolic							
Temp < 36							
Low Glucose							
Other							
Anaphylaxis							
Drug error							
Death							
Yes							
No							

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