An Evaluation of Severe Anesthetic-Related Critical Incidents and Risks From the South African Paediatric Surgical Outcomes Study: A 14-Day Prospective, Observational Cohort Study of Pediatric Surgical Patients

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Abstract

BACKGROUND: Severe anesthetic-related critical incident (SARCI) monitoring is an essential component of safe, quality anesthetic care. Predominantly retrospective data from low- and middle-income countries (LMICs) report higher incidence but similar types of SARCI compared to high-income countries (HIC). The aim of our study was to describe the baseline incidence of SARCI in a middle-income country (MIC) and to identify associated risk for SARCI. We hypothesized a higher incidence but similar types of SARCI and risks compared to HICs.

METHODS: We performed a 14-day, prospective multicenter observational cohort study of pediatric patients (aged <16 years) undergoing surgery in government-funded hospitals in South Africa, a MIC, to determine perioperative outcomes. This analysis described the incidence and types of SARCI and associated perioperative cardiac arrests (POCAs). We used multivariable logistic regression analysis to identify risk factors independently associated with SARCI, including 7 a priori variables and additional candidate variables based on their univariable performance.

RESULTS: Two thousand and twenty-four patients were recruited from May 22 to August 22, 2017, at 43 hospitals. The mean age was 5.9 years (±standard deviation 4.2). A majority of patients during this 14-day period were American Society of Anesthesiologists (ASA) physical status I (66.4%) or presenting for minor surgery (54.9%). A specialist anesthesiologist managed 59% of cases. These patients were found to be significantly younger ($P < .001$) and had higher ASA physical status ($P < .001$). A total of 426 SARCI was documented in 322 of 2024 patients, an overall incidence of 15.9% (95% confidence interval [CI], 14.4–17.6). The most common event was respiratory (214 of 426; 50.2%) with an incidence of 8.5% (95% CI, 7.4–9.8). Six children (0.3%; 95% CI, 0.1–0.6) had a POCA, of whom 4 died in hospital. Risks independently associated with a SARCI were age (adjusted odds ratio [aOR] = 0.95; CI, 0.92–0.98; $P = .004$), increasing ASA physical status (aOR = 1.85, 1,74, and 2.73 for ASA II, ASA III, and ASA IV–V physical status, respectively), urgent/emergent surgery (aOR = 1.35, 95% CI, 1.02–1.78; $P = .036$), preoperative respiratory infection (aOR = 2.47, 95% CI, 1.64–3.73; $P < .001$), chronic respiratory comorbidity (aOR = 1.75, 95% CI, 1.10–2.79; $P = .018$), severity of surgery (intermediate surgery aOR = 1.84, 95% CI, 1.39–2.45; $P < .001$), and level of hospital (first-level hospitals aOR = 2.81, 95% CI, 1.60–4.93; $P < .001$).

CONCLUSIONS: The incidence of SARCI in South Africa was 3 times greater than in HICs, and an associated POCA was 10 times more common. The risk factors associated with SARCI may assist with targeted interventions to improve safety and to triage children to the optimal level of care.

KEY POINTS

- **Question:** What is the incidence of pediatric severe anesthetic-related critical incidents (SARCIs) and associated perioperative cardiac arrest (POCA), and what are the independently associated risks for their occurrence?
- **Findings:** The incidence of SARCIs in South Africa is 3-fold higher and POCAs is 10-fold higher compared to high-income countries (HICs), with younger age, increasing American Society of Anesthesiologists (ASA) physical status, urgent/emergent surgery, acute preoperative respiratory infection, chronic respiratory

comorbidity, severity of surgery, and level of hospital identified as independent risks for a SARCI.

- **Meaning:** Preoperative identification of high-risk patients to allow triage to optimal levels of care as well as the need for targeted interventions to improve safety and increase capacity is essential.

GLOSSARY

ANOVA = analysis of variance; **aOR** = adjusted odds ratio; **ASA** = American Society of Anesthesiologists; **BMV** = bag mask ventilation; **CI** = confidence interval; **CRF** = case record form; **ENT** = otorhinolaryngology surgery; **ETT** = endotracheal tube; **GA** = general anesthetic; **HICs** = high-income countries; **HIV/AIDS** = human immunodeficiency virus/acquired immune deficiency syndrome; **In** = inhalational; **IRB** = Institutional Review Board; **IV** = intravenous; **LICs** = low-income countries; **LMICs** = low- and middle-income countries; **MICs** = middle-income countries; **MO** = medicalofficer; **OR** = odds ratio; **OSA** = obstructive sleep apnea; **PACU** = post-anesthesia care unit; **PHPT** = pulmonary hypertension; **POCA** = perioperative cardiac arrest; **RCIs** = respiratory critical incidents; **SAPSOS** = South African Paediatric Surgical Outcomes Study; **SARCIs** = severe anesthetic-related critical incidents; **SD** = standard deviation; **SGAD** = supraglottic airway device; **SSA** = Sub-Saharan Africa; **STROBE** = Strengthening the Reporting of Observational Studies in Epidemiology; **WHO-WFSA** = World Health Organization–World Federation of Societies of Anaesthesiologists

The study of severe anesthetic-related critical incidents (SARCIs) is important to understanding the safety and functioning of a perioperative service and health care system. The incidence of pediatric SARCI in high-income countries (HICs) varies from 2.4% to 5.2%.[1–5] Variability may reflect differences in care between institutions or differing study definitions of SARCIs, which may include less severe events.[3,6] Predominantly retrospective data from low- and middle-income countries (LMICs) report SARCI rates of up to 12% in middle-income countries (MICs),[4,7–12] and many-fold higher in certain low-income countries (LICs).[13–15]

Despite the differences in reported rates across country income categories, common themes emerge regarding types and risks for SARCIs. Perioperative respi-ratory critical incidents (RCIs) predominate,[1–5,9,11,15–17] while younger age, preexisting medical history (especially respiratory comorbidities), higher American Society of Anesthesiologists (ASA) physical status,[5] and emergency surgery are commonly identified risks for SARCIs.[3,5,16]

There are few prospective studies reporting pediatric perioperative outcomes and SARCIs from LMICs, including from Sub-Saharan Africa (SSA), an important cohort given that 42% of the SSA population are children <15 years.[18] The South African Paediatric Surgical Outcomes Study (SAPSOS) was undertaken to provide benchmark countrywide data on perioperative outcomes spanning all levels of care,[19] and included prospectively collected data on anesthetic-related events. The objectives of this substudy were to provide the baseline incidence of SARCIs, to describe the types of SARCIs including associated perioperative cardiac arrests (POCAs), to describe the relationship between age and SARCIs, and to identify risks independently associated with SARCIs in government-funded hospitals in a Sub-Saharan MICs. We expected the incidence of SARCIs to be higher than HICs but with a similar distribution of types and risks.

METHODS

Study Design, Setting, and Participants

Detailed methods for the 14-day multicentre, prospective, observational cohort SAPSOS study of pediatric patients undergoing surgery have previously been described.[19] Briefly, we aimed to compile a representative sample of patients in the country by inviting all South African universities and their affiliated government-funded hospitals to participate, each site selecting a single consecutive 14-day recruitment period between May and August 2017. Patients were followed from time of surgery to hospital discharge and censored at 30 days after study inclusion. The study was registered on ClinicalTrials.gov (NCT03367832). Primary ethics approval was obtained from the Institutional Review Board (IRB) of the University of KwaZulu-Natal Biomedical Research Ethics Committee (BE593/16). As required in South Africa, further IRB ethical approvals were obtained from each participating university and all hospital sites, and from the National Health Research Database (KZ_2016RP24_517). Five of 7 university IRBs waived the requirement for written informed consent. Two university IRBs required written informed consent from the parents (or legal guardian/surrogate) and assent from patients where possible. All such written informed consents were obtained from patients, including deferred written informed consent, which was allowed for patients who could not give consent before surgery.

Inclusion criteria were patients <16 years who underwent a general anesthetic (GA) or sedation for a surgical procedure. Exclusions were obstetric surgical procedures, where a GA was provided, but no procedure was performed (eg, noninterventional radiographic investigation); or where nonoperating room sedation for a procedure was provided. We aimed to include all consecutive eligible patients admitted to participating centers during the study period, thus addressing selection bias.

The primary objective of this substudy was to describe the incidence of SARCIs from government-funded hospitals in the prospectively collected SAPSOS anesthetic-related critical incident dataset. The secondary objectives were to describe the types of SARCIs, including associated POCAs, describe the relationship between age and SARCIs, and to identify risk factors independently associated with SARCIs.

Data Collection, Variables, and Outcomes

All perioperative data, including SARCIs, were collected prospectively and an anonymized electronic patient record was generated after hospital site investigators transcribed data from a case record form (CRF) onto a secure web-based application (Research Electronic Data Capture).[20] Data quality was improved by setting limits with investigator prompts for data entry. Study reporting was in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.[21]

The primary outcome variable for the current report was the incidence of SARCIs. "Incidence" in the study was calculated as the percentage of patients in whom one or more SARCIs was observed. SARCIs were defined as events where actual harm or physiological derangement occurred and excluded "near miss" events.[13] All study definitions, including SARCIs, were predefined and available to all investigators via the study website (www.SAPSOS.co.za) (Supplemental Digital Content 1, Supplemental Material S1, https://links.lww.com/AA/D713).

Variables describing the baseline characteristics cohort were collected and included age, sex, ASA physical status, and presence of acute and chronic comorbidities. The hospital level of care (first-level [district], second-level [regional], and third-level [tertiary and central] hospitals),[22] the type of operative procedure, severity of surgery (minor, intermediate, or major), urgency (routine or urgent/emergent), the most senior attending anesthesiologist (specialist, resident, or medical officer with >3 years of experience, medical officer with <3 years of experience), and use of a surgical checklist were also recorded.

Variables collected relating to anesthetic technique were daytime (07:00 to 17:00) or afterhours induction (17:01 to 06:59; or weekend from Friday 17:01 to Monday 06:59), type of anesthetic (GA or in-operating room sedation), induction technique (inhalational or intravenous), type of airway device used (facemask, supraglottic airway device [SGAD], and endotracheal tube [ETT]). Intraoperative SARCIs were recorded from a predefined list on the operative CRF (Supplemental Digital Content, Supplemental Material S2, https://links.lww.com/AA/D714) and included respiratory events (difficult bag mask ventilation, difficult intubation, failed intubation, laryngospasm, bronchospasm, aspiration, severe hypoxia), cardiovascular events (arrhythmia, bradycardia, severe hypotension), metabolic events (hypoglycemia, hyperthermia, hypothermia), and POCAs or death from induction of anesthesia to discharge from the postanesthesia care unit (PACU). Events in the PACU included emergence agitation and postoperative stridor. Entry of free text by investigators was possible for any "other" SARCIs, not on the predefined list. Text entries for "other" SARCIs were scrutinized and excluded from analysis if not deemed "severe" and the remainder were either reassigned to the predefined list of SARCIs as appropriate or assigned to a "miscellaneous" category for inclusion into the analysis (L.C. and A.M.T.).

Statistical Analysis

We reported mean and standard deviation (±SD) for age and then used a *t* test to test for difference in mean age between children with and without a SARCI. Analysis of variance (ANOVA) was used to compare the means (±SD) for patient age between different anesthesia providers and across levels of care. We used χ^2 test to test for differences in distribution of ASA physical status across hospital levels and between anesthesia providers.

To describe the cohort, variables relating to the surgery, hospital level, anesthesia provider, and anesthetic technique, we calculated the number and percentage of patients with and without SARCIs from the exposure variables listed above (in data collection, variables, and outcomes). Differences for categorical variables with more than 2 categories were compared using χ^2 or Fisher exact tests as appropriate. We then performed univariable analysis to study the association between each variable and our primary outcome (SARCI) and reported these as unadjusted odds ratios (OR) and 95% confidence interval (CI).

The incidence of composite SARCI was calculated and reported as number (percentage) and 95% CI. We also calculated (i) the proportion of each type of SARCI as a percentage of all SARCIs and (ii) their incidences which were reported as number (percentage) and 95% CI.

To assess the association between several exposure variables and development of a SARCI, we used logistic regression analysis and results are presented as unadjusted univariable and multivariable adjusted odds ratios (aOR) and 95% CIs. The study was expected to recruit 1750 patients and with a predicted SARCI event rate of 10%; we expected to be able to include up to 17 variables, not to violate the 10 events per variable rule of thumb.[23] A

decision was made to construct the model in 2 steps. Seven a priori candidate variables were included based on risk factors reported in the literature: age, ASA physical status, urgency of surgery, acute respiratory infection (a composite of upper and lower respiratory tract infection), chronic respiratory comorbidity (a composite of asthma/atopy, snoring, and obstructive sleep apnea), cardiac comorbidity (including pulmonary hypertension), and level of anesthesia provider. Six additional variables (severity of surgery, hospital level, cardiac surgery, neurosurgery, congenital syndromes, and neurological comorbidity) were included in the model based on their univariable association with SARCI and clinical utility. This would allow the exploration of candidate variables not initially anticipated. We aimed to construct an additional model for risk factors associated with RCI based on their univariable association and clinical utility while not violating the principle of 10 events per variable. Factors were tested for collinearity in both models and excluded if the variance inflation factor was >2.

As <5% of data were missing for the primary outcome, a complete case analysis was used.[24] Statistical analyses were performed using SPSS statistics version 26 (IBM). A *P* value of <.05 was considered statistically significant for all analyses.

RESULTS

Recruitment and Cohort Characteristics

Two thousand and twenty-four patients were recruited from 43 participating hospitals between May 22 and August 22, 2017 (Figure 1). The mean patient age was 5.9 (±4.2) including 59 (2.9%) neonates and 212 (10.5%) infants (29 days to 1 year old). Most patients had a low perioperative risk profile (1339 [66.4%] graded ASA physical status I) and presented for minor 1107 (54.9%) and elective 1311 (64.8%) surgery. There were 50 (2.5%) cardiac and 89 (4.4%) neurosurgical procedures performed. A comorbidity was present in 774 (38.2%) patients, the commonest being acute respiratory infection followed by chronic respiratory comorbidity, a congenital syndrome, and preoperative cardiac disease (Tables 1 and 2).

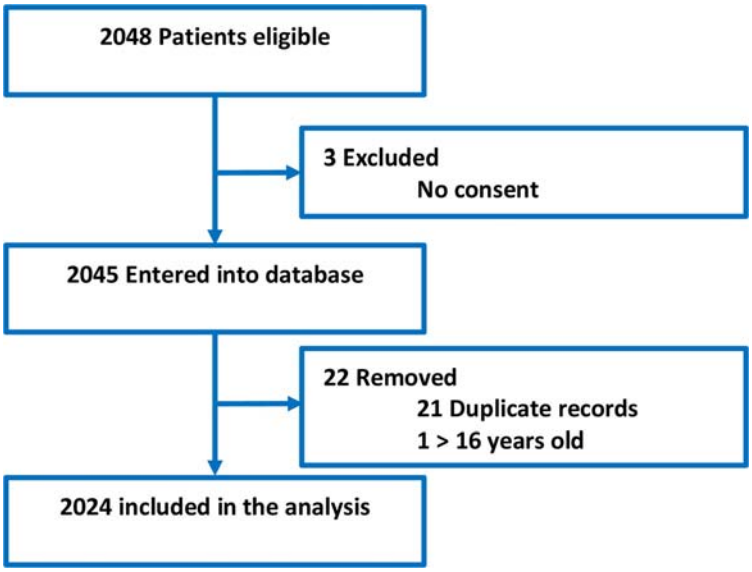

Figure 1.: Flow chart of patient recruitment and analysis.

Table 1. - Baseline Characteristics of the SAPSOS Anesthetic-Related Critical Incidents Cohort

Variable	All patients (N = 2024)	Patients with SARCI (n = 322)	Patients without SARCI (n = 1702)	Univariable odds ratio (95% CI)	*P* value
Age, y, mean (±SD)	5.86 (±4.20)	4.74 (±4.10)	6.08 (±4.19)	0.92 (0.89–0.95)	<.001
	n/N (%)	**n (n/N %)**	**n (n/N %)**		
Sex	N = 2015				.311
Male	1215 (60.3)	186 (15.3)	1029 (84.7)	Reference	
Female	800 (39.7)	136 (17.0)	664 (83.0)	1.13 (0.89–1.44)	.311
Age categories	N = 2024				<.001
Neonates (0–28 d)	58 (2.9)	20 (34.5)	38 (65.5)	4.41 (2.08–9.33)	<.001
29 d–1 y	227 (11.2)	59 (26.0)	168 (74.0)	2.94 (1.62–5.35)	<.001
2–5 y	832 (41.1)	130 (15.6)	702 (84.4)	1.55 (0.89–2.69)	.119
6–12 y	757 (37.4)	97 (12.8)	660 (87.2)	1.23 (0.70–2.16)	.468
13–16 y	150 (7.4)	16 (10.7)	134 (89.3)	Reference	
ASA physical status	N = 2017				<.001
I	1339 (66.4)	144 (10.8)	1195 (89.2)	Reference	
II	418 (20.7)	100 (23.9)	318 (76.1)	2.61 (1.96–3.46)	<.001
III	218 (10.8)	59 (27.1)	159 (72.9)	3.08 (2.18–4.35)	<.001
IV–V	42 (2.1)	19 (45.2)	23 (54.8)	6.85 (3.64–12.89)	<.001
Comorbidities	N = 2024				
Composite					
Any comorbidity	774 (38.2)	194 (25.1)	580 (74.9)	2.93 (2.30–3.74)	<.001
Acute respiratory infection	139 (6.9)	48 (34.5)	91 (65.5)	3.10 (2.14–4.50)	<.001
Chronic respiratory disease	121 (6.0)	32 (26.4)	89 (73.6)	2.00 (1.31–3.05)	.001
Preoperative cardiac disease	99 (4.9)	36 (36.4)	63 (63.6)	3.27 (2.13–5.03)	<.001
Individual					
Cancer	61 (3.0)	9 (14.8)	52 (85.2)	0.91 (0.44–1.87)	.802
Cerebral palsy	30 (1.5)	6 (20.0)	24 (80.0)	1.33 (0.54–3.27)	.538
Congenital syndrome	132 (6.5)	30 (22.7)	102 (77.3)	1.61 (1.05–2.47)	.028
Endocrine	9 (0.4)	2 (22.2)	7 (77.8)	1.51 (0.31–7.32)	.606
HIV/AIDS	51 (2.5)	7 (13.7)	44 (86.3)	0.84 (0.37–1.88)	.666
Neurological	63 (3.1)	19 (30.2)	44 (69.8)	2.36 (1.36–4.10)	.002
Muscle disorder	4 (0.2)	2 (50.0)	2 (50.0)	5.31 (0.75–37.85)	.096
Other	231 (11.4)	54 (23.4)	177 (76.6)	1.74 (1.25–2.42)	.001

Abbreviations: ASA, American Society of Anesthesiologists; CI, confidence interval; HIV/AIDS, human immunodeficiency virus/acquired immune deficiency syndrome; SAPSOS, South African Paediatric Surgical Outcomes Study; SARCI, severe anesthetic-related critical incident; SD, standard deviation.

Table 2. - Hospital Level, Surgical, and Anesthetic Information

Variable	All patients (N = 2024)	Patients with SARCI (n = 322)	Patients without SARCI (n = 1702)	Univariable odds ratio (95% CI)	*P* value
Hospital level	N = 2024				<.001
First-level (district)	154 (7.6)	28 (18.2)	126 (81.8)	Reference	
Second-level (regional)	424 (20.9)	38 (9.0)	386 (91.0)	0.43 (0.26–0.75)	.003
Third-level (tertiary/central)	1446 (71.4)	256 (17.7)	1190 (82.3)	0.88 (0.63–1.49)	.883
Urgency of surgery	N = 2024				.064
Elective	1311 (64.8)	194 (14.8)	1117 (85.2)	Reference	
Urgent/emergent	713 (35.2)	128 (18.0)	585 (82.0)	1.26 (0.99–1.61)	.064
Severity of surgery	N = 2017				<.001
Minor	1107 (54.9)	127 (11.5)	980 (88.5)	Reference	
Intermediate	759 (37.6)	150 (19.8)	609 (80.2)	1.90 (1.47–2.46)	<.001
Major	151 (7.5)	44 (29.1)	107 (70.9)	3.17 (2.13–4.72)	<.001
Type of surgery	N = 2016				
Cardiac	50 (2.5)	24 (48.0)	26 (52.0)	5.19 (2.94–9.16)	<.001
ENT	260 (12.8)	39 (15.0)	221 (85.0)	0.92 (0.64–1.33)	.668
Neurosurgery	89 (4.4)	23 (25.8)	66 (74.2)	1.91 (1.17–3.11)	.010
Surgical checklist used	N = 1993				
Surgical Checklist used	1415 (71.0)	212 (15.5)	1196 (84.5)	0.865 (0.67–1.12)	.271
Most senior anesthetist	N = 2017				<.001
Specialist	1190 (59.0)	231 (19.3)	964 (80.7)	Reference	
Resident/MO > 3 y	604 (29.8)	74 (12.3)	530 (87.7)	0.58 (0.44–0.77)	<.001
MO < 3 y	225 (11.1)	17 (7.6)	208 (92.4)	0.34 (0.20–0.57)	<.001
Anesthetic	N = 2018				
General (GA)	2008 (99.5)	321 (16.0)	1687 (84.0)	-	-
Sedation	10 (0.5)	0 (0.0)	10 (100.0)	-	-
Time of induction	N = 2013				.015
Daytime	1716 (85.2)	287 (16.7)	1429 (83.3)	Reference	
Afterhours	297 (14.8)	33 (11.1)	264 (88.9)	0.622 (0.42–0.91)	.015
Type of induction	N = 2017				.136
IV	345 (17.0)	55 (15.9)	290 (84.1)	Reference	
In	1545 (76.3)	240 (15.5)	1305 (84.5)	0.97 (0.71–1.33)	.850
Combined (IV + In)	117 (5.8)	26 (22.2)	91 (77.8)	1.51 (0.89–2.54)	.124
Sedation	10 (0.5)	0	10 (100%)	-	-
Definitive airway (GA)	N = 1965				<.001
Facemask	223 (11.3)	31 (13.9)	192 (86.1)	Reference	
SGAD	777 (39.5)	70 (9.0)	707 (91.0)	0.61 (0.39–0.96)	.034
ETT	951 (48.4)	213 (67.8)	738 (44.7)	1.79 (1.19–2.69)	.005
Other (eg, tracheostomy)	14 (0.7)	0 (0.0)	14 (100.0)	-	-

Abbreviations: CI, confidence interval; ENT, otorhinolaryngology surgery; ETT, endotracheal tube; GA, general anesthetic; In, inhalational; IV, intravenous; MO, medical officer; SARCI, severe anesthetic-related critical incident; SGAD, supraglottic airway device.

Most children (2008; 99.5%) underwent GA, 679 (33.5%) in combination with a regional block/local infiltration technique. An inhalational induction was used in 1545 (76.3%)

children, and they were younger compared to those who had an intravenous induction (mean age 5 years ± 3.5 vs 9.6 years ± 4.6; $P < .001$). Sevoflurane was used for most inhalational inductions, but halothane was used in 110 (6.6%) children of whom 87 of 110 (79.1%) were at first-level hospitals. The most common device for airway management was an ETT (951; 48.4%), followed by a SGAD (777; 39.5%).

Third-level hospitals managed 1446 (71.5%) of the SAPSOS cohort and while there was no difference in mean age of patients ($P = .300$) between the 3 different levels of care, there was a significant difference in ASA physical status distribution ($P < .001$). Sicker children (as graded by ASA physical status) were managed at progressively higher levels of care; first-level hospitals managed 143 (92.9%) ASA I, and no ASA III–V physical status patients. In comparison, third-level hospitals managed 251 of 260 (96.5%) of the ASA III–V physical status patients, comprising 17.4% of third-level hospitals' case load. A specialist anesthesiologist was the primary caregiver in 1190 (59%) cases. Compared to other anesthesia providers, specialists managed younger ($P < .001$) and sicker patients ($P < .001$); 81% of ASA III–V physical status patients were managed by specialists (Supplemental Digital Content 3, Supplemental Material S3, Table 1 and Figures 1 and 2, https://links.lww.com/AA/D715).

Incidence and Types of SARCI

A total of 426 SARCI were documented in 322 patients, an overall incidence of 15.9% (95% CI, 14.4–17.6) (Table 3), with 246 children having 1 event, and 76 children having between 2 and 6 events. Most events occurred during the intraoperative phase (incidence 14.2%; 95% CI, 12.8–15.8). Intra and postoperative RCI comprised 50.2% of all events recorded with an overall incidence of 8.5% (95% CI, 7.4–9.8). Metabolic critical incidents were the second most reported incidents (4.5%; 95% CI, 3.6–5.4) followed by cardiovascular incidents (2.6%; 95% CI, 1.9–3.2).

Table 3. - Incidence and Types of SARCI

Type of SARCI	No. of events (% of total no. of events)	Incidence (no. of patients with SARCI/no. of patients)
	n (% of 426)	% (95% CI)
Overall	426 (100)	15.9 (14.4–17.6)
Intraoperative	377 (88.49)	14.2 (12.8–15.8)
Postoperative	42 (9.86)	1.6 (1.1–2.2)
Respiratory	214 (50.2)	8.5 (7.4–9.8)
Difficult BMV	12 (2.82)	0.6 (0.3–1.0)
Difficult intubation	38 (8.92)	1.9 (1.4–2.5)
Failed intubation	5 (1.17)	0.2 (0.1–0.5)
Other intraoperative airway/respiratory	12 (2.82)	0.6 (0.2–0.9)
Laryngospasm	71 (16.67)	3.5 (2.8–4.4)
Bronchospasm	20 (4.69)	1.0 (0.6–1.5)
Aspiration	3 (0.70)	0.1 (0.0–0.4)
Severe hypoxia	44 (10.33)	2.2 (1.6–2.9)
Postoperative stridor	7 (1.64)	0.3 (0.2–0.7)
Other postoperative airway/respiratory	2 (0.46)	0.1 (0.0–0.2)
Metabolic	93 (21.83)	4.5 (3.6–5.4)
Low glucose	16 (3.76)	0.8 (0.5–1.3)
Temp > 38 °C	19 (4.46)	0.9 (0.6–1.4)
Temp < 36 °C	58 (13.62)	2.9 (2.2–3.7)
Cardiovascular	59 (13.85)	2.6 (1.9–3.2)
Arrhythmia	9 (2.11)	0.4 (0.2–0.8)
Bradycardia	16 (3.76)	0.8 (0.5–1.3)
Severe hypotension	24 (5.63)	1.2 (0.8–1.7)
Other cardiovascular	4 (0.94)	0.2 (0.1–0.5)
Cardiac arrest	6 (1.41)	0.3 (0.1–0.6)
Miscellaneous	26 (6.10)	1.3 (0.8–1.8)
Emergence agitation	33 (7.75)	1.6 (1.1–2.2)
Death[a]	1 (0.23)	0.0 (0.0–0.2)

Abbreviations: BMV, bag mask ventilation; CI, confidence interval; SARCI, severe anesthetic-related critical incident.

[a]From induction of anesthesia to discharge from the postanesthesia care unit.

The most common RCIs were laryngospasm (3.5%; 95% CI, 2.8–4.4) and severe hypoxia (2.2%; 95% CI, 1.6–2.9). A difficult intubation was encountered in 38 patients (1.9%; 95% CI, 1.4–2.5) and there were 5 failed intubations, one of which resulted in the patient dying before surgery commencing. The majority of metabolic critical incidents were due to low temperature (only 5 of 58 following cardiac surgery). Emergence agitation occurred in 1.6% (95% CI, 1.1–2.3) of patients (Table 3).

Six patients (0.3%; 95% CI, 0.1–0.6) had a POCA. All POCAs occurred at third-level (central) hospitals and were managed by a specialist anesthesiologist. Patients were ≤4 months old, 5 of 6 had significant comorbidities and had multiple SARCIs. Four of the 6 patients (66.7%) died before hospital discharge (1 on the operating table due to failed intubation; Supplemental Digital Content 3, Supplemental Material S3, Table 2, https://links.lww.com/AA/D715).

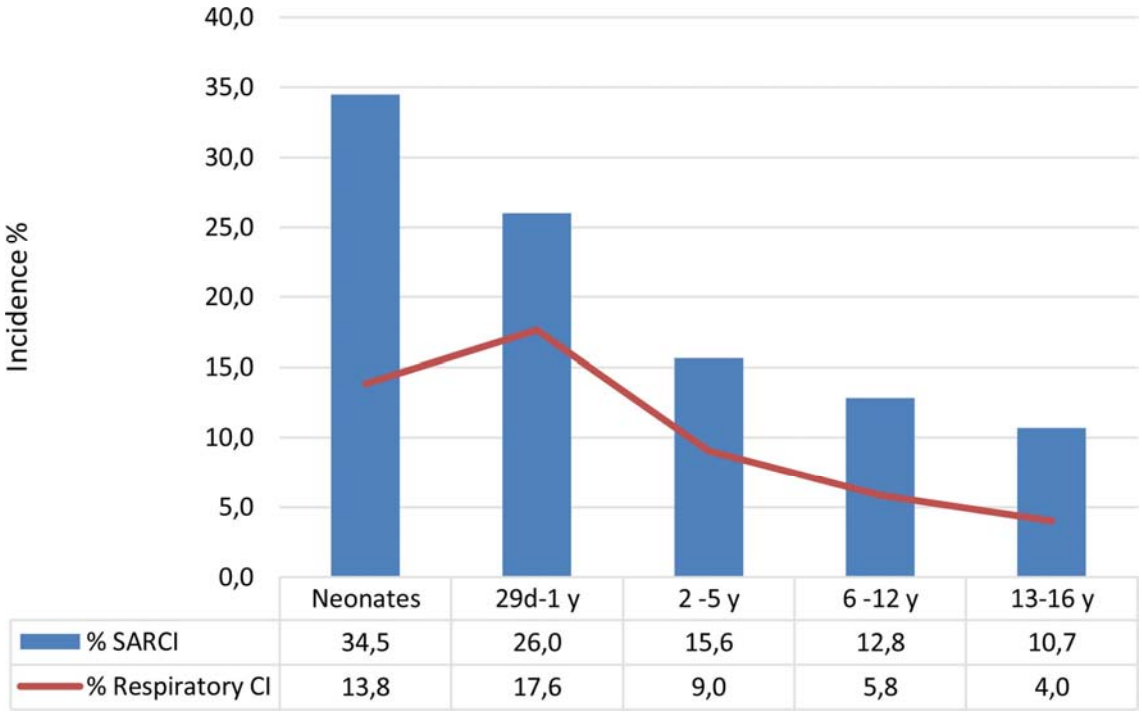

Figure 2.: Incidence of SARCI, by age group. CI indicates critical incident; SARCI, severe anesthetic-related critical incident.

Overall, children with a SARCI were significantly younger than those without a SARCI (mean age 4.7 years [±4.1] vs 6.1 [±4.2]; $P < .001$). Figure 2 depicts the incidence of SARCIs and RCIs by age categories. The incidence of SARCIs in neonates was 34.5% (95% CI, 23.2–47.2) and they had 4-fold increased odds for SARCIs (OR = 4.4; 95% CI, 2.1–9.3; $P < .001$). Infants (29 days to 1 year) had an incidence of SARCIs of 26.0% (95% CI, 20.6–32.0), and the odds were increased 3-fold for SARCIs (OR = 2.9; 95% CI, 1.6–5.3; $P < .001$).

Factors Associated With SARCI

To construct the multivariable model for SARCIs, 7 a priori variables and the following 6 additional variables were entered into the model based on univariable association and clinical utility; severity of surgery, hospital level (second-level hospitals entered as reference category), cardiac surgery, neurosurgery, congenital syndromes; and neurological comorbidity (Table 4). Multivariable analysis identified age, ASA physical status, urgent/emergent surgery, preoperative respiratory infection, chronic respiratory comorbidity, severity of surgery, and level of hospital as risks for occurrence of SARCIs.

Table 4. - Multivariable Analysis of Factors Associated With Critical Incidents

Variable	n (%) (N = 2024)	Univariable analysis		Multivariable analysis	
		OR (95% CI)	*P* value	aOR (95% CI)	*P* value
Factors for severe anesthetic-related critical incidents					
Age	2024 (100)	0.92 (0.89–0.95)	<.001	0.95 (0.92–0.98)	.004
ASA physical status	N = 2017				.001
I	1339 (66.4)	Reference		Reference	
II	418 (20.7)	2.61 (1.96–3.46)	<.001	1.85 (1.33–2.57)	<.001
III	218 (10.8)	3.08 (2.18–4.35)	<.001	1.74 (1.13–2.69)	.012
IV–V	42 (2.1)	6.85 (3.64–12.89)	<.001	2.73 (1.29–5.76)	.009
Urgency of surgery	N = 2024				.036
Routine	1311 (64.8)	Reference		Reference	
Urgent/emergent	713 (35.2)	1.26 (0.99–1.61)	.064	1.35 (1.02–1.78)	.036
Acute respiratory infection	139 (6.9)	3.10 (2.14–4.50)	<.001	2.47 (1.64–3.73)	<.001
Chronic respiratory disease	121 (6.0)	2.00 (1.31–3.05)	.001	1.75 (1.10–2.79)	.018
Preoperative cardiac disease/PHPT	101 (5.0)	3.32 (2.17–5.07)	<.001	1.08 (0.55–2.12)	.819
Most senior anesthetist	N = 2017				.089
Specialist	1195 (59.0)	Reference		Reference	
Resident/MO > 3 y	604 (29.8)	0.58 (0.44–0.77)	<.001	0.79 (0.58–1.08)	.145
MO < 3 y	225 (11.1)	0.34 (0.20–0.57)	<.001	0.58 (0.36–1.01)	.053
Severity of surgery	N = 2017				<.001
Minor	1107 (54.9)	Reference		Reference	
Intermediate	759 (37.6)	1.90 (1.47–2.46)	<.001	1.84 (1.39–2.45)	<.001
Major	151 (7.5)	3.17 (2.13–4.72)	<.001	1.5 (0.88–2.57)	.138
Hospital level	N = 2024				.001
Second-level (district)	424 (20.9)	Reference		Reference	
First-level (regional)	154 (7.6)	2.26 (1.33–3.83)	.003	2.81 (1.60–4.93)	<.001
Third-level (tertiary/central)	1446 (71.4)	2.19 (1.53–3.13)	<.001	1.48 (1.00–2.19)	.051
Type of surgery	N = 2016				
Cardiac	50 (2.5)	5.19 (2.94–9.16)	<.001	2.34 (0.92–5.92)	.074
Neurosurgery	89 (4.4)	1.91 (1.17–3.11)	.010	0.80 (0.42–1.56)	.516
Comorbidities	N = 2024				
Congenital syndrome	132 (6.5)	1.61 (1.05–2.47)	.028	1.07 (0.66–1.72)	.788
Neurological	63 (3.1)	2.36 (1.36–4.10)	.002	1.85 (0.90–3.79)	.093
Factors for respiratory critical incidents					
Age	2024 (100)	0.881 (0.84–0.92)	<.001	0.911 (0.8–0.96)	<.001
ASA physical status	N = 2017				.001
I	1339 (66.4)	Reference		Reference	

II	418 (20.7)	2.74 (1.90–3.95)	<.001	2.10 (1.41–3.09)	<.001
III	218 (10.8)	2.98 (1.92–4.65)	<.001	1.79 (1.09–2.92)	.021
IV–V	42 (2.1)	6.15 (2.97–12.73)	<.001	2.76 (1.25–6.08)	.012
Comorbidities	N = 2024				
Acute respiratory infection	139 (6.9)	4.07 (2.66–6.21)	<.001	2.98 (1.88–4.74)	<.001
Chronic respiratory disease	121 (6.0)	1.83 (1.07–3.14)	.028	1.19 (0.64–2.20)	.589
Induction technique	N = 2003				.929
Intravenous	345 (17.0)	Reference		Reference	
Inhalational	1545 (76.3)	1.01 (0.71–1.75)	.067	0.93 (0.56–1.53)	.773
Combined	117 (5.8)	2.53 (1.35–4.73)	.004	1.92 (0.56–1.53)	.063
Airway device	N = 1965				.003
Mask	218 (11.1)	Reference		Reference	
SGA versus mask	776 (39.6)	1.30 (0.612–2.70)	.499	1.90 (0.88–4.07)	.101
Tracheal tube versus mask	951 (48.5)	3.40 (1.70–6.81)	.001	3.19 (1.55–6.57)	.002
Other versus mask	14 (0.7)	-	-	-	-

Abbreviations: aOR, adjusted odds ratio; ASA, American Society of Anesthesiologists; CI, confidence interval; MO, medical officer; OR, odds ratio; OSA, obstructive sleep apnea; PHPT, pulmonary hypertension; SGA, supraglottic airway device.

We were able to construct a model for risk factors associated with RCI by including 6 variables (age, ASA physical status, preoperative respiratory infection, chronic respiratory comorbidity, induction technique, and airway device used), based on their univariable association (while not violating the principle of 10 events per variable). RCI were independently associated with age, ASA physical status, preoperative respiratory infection, and use of an ETT.

DISCUSSION

The principal findings of this study are an incidence of SARCIs of 15.9% (95% CI, 14.4–17.6), with over half being RCI. The incidence of POCAs was 0.3% (95% CI, 0.1–0.6). Younger age, ASA physical status ≥II, urgent/emergent surgery, preoperative respiratory infection, chronic respiratory comorbidity, severity of surgery, and hospital level were independently associated with SARCIs.

While we describe similar patterns of, and risks for, SARCIs to those reported from both HICs and LMICs, this study has identified severity of surgery and hospital level as important additional risk factors for SARCIs. These factors have both clinical and health system implications for planning surgical health services and increasing safety and capacity in LMICs. We highlight that even low-risk children are at increased risk for a SARCI in LMICs.

The finding that the overall incidence of SARCIs in our study was 3 times higher than in HICs and that respiratory events predominate was not unexpected.[1–5,9,11,15–17,25,26] Similar to other studies, we identified 4 independent risks associated with RCIs, those being younger age group, increasing ASA physical status, preoperative respiratory infection, and airway

management with an ETT.[5,27] Despite high use of inhalational inductions in our study compared to von Ungern-Sternberg et al[27] (76% vs 39%), we did not identify inhalational induction, or otorhinolaryngology surgery (ENT) as independent risks associated with RCI.[2,28] Habre et al[5] suggested that children <3 to 3.5 years old should be managed by tertiary care providers or anesthesiologists with a pediatric interest or specialization. Specialists did manage younger and sicker children, but our study did not corroborate the experience of the anesthesiologist,[5] nor care provided by specialist anesthesiologists as protective.[27,28]

POCA was equivalent to 30 per 10,000 anesthetics in our study, 10-fold that of HICs with similar case mix, and mortality was at least doubled compared to HICs.[3,5] These findings are on par with other MICs.[25,29] LICs and those with low human-development index report POCA rates of 150 per 10,000 anesthetics,[14,30] with perioperative mortality up to 100-fold higher than in HIC,[31] highlighting the burden of POCAs in anesthetized children in LMIC. Reasons for higher rates and poorer outcomes of POCAs in LMICs are multifactorial,[14,25,29–33] and were not explored in our study as the number of POCAs was too small to identify associations. All POCA cases were managed by specialists and performed during normal hours and although young age and higher ASA physical status were common factors, half were elective cases, raising potential questions about case selection.

The SAPSOS study estimated that the number of pediatric surgical cases performed in South Africa achieved between one-third and one fifth of its potential surgical need.[19,34] Third-level hospitals currently perform 3 quarters of all pediatric surgeries and manage younger and sicker children. Although our study did not investigate delays in access or escalation to higher levels of care, the findings suggest that those children that have reached care, are generally managed at an appropriate hospital level and by a specialist anesthesiologist. To increase surgical capacity and access, ASA physical status I and II children coming for minor surgery should be able to be safely managed at first- and second-level hospitals.[35] This could help to unload the overburdened higher-level facilities. Although not focusing on anesthetic morbidity, Newton et al[31] identified increased perioperative mortality in first-level hospitals in Kenya compared to higher levels of care. The SAPSOS study identified a near 3-fold increase in anesthesia morbidity at first-level hospitals, compared to second-level hospitals, despite a very low-risk profile of patients. Safe expansion of service to these lower levels of care therefore requires identification of risk factors for SARCIs.

Our study has confirmed previously identified risks (younger age especially neonates and infants, preexisting respiratory comorbidities, higher ASA physical status,[5] and emergency surgery[3,5,16]). Although the utility of ASA physical status has been questioned in children,[36] increasing ASA physical status risk categories have consistently been identified as the increasing odds for SARCIs.[3–5,9,10,14] In our study, risk was almost doubled for ASA physical status II and III patients compared to ASA physical status I patients and increased 3-fold in ASA physical status IV to V patients. Increased risk in low-risk patients (ASA physical status II), and the identification of severity of surgery and first-level hospitals as independent risks for SARCIs suggest that currently no more than minor surgery in well children should occur at the lower levels of care. Follow-up studies should identify limitations at these hospitals to identify potential shortcomings in training and resources, for example, availability of medication, equipment, monitoring, training, and appropriate supervision.

Strengths

The study's simple design including using a predefined list of severe anesthesia-related critical incidents ensured high levels of participation. Compared to predominantly retrospective data from LMICs, the incidence of SARCIs in our study would therefore be closer to the true incidence.

Limitations

Errors in the true incidence of SARCIs or risks for SARCIs may have occurred due to study design, definitions, and analysis. Due to the pragmatic nature of the study, it was decided to collect only a core set of critical incidents, which may have underestimated the true incidence of SARCIs. Overestimation or underestimation may also have occurred as some of the SARCI definitions required subjective assessment.

As multiple associations for SARCIs were studies without multiplicity adjustments, the chance of type I errors may have increased. The use of logistic regression analysis to identify risks for SARCIs (as a composite end point of binary events) was chosen to allow comparison of our results with similar studies performed in HICs. Mascha and Sessler[37] suggests that this "all or none" approach to SARCIs has limitations as higher-frequency or clinically unimportant components may be overweighted. A potential solution for future studies should consider using a multivariate approach (ie, multiple outcomes per patient) to improve the clinical utility and interpretation of results.[37]

Heterogeneity in reported rates of SARCIs are partly due to different definitions and timing of adverse events,[1,3,16] but may also reflect differential training, resources, and infrastructure to support specialized pediatric surgical and anesthesia care.[6] We did not explore the specific pediatric experience nor training of the anesthesiologists providing care, which may explain the findings that the experience of the anesthesiologist or care provided by a specialist were not protective. There is no recognized pediatric anesthesia subspeciality in South Africa, and only 2 of the 43 participating hospitals provided dedicated pediatric care. Most anesthesiologists were thus working in a mixed adult and pediatric practice, as is common in LMICs.

Reasons for the higher incidence of SARCIs were not explored in our study but we would recommend follow-up studies to identify factors suggested from the literature including (i) lack of specific pediatric anesthesia experience, training, and care in nonspecialized hospitals[33,38]; (ii) resource limitations[38] including inadequate workforce, equipment, monitoring, or medication (eg, continued use of halothane in first-level hospitals; lack of forced air warmers or adequate operating room temperature control leading to the high incidence of hypothermia identified)[4]; (iii) system factors (eg, limited or delayed access to an appropriate level of care).[39]

Generalizability

As there are limited studies on risks in LMICs, we chose a priori variables as identified in the literature. However, we were concerned that SARCIs may have additional or different risks in LMICs not yet identified, thus decided to include other variables with a univariable association with SARCIs. Our study may enable future researchers to add the identified

associations with SARCIs in this study as a priori variables for consideration in LMIC research.

We estimated our sample represented more than half the potential pediatric surgical population in South Africa and thus believe our study is generalizable to other government-funded hospitals in South Africa, and potentially more broadly to other MICs due to the wide distribution of hospitals geographically and by levels of care. We did not include privately funded hospitals and are unable to generalize outcomes to this sector. Future studies should include this sector which provides health care to approximately 16% of the population.

Recommendations for future planning of pediatric surgical and anesthesiology services should include (1) Increased investment in resources at first-level hospitals—improved education and training of anesthesia providers, adoption of the World Health Organization–World Federation of Societies of Anaesthesiologists (WHO-WFSA) International Standards for a Safe Practice of Anesthesia,[40] provision of appropriate equipment and monitors, and a reliable source of anesthetic medications. Age limits should be considered, for example, neonates and infants should not be managed at first-level hospitals. (2) Improved capacity at second-level level hospitals to increase the number of surgeries available for low-risk patients. (3) Continued triage of high-risk children to third-level hospitals.

CONCLUSIONS

This prospective, observational study in South African pediatric surgical patients reports that 1 in 6 patients suffer a SARCI, a rate 3 times higher than in HICs. Furthermore, 1 in 330 had an associated POCA, a rate 10-fold that of HICs. Children at risk for severe anesthesia-related critical incidents can be identified preoperatively (younger age, ASA physical status, urgent/emergent surgery, preoperative respiratory infection, chronic respiratory comorbidity, severity of surgery, and hospital level) and should be managed at an appropriate level of care. Ongoing critical incident monitoring will improve the quality and safety of anesthesia. It may identify areas requiring training, improved resource allocation including workforce, equipment, monitoring and medications, and capacity building.

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