

## Original Article

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## Burden and outcome of neonatal surgical conditions in Nigeria: A countrywide multicenter cohort study

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## KEYWORDS

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Complications,  
Mortality,  
Predictors,  
Quality improvement

## ABSTRACT

**Background:** Despite a decreasing global neonatal mortality, the rate in sub-Saharan Africa is still high. The contribution and the burden of surgical illness to this high mortality rate have not been fully ascertained. This study is performed to determine the overall and disease-specific mortality and morbidity rates following neonatal surgeries; and the pre, intra, and post-operative factors affecting these outcomes.

**Methods:** This was a prospective observational cohort study; a country-wide, multi-center observational study of neonatal surgeries in 17 tertiary hospitals in Nigeria. The participants were 304 neonates that had surgery within 28 days of life. The primary outcome measure was 30-day postoperative mortality and the secondary outcome measure was 30-day postoperative complication rates.

**Results:** There were 200 (65.8%) boys and 104 (34.2%) girls, aged 1-28 days (mean of 12.1 ± 10.1 days) and 99(31.6%) were preterm. Sepsis was the most frequent major postoperative complication occurring in 97(32%) neonates. Others were surgical site infection (88, 29.2%) and malnutrition (76, 25.2%). Mortality occurred in 81 (26.6%) neonates. Case-specific mortalities were: gastroschisis (14, 58.3%), esophageal atresia (13, 56.5%) and intestinal atresia (25, 37.2%). Complications significantly correlated with 30-day mortality (p <0.05). The major risk predictors of mortality were apnea (OR=10.8), severe malnutrition (OR =6.9), sepsis (OR =7.1), deep surgical site infection (OR=3.5), and re-operation (OR=2.9).

**Conclusion:** Neonatal surgical mortality is high at 26.2%. Significant mortality risk factors include prematurity, apnea, malnutrition, and sepsis

## INTRODUCTION

Sustainable Development Goal (SDG) number 3 sets out among other things to decrease neonatal mortality to as low as 12 per 1000 live births by 2030. [1] It is estimated that at the current trend, more than 60 countries will miss the SDG target by 2030. [2] Most sub-Sahara African countries belong to this category. There is thus an urgent need to improve the accessibility and quality of surgical care.

Despite a decreasing global Neonatal Mortality Rate (NMR), there is still a huge disparity in sub-Saharan Africa with a slower decline when compared to the global statistics. Congenital anomalies which form the bulk of most neonatal surgical cases globally constitute 10.6% of NMR. Congenital anomaly is currently the 5th leading cause of neonatal mortality worldwide and is likely to continue rising in profile. [4] Low- and

Middle-Income Countries (LMICs) may have high mortality from surgical deaths given the high incidence of congenital anomalies and the prevalent high underreporting rate. [4]

With 359,081 neonates dying in Nigeria in 2019, NMR in Nigeria is among the highest globally at 47.7 per 1000 population. [5]

Nigeria as classified by the World Bank based on Gross National Income is a lower-middle-income country. The practice of neonatal surgery in Nigeria as in most LMICs is still faced with multiple challenges. Although some isolated improvements have been made in some centers, recent outcome reports still have mortality rates of up to 50%, with a range across institutions as 12% to 62%. [6-10] Not much has changed regarding the challenges militating against good outcomes. [11] The contribution of surgical ill-

ness to this high mortality rate has not been fully ascertained.

There is thus a need to determine the actual burden and outcome of neonatal surgical conditions in Nigeria to plan and implement strategies to improve the outcomes. The objectives of this study are first, to determine the overall and disease-specific mortality and morbidity rates following neonatal surgery in Nigeria. Secondly, to study the pre-, intra-, and postoperative factors affecting the outcome of neonatal surgery. These will provide a baseline for planning the implementation of mitigation strategies.

## METHODS

### Study Design and Setting

This was a collaborative prospective cohort study conducted from May 2018 -December 2019 involving twenty-eight investigators from 17 tertiary hospitals.

### Data Collection Tool

The study tool was adapted from the American College of Surgeons National Surgical Quality Improvement Programme Paediatric (ACS NSQIP-P). [12]

Information from enrolled participants on demography, presentation, diagnosis, treatment, outcome, and factors affecting outcome was collated using a customized web-based data capture tool.

Patients were monitored and data was collected up to 30 days post-surgery.

Collaborators were trained virtually on the study protocol and study progress was regularly monitored by the principal investigator.

### Inclusion and Exclusion Criteria

Consecutive neonates from the selected centers aged 0-28 days at the time of presentation, who had a surgical disease and surgical intervention in the neonatal period were enrolled in the study and were followed up for 30 days after surgery.

Circumcision, orthopedic, plastic, neurosurgical, or cardiac surgeries were excluded.

### Sample Size and Sampling

Most pediatric centers in Nigeria perform on average, about 50 general neonatal surgical operations in a year. [6,9,13] Although 800 subjects were the total predicted population, the minimum sample size at 95% confidence level and 5% margin of error was 260. However, we enrolled 304 patients for the study. [14]

Seventeen centers were selected by purposive sampling method based on the frequency of neonatal surgeries and evenly distributed across the six regions. Each included hospital has at least one trained pediatric surgeon.

### Data Capture Monitoring and Validation

A two-week pilot study was conducted to test and validate the study tool and the customized web-based data capture before the commencement of the study and necessary adjustments made. Monthly interactions with study centers via phone calls and media messaging were used to monitor compliance and ensure data integrity.

### Ethics

Ethical approval for the study was obtained from the Health Research and Ethics Committee (HREC) of Nnamdi Azikiwe University Teaching Hospital (NAUTH/CS/66/VOL 10/208/2017/106).

Informed consent was obtained from the participants. Being an observational study with little or no influence on the choice of treatment, no parent declined consent or withdrew from the study.

### Data Analysis

Data were analyzed using STATA® Statistics/Data Analysis version 16.0 (StataCorp LLC Texas USA). Tables and charts were used to present the data. A Chi-square test was done to test associations between variables. Logistic regression analysis was done to assess the risks of mortality. The level of statistical significance was set at  $p \leq 0.05$ .

### Outcome Measures

The primary outcome measure was 30-day postoperative mortality. Secondary outcome measures were 30-day postoperative complication rates and adverse perioperative events.

## RESULTS

### Demographics

There were 104 (34.2%) girls and 200 (65.8%) boys aged 0-28 days (mean  $12.1 \pm 10.1$  days). While 99(31.6%) were born preterm; 18(5.0%) were extremely preterm (Table 1). Only 72(23.7 %) of the infants lived within 30 km distance from the hospital, 172(56.6%) had to travel more than 50 km, and 18(5.9%) more than 100 km to access care. The most commonplace delivery of the neonates was in private non-governmental hospitals (92, 30.3%) followed by unsupervised delivery at home in 61 (20.0%). One hundred and forty-five (47.2%) infants arrived at the hospital with their caregivers using public transportation while 11(3.6%) arrived with an ambulance service. Surgical neonates were managed mostly in Special Care Baby Units or High Dependency Units.

### Time of presentation

The duration of presentation from the onset of symptoms ranged from 1 hour to 26 days (mean  $34.7 \pm 21.1$  hours). While 205(68.4%) presented early, 99

(31.6%) infants presented for surgical care more than 48 hours after the onset of symptoms. There were multiple reasons for presenting late but the most common reason was late referral from the initial hospital of care 28(38%) (Figure 1).

**Diagnosis and surgical procedures**

Anorectal malformation in 69 (22.7%) neonates was the most common diagnosis followed by intestinal (duodenal, jejunoileal, and colonic) atresia in 67 (22.0%), omphalocele in 27 (8.9%), gastroschisis in 24 (7.9%), and esophageal atresia in 23 (7.6%) neonates. The most common procedures were intestinal resection and anastomosis in 90 (29.6%), colostomy in 64 (21.1%), primary repair of anterior abdominal wall defect in 39 (12.7%), and silo or modified silo application in 21 (6.9%) neonates (Table 2). Modified silo implies the use of materials like urine bags, female condoms, and intravenous infusion bags to achieve temporary improvised housing for the intestine. The total number of days on admission was 1 to 81 days (Mean = 34.7 ±21.1 days).

One hundred and twenty (39.7%) neonates had a need for total parenteral nutrition (TPN). However, TPN could not be administered in 74 (61.7%) of them. The reasons were due to non-availability (29, 39.2%), non-affordability (5, 6.8%) or both (40, 54.0%).

**Mortality**

There were a total of 81 deaths giving a mortality rate of 26.6%. The fatality rate was highest among those who had a reduction of gastroschisis (15/21, 71.4%), intestinal resection and anastomoses for atresias, and gut perforations (34/90, 37.8%).

**Complications and Determinants of Mortality**

Postoperative Complications: The most common postoperative complications included sepsis (97, 32.0%), surgical site infections (88, 28.7%), malnutrition (76, 25.2%), hypothermia (59, 19.5%) and apnea (51, 17.0%) (Table 3).

Sepsis occurred most frequently in neonates that had intestinal resection and anastomosis (35/90, 38.0%), colostomy (17/45, 37.8%), and modified silo reduction (12/21, 57.1%). Surgical wound classification type did not correlate with the development of sepsis (p=0.370). Fifty-three (54.6%) of the neonates that developed sepsis died (p = 0.001) Again, delayed presentation did not have a statistically significant impact on 30-day mortality (p=0.075) nor on serious complications like sepsis (p=0.131).

Of the surgical site infections (SSIs), 66 (21.9%) were superficial, 15 (5.0%) were deep and 7(2.3%) were

organ/ space infections. Mortality was 100% among those that had organ /space infection (p = 0.001), while 8(53.3%) of those with deep SSIs died (p = 0.025).

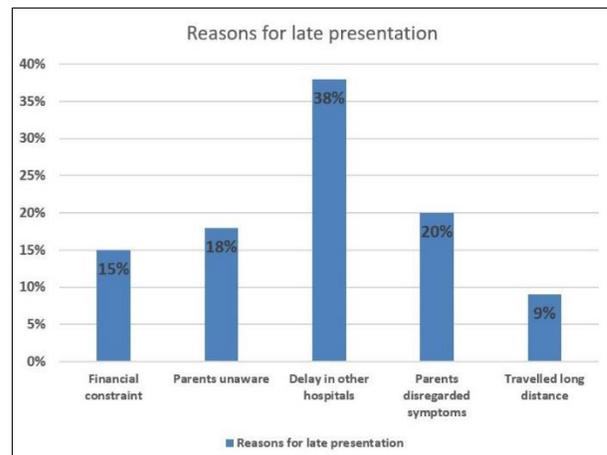


Figure 1: Reasons for late presentation

Table 1: Perinatal characteristics and frequencies

Variable	Frequency	Percentage
<b>Birth-weight (g)</b>		
≤1000	2	0.7
>1000 ≤ 1500	0	0.0
>1500≤2500	1	0.3
>2500	315	99.0
<b>Gestational age(weeks)</b>		
<28 (extremely preterm)	18	5.0
>28≤32 (very preterm)	11	3.6
>32≤37 (late preterm)	70	23.0
>37 (term)	206	67.5
<b>Mode of delivery</b>		
Vaginal delivery	245	80.6
Elective caesarean operation	12	4.0
Emergency caesarean operation	47	15.5
<b>Place of delivery</b>		
Traditional birth attendants(TBA)	15	4.9
Home	61	20.0
Maternity primary health centre	55	18.1
Private hospital	92	30.3
General hospital	49	16.1
Tertiary hospital	32	10.5
<b>Distance from residence to hospital (km)</b>		
<10	34	11.2
11 – 30	38	12.5
31 -50	60	19.7
51 – 70	52	17.1
71 – 100	102	33.6
>100	18	5.9
<b>Mode of transportation to the hospital</b>		
Carried/backed	25	8.2
Motorcycle	6	2.0
Private car	110	36.2
Public transport	145	47.2
Ambulance	11	3.6
Born at the facility	7	2.3

Table 2: showing the common conditions and surgical procedures done with case specific mortalities

Diagnosis/Surgical Procedures	Frequency	%	No of mortality	Disease / procedure specific mortality rate (%)
<b>Most common disease conditions</b>				
Anorectal malformation	69	22.7	6	8.7
Intestinal atresias	<b>67</b>	<b>22.0</b>		
Jejunioileal atresia	35	11.5	16	45.7
Duodenal atresia	27	8.9	7	25.9
Colonic atresia	5	1.6	2	40.0
Omphalocele	27	8.9	10	37.0
Gastroschisis	24	7.9	14	58.3
Oesophageal atresia	23	7.6	13	56.5
Malrotation syndrome	13	4.3	2	15.4
Necrotising enterocolitis	11	3.6	5	45.5
Posterior urethral valve	11	3.6	0	0.0
Gastrointestinal perforation	4	1.3	2	50.0
Bladder extrophy	7	2.2	0	0.0
Obstructed inguinal hernia	4	3.4	0	0.0
Sacrococcygeal tumour	3	1.0	0	0.0
Infantile hypertrophic pyloric stenosis	3	1.0	1	33.3
Multiple abscesses	4	1.3	2	50.0
Hirschsprung's disease	2	0.7	0	0.0
Omphalopagus twins	1	0.3	0	0.0
<b>Most common surgery performed</b>				
Intestinal resection/anastomosis	90	29.6	34	37.8
Colostomy	64	21.1	6	9.4
Primary closure of abdominal wall defect	27	8.9	6	22.2
Modified Silo reduction	21	6.9	15	71.4
Valvotomy	11	3.6	0	0.0
Feeding gastrostomy	10	3.3	7	70.0
Anoplasty	7	2.3	0	0.00
Primary repair of trachea-oesophageal fistula	8	2.6	2	25.0
Functional bladder closure	7	2.3	0	0.0
Excision of tumours	7	2.3	0	0.0
Ladd's procedure	5	2.0	1	20.0
Ileostomy	5	1.7	2	40.0
Cervical oesophagostomy	4	1.3	3	75.0
Posterior sagittal anorectoplasty(PSARP)	4	1.3	0	0.0
Drainage of abscess	4	1.3	2	50.0
Duodenal web excision	3	1.0	1	33.3
Pyloromyotomy	3	1.0	1	33.3
Inguinal herniotomy	3	1.0	0	0.00
Emergency separation for conjoint twin	1	0.3	0	0.00

Table 3: Post-operative complications, fatality rates from the complications and correlation with 30-day mortality

Complications	Frequency	Percentage	No of deaths attributable to the complication	Fatality rate (%)	p-value (co-relating complication with 30 day mortality)
Sepsis	97	32.0	53	54.6	0.001
Surgical site infection	88	29.2	32	36.4	0.001
Malnutrition	76	25.2	57	75.0	0.001
Hypothermia	59	19.5	32	54.2	0.001
Apnoea	51	17.0	37	72.5	0.001
Renal failure	27	8.9	25	92.9	0.001
Stress gastritis	22	7.3	12	54.5	0.001
Pneumonia	20	6.7	17	85.0	0.001
Prolonged recovery from anaesthesia	20	6.7	12	60.0	0.001
Urinary tract infection	12	4.0	1	8.3	0.139
Unconsciousness	3	1.0	3	100.0	0.003
Seizure	3	1.0	2	66.7	0.116

Catheter-associated urinary tract infection (CAUTI) occurred in 12 (5.3%) of 225 infants that were catheterized; this correlated significantly with the duration of urethral catheterization ( $p=0.001$ ). The median duration of catheterization was 14 days (interquartile range (IQR) 1 - 26 days). The risk of development of UTI from catheterization increased by 1.05 times after 72 hours (OR 1.05, 95 % CI = 0.28-3.98) and 3.9 times after 7 days (OR 3.88, 95%CI= 0.31-47.17) on the urethral catheter. More boys (9) had UTI than girls (3) ( $p = 0.39$ ).

Apnea and Anesthesia: Postoperative apnea, the most frequent anesthetic complication occurred in 51(17.0%) neonates. Thirty-six neonates died from anesthesia-related complications representing 44.4%of the total mortality. The risk of mortality increased by 11 times in those that developed apnea (OR =10.83,  $p= 0.001$ , 95% CI =5.47-21.44).

Anesthesia time lasted more than 2 hours in 198(66.0%) neonates. Anesthesia time longer than 2 hours did not correlate with the development of apnea ( $p = 0.67$ ) and 30-day mortality ( $p = 0.50$ ).

Mortality was higher with the high ASA class. Mortality among ASA I was 21.9% ( $n=25/114$ ), and ASA II was 20.3% ( $n=16/79$ ); while ASA III was 36.5% ( $n=31/85$ ), ASA IV was 38.1% ( $n= 8/21$ ) and ASA V was 20% ( $n = 1/5$ ). P-value was insignificant at =0.07.

Residents in anesthesiology administered anesthesia in 179(60,0%) of the cases, while consultants did in 92(30.8%) and anesthetic nurses 27(9.1%). Mortality across the groups was not significant ( $p=0.814$ ).

Distance from Hospital: Although 172 (56.96%) neonates traveled more than 50 km to access care, there

was no associated significant risk of death compared to those closer to the hospital (OR= 0.83, 95% CI 0.50-1.39,  $p = 0.48$ ).

Gestational Age and Birth Weight: While 99 (32.5%) patients were preterm, only 3 (0.9%) neonates weighed less than 2500 gm at birth. Proportionately, more deaths occurred in the preterm (39/99, fatality rate 39.4%) compared to the term neonates (42/205, fatality rate 20.5%) ( $p=0.001$ ).

Other factors: Consultant pediatric surgeons performed 196(64.5%) of the initial surgical procedures while Senior Registrars (trainees in pediatric surgery) did 87(28.6%) and Registrars (junior surgical trainees) did 21(6.9 %). Mortality did not differ significantly across groups ( $p = 0.760$ ).

Re-operation increased the risk of mortality by 2.9 times (OR 2.93, 95% CI 1.06-8.09,  $p=0.038$ ). Sixteen (5.7%) neonates were re-operated; 9 (3.0%) were operated twice and 7 (2.7%) thrice. Repeat operations were done within 30 days of the first. Indications for re-operation were failed intestinal anastomosis for intestinal atresia (9), complications of anterior abdominal wall defect closure (3), colostomy revision (1), gastrotomy revision (1), failed gastric perforation closure (1), and complications from sacrococcygeal tumor excision (1).

Oxygen saturation was measured and recorded at admission in only 81 (26.6%) neonates. Out of these, 40 (23.8%) neonates were admitted with oxygen saturation of less than 90%. SpO<sub>2</sub> at admission less than 90% did not adversely affect the 30-day mortality ( $p=0.20$ ). Thirty-one neonates had postoperative cardiac arrest, 29(93.6%) of them died ( $p=0.001$ ). Another two died intra-operation.

## Risk Predictors

Logistic regression analysis showed that the risk of death is highest in those that developed apnea (OR=10.8). Other risk predictors are shown in Table 4.

Table 4: Determinants of mortality (binary logistic regression analysis)

Variable	Odds Ratio	Std Error(b)	P>[z]	95%CI of OR
Apnoea	10.83	3.78	0.001	5.47-21.44
Sepsis	7.61	2.19	0.001	4.33-13.39
Malnutrition	6.99	2.05	0.001	3.93-12.43
Deep SSI	3.50	1.88	0.025	1.22-10.01
Re-operation	2.93	1.52	0.038	1.06-8.09

CI –confidence interval OR –Odds ratio SSI-surgical site infection

## DISCUSSION

### Mortality

A systematic review comparing mortality in surgical neonates in Africa in the last two decades showed an improvement from a rate of 36.9 % to 29.1%. [11] The overall mortality rate of neonatal surgery in Nigeria in this study was 26.6%. Although this compares with the overall trend reported across Africa, it is still more than double the projected SDG 3.2 target and much higher when compared to less than 5% reported in high-income countries. [15]

Comparing different systems, gastrointestinal pathologies contributed to the overwhelming majority (76, 93.8%) of the mortalities in the present report of general pediatric surgical neonates. Most mortalities were from surgery for intestinal atresias, gastroschisis, esophageal atresia, omphalocele, anorectal malformation, and intestinal malrotation, similar to previous single institutional reports from Nigeria and Africa, [16, 17] but much higher than HICs. For instance, the mortality from gastroschisis in the present report was 58.3% compared to 1% in HICs. [18] Most of the patients with gastroschisis were managed using an improvised surgical silo (made from several materials, including urine bag, female condom, intravenous fluid bag, and surgical gloves). Incidentally, most of the deaths were from sepsis and aspiration pneumonitis. The 70% mortality from this method of treatment may be explained by the absence of a protocol to improve outcomes. Wesonga et al were able to reduce gastroschisis mortality in Uganda from 90% to 58 % in one year by using a locally designed protocol. [19]

The absence of NICU and support facilities like in most sub-Saharan Africa no doubt also played a role in the high mortality. The majority of the neonates were managed in special care baby and high dependency units. Many other improvisations were often made as regards temperature control and nutritional needs of the neonates. Patient monitoring also often

takes a lot of man-hours from the surgical teams due to the paucity of intensivists and monitoring gadgets.

### Morbidities

As shown in Table 3, the occurrence of postoperative complications was common and greatly affected the survival of the neonates. Sepsis has been documented in several reports from developing countries as the most common cause of neonatal postoperative death. [9, 20, 21] Neonates have deficient cellular and humoral immunity; surgery additionally breaches the physical barrier to organisms, further increasing the risk of SSI and sepsis. From our study, nearly one-third of the neonates had sepsis, and more than half of this number died. Delayed presentation unlike in many LMICs did not significantly affect the development of sepsis in our study (p=0.075). As observed from the study, the major reason for the delayed presentation was a late referral from peripheral hospitals (32.8%). However, most of these neonates must have been on antibiotics besides from other resuscitative measures prior to arrival at the specialist centers, thus accounting for the low incidence of sepsis among late presenters. On the other hand, it might be possible that poor unsupervised deliveries at home, long and unsupervised transportation as well as nursing surgical neonates in sick pediatric wards as seen in many LMICs may have contributed to the overall high rates of SSI and sepsis. [22] Surgical site infection is common in sub-Saharan Africa and significantly affects the postoperative outcome. [7, 23]

Besides pre-existing preoperative malnutrition, a catabolic metabolic response from disease, surgery, and delayed onset of feeding also pushes the neonate further into negative nutritional balance, increasing the risk of death. Over 60% of infants that needed TPN never received it due to non-availability and non-accessibility, a situation that also exists in most sub-Saharan African countries. [7] Further studies on the burden of neonatal surgical malnutrition, the development of surgical nutrition guidelines, and the provision of TPN are needed to improve outcomes.

### Challenges of anesthesia

In the present report anesthesia-related deaths accounted for 44.4% of overall mortality, with the development of postoperative apnea as the most common risk factor. The most used modality was general anesthesia indicating an improvement in the choice of anesthesia for neonatal surgeries over the earlier preferred choice of local anesthesia. [24] This may be explained by an increase in the number of physician anesthetists involved in neonatal surgeries. In one report from Ghana, an increase in the number of physician anesthetists contributed to improving the outcome of neonatal surgery. [25] However specialist pediatric anesthetists are still quite a few, and the

density of anesthetists in Nigeria is still low. [26] Encouraging and training pediatric anesthetists along with the provision of appropriate facilities should lead to improvements in the safety and outcome of anesthesia in the setting.

### Preoperative factors

Majority of the neonates traveled more than 50 km to the hospital of care on public transportation unsupervised. While 20% were born at home with poor care, only a small fraction (2.3%) was born in the tertiary hospital of care. The low in-hospital delivery might be related to low prenatal diagnosis. Low utilization and uptake of prenatal ultrasonography especially in rural areas of sub-Saharan Africa where access to ultrasound services may be as low as 6% has been documented. [11, 27] The long-distance travel and low in-hospital delivery may worsen the physiologic status of the already severely ill infants, and some may die before accessing care. [24]

Again, it is noteworthy that the majority of the reported cases in this study weighed  $\geq 2.5$ kg. The preterm and low birth weight neonates are probably not reaching the pediatric surgeons and are a subject for further research.

At present, most pediatric surgeons in Nigeria are still concentrated mainly in the tertiary institutions in the urban areas leaving a vast population in rural areas without access to a pediatric surgeon. [28] The majority of the infants were referred from these distant rural areas.

### Conclusion

Although there have been some improvements in the practice of neonatal surgery in Nigeria, the national mortality is still high at 26.6%. The outcome is worse in the preterm and in neonates that developed apnea, sepsis, or disease-induced malnutrition.

### Recommendation

Development and implementation of treatment protocols and guidelines; and collaboration across centers is needed to ensure a continuous neonatal surgical quality improvement for a sustained good outcome. District and secondary level hospitals should be equipped and staffed to handle basic

neonatal surgical emergencies along with strengthening of referral and transfer strategies to higher-level hospitals. Advocacy should be increased towards the training of more pediatric surgeons, pediatric anesthetists, and support staff and motivating them to work in the district and secondary level hospitals.

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