

Original Article

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Predictors of postoperative mortality among neonates after major-risk surgery: A one-year experience from a Tunisian hospital

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KEYWORDS

Anesthesia; Neonatal mortality; Predictors; Neonatal surgery; Perioperative management.

ABSTRACT

Background: Neonatal surgery in developing countries remains a high-risk modality p and its outcomes depend on various patient-related, system-related, and management-related factors. This study aims to describe our experience in managing newborns requiring surgical interventions and to investigate the primary predictors of postoperative mortality.

Methods: In this observational study, we included all newborns aged less than 28 days who underwent surgery in the pediatric surgery department under general anesthesia with tracheal intubation for major-risk surgery. Patients were categorized into two groups based on the outcome (survival or death) during the two months following surgery. Following a comparison of the two groups, univariable and multivariable logistic regression analyses were conducted to explore predictors of perioperative mortality among neonates.

Results: Sixty-seven newborns were included in this study, with an early mortality incidence of 28.3%. Anesthesia management did not impact neonatal mortality. The main predictors of neonatal mortality were revision surgery [aOR=35.5; 95% CI: 1.33- 94.1], surgery duration ≥ 120 minutes [aOR=36.5; 95% CI: 1.48- 312], preoperative mechanical ventilation [aOR=3.88; 95% CI: 1.12- 30.8], and the occurrence of perioperative adverse events [aOR=5.7; 95% CI: 1-29.5] or postoperative surgical complications [aOR=32.5; 95% CI: 1.05-101].

Conclusion: The early mortality rate after major neonatal surgery remains high in our department. It appears that preoperative poor conditions can elevate the risk. Additionally, major-risk surgeries requiring prolonged procedures and revision surgery, along with the incidence of postoperative infections, significantly increase the risk of neonatal mortality.

INTRODUCTION

Neonatal surgery is one of the most challenging specialties. [1] It generally requires a multidisciplinary management approach, sophisticated and expensive surgical and anesthetic procedures, as well as skilled neonatal anesthesiologists and intensivists. [1, 2] Nevertheless, there is a wide global disparity in the reported neonatal surgical mortality rates, varying from 4% to 80%l [3] In low and middle-income countries (LMICs), perioperative neonatal mortality remains high because of several insufficiencies, such as the lack of diagnostic facilities, adequate airway and vascular access devices, consensual management and nursing protocols, and skilled multidisciplinary teams. [4,5]

In our country, neonatal mortality after surgery remains high despite improvements in diagnostic facilities and neonatal intensive care units (NICU). [6]

However, we don't have any idea about the impact of management strategies and protocols, particularly anesthesia management of neonates, on perioperative neonatal mortality. Knowledge of independent risk factors for early perioperative mortality is mandatory, as it can guide and improvise our perioperative practice, which may help improve practices and try to understand what substantial points need to be changed according to our internal team audit that can serve as a starting point of a quality improvement process. [6] However, even if there are several studies investigating predictors of early neonatal mortality after surgery, there is still poor data on the impact of anesthesia techniques and perioperative management protocols, particularly in LMICs. [7]

Our study aimed to describe our experience of managing newborns that require major surgical interventions and investigate the main predictors of postoperative mortality.

METHODS

Study Design and Setting:

After obtaining approval from the local ethics committee (HCUH 025/2022) and securing informed written consent from the parents, we conducted a prospective observational study on postoperative neonatal mortality. Data collection occurred for newborns undergoing neonatal surgery in the pediatric surgery department between July 2022 and August 2023.

Inclusion Criteria:

This study included newborns aged less than 28 days undergoing major neonatal surgery, regardless of the emergent condition or anesthesia technique. Major surgery encompassed interventions with the potential for bleeding, hemodynamic or respiratory disorders, requiring deep anesthesia with tracheal intubation, such as procedures on the esophagus, digestive tract, urinary tract, and pulmonary surgery. Exclusions comprised patients whose parents did not provide consent, as well as newborns aged more than 28 days and those who died before surgical intervention.

Variables and Data Sources:

Demographic data, including age, post-conceptual age, weight, maternal age, mode of delivery, and pregnancy-related diseases, were recorded. Surgeryrelated information covered the type of surgery (elective, emergent, or revision), duration, and timing (day or night), surgeon and anesthesiologist experience (considered experienced with two years in neonatal surgery). Preoperative assessment data encompassed malformation syndrome, preoperative anemia or hemostasis issues, and patient blood management. In critically ill neonates, preoperative management included correction of hemodynamic or fluid and electrolyte disorders, antibiotherapy, oxygen support, and preoperative mechanical ventilation. Anesthetic management data included induction technique, intubation, vascular access, extubation timing, and peroperative incidents like difficult intubation, excessive bleeding, and adverse events related to anesthesia or surgery.

Study Groups:

Patients were categorized into two groups based on their outcome during the two months following surgery: Group 1 (surviving neonates) and Group 2 (neonatal deaths).

Statistical Methods:

Statistical analyses were performed using SPSS V.25.0. Student's t-test and x2 test were used for continuous and categorical variables, respectively. Fisher's exact test was applied when the x2 test was

not applicable. Univariable and multivariable logistic regression models were employed to identify risk factors for neonatal mortality. Odds ratios (ORs) with 95% confidence intervals (CIs) were reported, with p<0.05 considered statistically significant.

RESULTS

In this study, we included 67 neonates who underwent surgery and were managed in our institution. The main types of interventions were as follows: esophagus atresia surgery (n = 17), laparotomy (n = 47), urinary tract surgery (n = 2), and pulmonary resection for pulmonary lung malformation (n = 1).

The esophageal atresia cohort included 16 cases of Type III and 1 case of Type I esophageal atresia; one patient was a severely premature newborn. Laparotomy was indicated for 4 cases of diaphragmatic hernia, 2 cases of omphalocele, and 41 cases of neonatal abdominal conditions (3 cases of volvulus, 17 cases of duodenal atresia, and 21 cases of peritonitis due to necrotizing enterocolitis or postoperative peritonitis).

Of the 67 neonates operated on, nine patients required revision surgery (13.4%): eight for postoperative peritonitis and one for esophagus atresia revision. The emergency context was noted for all patients. However, 55 patients (82%) were operated on the same day of being diagnosed, and 12 patients were operated on after 24 hours or more. The proportion of postoperative early mortality was 28.3%.

The main causes of death were surgical complications (6 cases of anastomosis leakage and postoperative infectious complications) and severe prematurity complications (6 cases of sepsis, meningitis, multiple organ failure syndrome, or disseminated intravascular coagulation after prolonged surgery). Other causes of newborn deaths included nosocomial infection, severe postoperative hyponatremia, and renal failure (7 cases).

The comparison between the two study groups showed lower weight and a higher incidence of prematurity in the death group (Table 1). The mode of delivery and pregnancy-related diseases were comparable in both groups. Revision surgery and long duration of surgery (>120 min) were higher in the death group, with p = 0.025 and p = 0.0001, respectively. However, the emergency context and the experience of the physicians were comparable in both groups (Table 2). The preoperative assessment revealed poor preoperative conditions in the death group, with higher rates of anemia, transfusions, oxygen support, fluid and electrolyte disorders, and the use of antibiotics (Table 3). Although anesthesia management was comparable between the two groups, early extubation (at the end of surgery or

during the 48 hours following surgery) was more frequent in the surviving group (Table 4). The incidence of a peroperative adverse event was 18.7% in the surviving group versus 89.4% in the death

group, with p = 0.0001 (Table 4). Furthermore, the incidence of referrals and the duration of stay in the neonatal intensive care unit were significantly higher in the death group.

Table 1: Demographic parameters

	Group 1	Group 2		
	Surviving group	Neonatal Deaths		
	N= 48	N=19		
Age at surgery (days)	10.94 ± 10.5	9.94 ± 10.3	0.729	
Post conceptual age at surgery (WG)	36.9 ± 5.8	35.1 ± 3.4	0.212	
Weight at birth (Kg)	3.92 ± 0.7	2.13 ± 0.9	0.0001	
Weight at surgery	2.96 ± 0.7	2.09 ± 0.9	0.0001	
Weight ≤ 3kg	15 (31.2%)	14 (73.6%)	0.002	
Weight loss	12 (25%)	7 (36.8%)	0.249	
Premature newborn (≤34 WG)	15 (31.2%)	14 (73.6%)	0.002	
Maternal age ≥ 40 years	13 (27%)	2 (10.5%)	0.125	
Mode of delivery (vaginal/ cesarean)	28/20	6/13	0.057	
Anesthesia technique for delivery				
Spinal anesthesia	17	12	0.300	
Epidural anesthesia	8	1	0.085	
General anesthesia	3	2	0.305	
No anesthesia	20	4	0.152	
Pregnancy-related disease				
Fetal distress	13	11	0.051	
Severe preeclampsia	5	5	0.105	
Gestational diabetes	4	3	0.311	
Infections	1	0	0.711	

Table 2: surgery parameters:

	Group 1	Group 2	P value
	Surviving group	Neonatal Deaths	
	N= 48	N=19	
Emergency context:			
operated the same day of diagnosis	38 (79.1%)	17 (89.4%)	0.270
operated after 24 hours or more	10 (20.8%)	2 (10.5%)	0.096
Revision surgery	4 (8.3%)	6 (31.5%)	0.025
Duration of surgery (min)	111 ± 54	139 ± 54	0.05
Duration ≥ 120 min	29 (60.4%)	19 (100%)	0.0001
Time of surgery (day/ night)	40 /8	15 /4	0.459
Experience of the surgeon ≥ 2 years	37 (77%)	15 (78.9%)	0.574
Experience of the anesthetist ≥ 2 years	41 (85.4%)	17 (89.4%)	0.542
Type of surgery:			
Esophagus atresia	11 (22.9%)	6 (31.5%)	0.102
Laparotomy	34 (70.8%)	13 (68.4%)	0.452
Urinary tract surgery	2 (4.1%)	0	-
Pulmonary lung malformation	1 (2%)	0	-

In univariable logistic regression, low weight, prematurity, poor preoperative conditions, and the incidence of a peroperative adverse event or postoperative complications were correlated with an increased risk of postoperative mortality (Table 5).

In multivariable logistic regression, revision surgery [aOR=35.5; 95% CI: 1.33- 94.1], duration of surgery \geq 120 min [aOR=36.5; 95% CI: 1.48- 312], preoperative mechanical ventilation [aOR=3.88; 95% CI: 1.12-30.8], and the incidence of peroperative adverse

events [aOR=5.7; 95% CI: 1–29.5] or postoperative complications [aOR=32.5; 95% CI: 1.05–101] were identified as the main predictors of neonatal mortality after major-risk surgery (Table 5).

DISCUSSION

In this study, we demonstrated that early neonatal mortality after major-risk surgery remains high at our centre. The main risk factors identified were poor preoperative conditions, specifically mechanical ventilation, prolonged duration of surgery, peroperative adverse events, postoperative complications, and revision surgeries. These findings, specific to our department, not only raise awareness of our current situation but also serve as a basis for guiding future improvement actions concerning our management protocols.

Table 3: preoperative assessment of the newborns

	Group 1 Surviving group N= 48	Group 2 Neonatal Deaths N=19	P value
Malformation syndrome	10 (20.8%)	7 (36.8%)	0.148
Preoperative anemia	11 (22.9%)	13 (68.4%)	0.001
Preoperative transfusion	5 (10.4%)	10 (52.6%)	0.001
Abnormal hemostasis requiring FFP or platelet transfusions	1 (2%)	7 (36.8%)	0.0001
Low blood pressure before surgery	5 (10.4%)	2 (10.5%)	0.645
Fluid and electrolyte disorders requiring supplementations	4 (8.3%)	13 (68.4%)	0.0001
Preoperative antibiotherapy	18 (37.5%)	16 (84.2%)	0.003
Oxygen desaturation ≤ 94%	9 (18.7%)	10 (52.6%)	0.008
Preoperative Mechanical ventilation	4 (8.3%)	8 (42.1%)	0.003
Need for preoperative oxygen support	22 (45.8%)	18 (94.7%)	0.0001

Table 4: anesthesia technique and perioperative management

	Group 1	Group 2	P value
	Surviving group	Neonatal Deaths	
	N= 48	N=19	
Intravenous induction (propofol)	44 (91.6%)	18 (94.7%)	0.560
Inhalatory induction	4 (8.3%)	1 (5.2%)	0.560
Opioids at induction	7 (14.5%)	2 (10.5%)	0.510
Non-depolarizing Muscle relaxant	2 (4.1%)	3 (15.7%)	0.134
Depolarizing muscle relaxant at induction	26 (54.1%)	6 (31.5%)	0.072
and/ or maintenance			
Opioids for maintenance			
Remifentanyl / Fentanyl / alfentanil	28/ 14/ 6	10/ 9/ 0	0.125
Difficult intubation (≥ 2 attempts)	8 (16.6%)	5 (26.3%)	0.522
Nasotracheal intubation	20 (41.6%)	10 (52.6%)	0.623
Orotracheal intubation	28 (58.3%)	9 (47.3%)	
Per-operative adverse event	9 (18.7%)	17 (89.4%)	0.0001
Per-operative Oxygen desaturation ≤ 94%	7 (14.5%)	9 (47.3%)	0.007
Per-operative hypotension and/or	4 (8.3%)	7 (36.8%)	0.007
catecholamine infusion			
Per-operative bleeding and / or transfusion	2 (4.1%)	7 (36.8%)	0.01
Incidence of anesthesia-related complication	0	0	-
Incidence of surgery-related complication	6 (12.5%)	17 (89.4%)	0.0001
Broviac catheter placement	16 (33.3%)	9 (47.3%)	0.214
Extubation at the end of the intervention	18 (37.5%)	1 (5.2%)	0.006
Early extubation ≤ 48 h	30 (62.5%)	3 (15.7%)	0.0001
Late extubation ≥ 48h or non-extubated	0	15 (78.9%)	0.0001
NICU admission	34 (70.8%)	19 (100%)	0.005
Duration of stay in NICU	3.0 ± 3.11	8.4 ± 13	0.010

There exists a significant disparity in the incidence of postoperative neonatal mortality between developed countries and LMICs. [3, 8] We believe that improving healthcare facilities for surgical neonates in LMICs could potentially prevent several cases of death. Despite all study patients having access to perioperative neonatal intensive care and surgical care, it is noteworthy that our university hospital, serving as the sole neonatal surgery center in the southern part of the country, receives newborns from various far-flung regions, potentially up to 300 kilometers away. This geographical constraint can lead to delays in managing surgical newborns, exacerbating morbidity and mortality. [9] However, it is crucial to acknowledge that our study did not

include newborns who died before surgery, which could impact the interpretation of our results.

Our study highlighted that poor preoperative conditions increase the risk of postoperative mortality, aligning with previous literature emphasizing the role and benefits of adequate preoperative optimization. [10] The quality of healthcare and the availability of intensive care resources often dictate preoperative health conditions. It's essential to recognize the importance of antenatal diagnosis tools, generally unavailable in LMICs, to improve preoperative well-being for neonatal diaphragmatic malformations like hernia esophagus atresia. [11] We advocate for early surgical

treatment of congenital malformations to avoid preoperative mechanical ventilation, correlated with an increased risk of neonatal mortality. [6] Furthermore, improving pregnancy conditions through an adequate maternal healthcare protocol could reduce the incidence of low birth weight and

prematurity, both of which worsen the prognosis of surgical newborns. [12] Our study noted an overuse of preoperative antibiotics, raising concerns about potential bacterial resistance development in the event of postoperative infection, suggesting that antibiotic use should be justified. [13]

Table 5: Risk factors of perioperative neonatal mortality

	OR [95% CI]	aOR [95% CI]	sign
Weight ≤ 3kg	6.16 [1.87-20.2]	9.13 [0.589- 142]	0.115
Premature newborn (≤34 WG)	6.1 [1.875-20.24]	2.16 [0.164- 28.5]	0.558
Revision surgery	5.07 [1.24- 20.7]	35.5 [1.33- 94.1]	0.033
Duration of surgery ≥ 120min	32.3 [3.62- 325]	36.5 [1.48- 312]	0.0001
Preoperative anemia	7.28 [2.24- 23.68]	0.60 [0.073- 5.03]	0.643
Preoperative transfusion	5.95 [2.62- 34.7]	2.16 [0.165- 25.01]	0.615
Abnormal hemostasis/transfusion	27.4 [3.07-244]	2.19 [0.48- 107]	0.060
Fluid and electrolyte disorders	23.8 [5.82- 97.4]	9.3 [0.092- 65.2]	0.064
Preoperative antibiotherapy	8.59 [2.19- 33.68]	5.4 [0.998- 29.4]	0.051
Preoperative Oxygen desaturation	4.81 [1.51- 15.29]	3.3 [0.727- 15.12]	0.121
Preoperative Mechanical ventilation	8.0 [2.03- 31.4]	3.88 [1.12- 30.8]	0.036
Need for preoperative oxygen support	21.2 [2.625- 172.3]	6.82 [0.64- 74.3]	0.112
Peroperative adverse event	4.87 [1.596- 39.9]	5.7 [1- 29.5]	0.05
Extubation at the end of surgery	0.093 [0.011- 0.754]	0.190 [0.011- 3.11]	0.250
Early extubation (postoperative mechanical ventilation ≤48h)	0.085 [0.022- 0.337]	0.144 [0.013-1.64]	0.119
Late extubation (postoperative mechanical ventilation ≥ 48h)	5.76 [1.826- 18.207]	1.422 [0.166- 12.14]	0.748
Incidence of postoperative surgical complication (infection)	62.3 [8.62- 425]	32.5 [1.05- 101]	0.002

Contrarily, anesthesia management did not show a correlation with neonatal mortality. While neonatal anesthesia remains controversial regarding muscle relaxant use, intubation type (nasal or oral), and analgesia protocols, we stress the role of enhanced recovery and early extubation in reducing the risk of morbidity and mortality. [14] Fast-track surgery with early extubation can shorten NICU stays and mitigate the risk of nosocomial and postoperative infections, a primary predictor of mortality. However, like many LMICs, we also face a shortage of pediatric anesthesiologists and surgeons with the requisite skills to manage neonates. [15] Challenges in our setting include delays in neonatal surgery due to a lack of specialized anesthesiologists and insufficient devices for difficult intubation [16], ultrasound-guided vascular access [17], and temperature monitoring. [18] We advocate for a multidisciplinary approach involving surgeons, anesthetists, neonatologists, and trained nurses. [19] Continuous education and training for nurses and anesthesia technicians in neonatal healthcare can reduce the risk of postoperative infection, a main complication whose incidence remains high in our setting, necessitating urgent quality improvement programs to save neonates. [20]

Furthermore, revision surgery was correlated with an increased risk of neonatal mortality, primarily related to postoperative complications such as anastomotic leakage leading to severe infections. [21, 22] We posit that preoperative conditions, including anemia, fluid and electrolyte disorders, and hemodynamic disorders, can heighten the risk of anastomotic leakage. Additionally, prolonged surgery duration can lead to hypothermia, hemodynamic, and fluid and electrolyte disorders, potentially increasing the risk of infection. [23]

This study serves as an internal audit, initiating a quality improvement process. We propose a campaign targeting general practitioners and regional decisionmakers to raise awareness of warning factors, conditions including poor preoperative geographical distance, which often delay the care of newborns and may worsen the prognosis. Additionally, assessing outcomes after implementing a quality process is essential. Continuous medical anesthesiologists training pediatric intensivists is crucial to improving physician skills and nursing quality, reducing the incidence of postoperative nosocomial infections and complications. However, a national strategy is

imperative to decrease referrals of newborns requiring surgery.

The main limitations of this study include the inclusion of various types of major-risk surgeries and a small sample size, preventing a comparison of different anesthesia and perioperative procedures. Another limitation is the absence of data collection on neonates who died before surgery or the causes of death in this particular population.

CONCLUSION

Early postoperative neonatal mortality continues to be a significant concern in our country. Understanding the primary predictors of mortality is crucial for promoting awareness and implementing safety measures during newborn surgeries. Notably, neonatal mortality did not show a correlation with the anesthesia technique. However, preoperative poor health conditions, particularly the use of preoperative mechanical ventilation, emerged as risk factors for

increased mortality. Additionally, the incidence of peroperative adverse events, such as hemodynamic instability, oxygen desaturation, or excessive bleeding requiring blood transfusions, along with prolonged surgical procedures and the necessity for revision surgery, were identified as predictors of postoperative neonatal mortality. A notable observation was the high incidence of postoperative infections, indicating a rising trend that significantly contributes to the risk of neonatal mortality.

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