

Factors associated with infection and mortality in neonates following abdominal surgery

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Abstract

Background The outcomes of neonatal surgical cases has steadily improved in the last decade. However, limited local data are available in Indonesia regarding the contributing factors and outcomes of surgical procedures in neonates.

Objective To determine the incidence of infection and mortality in neonatal surgical cases in Saiful Anwar Hospital, Malang, East Java, Indonesia.

Methods This retrospective cohort study included neonates who underwent abdominal surgery over a period of 20 months from January 2021 to August 2022. Data collected included subjects' basic demographics, primary surgical diagnoses, associated congenital anomalies, pre-operative conditions, and referral status. These parameters were analyzed in relation to the incidence of infection and mortality in the 30 days after surgical procedure.

Results Of fifty-four neonates in this study, the most common neonatal surgical conditions were anorectal malformation, followed by necrotizing enterocolitis and Hirschsprung's disease. The mortality rate at 30 days was 48%. The most common associated factors was sepsis (OR 2.129; 95%CI 1.039 to 3.126; $P < 0.001$). Other factors, such as: age at presentation, gender, gestational age, birth weight, referral patient, pre-operative respiratory failure/hemodynamic instability, associated congenital anomalies, and emergency procedures, were not associated with mortality. The survival time in the sepsis group [17.30 (1.68-13.98) days] was significantly lower than in the non-sepsis group [25.95 (1.63-22.76) days] ($P < 0.001$).

Conclusion Sepsis is a risk factor for mortality in neonates following abdominal surgery. Identification of this risk factor and early intervention are important to improve outcomes. [Paediatr Indones. 2023;63:S8-S13; DOI: <https://doi.org/10.14238/pi63.01.2022.S8-S13>].

Keywords: neonates; abdominal surgery; infection; mortality

The outcomes of neonatal surgical cases has steadily improved in developed countries. This has been attributed to a better understanding of neonatal physiology, improvement in specialist surgical techniques and anesthesiology, as well as improved diagnostic facilities and neonatal intensive care.¹ UNICEF reported in 2016 that mortality due to congenital abnormalities was estimated to be 10% of the overall neonatal mortality rate, many of whom require surgery in the neonatal period.² Unfortunately, there are limited data regarding the contributing factors and outcomes of surgical conditions in neonates that contribute to the significant portion of neonatal mortality.

There are several challenging aspects of surgical management of neonates. Neonates have unique differences in physiology, such as vulnerability to electrolyte and fluid imbalances compared to older children and adults. They also have a different

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disease profile, and often have associated congenital anomalies, as well as increased risk for sepsis due to an immature immune system. Many factors could be potentially responsible for neonatal surgical outcomes, including infections. Infection was a major risk factor associated with morbidity and mortality in neonates following surgical procedures.³ A study in South Africa reported that sepsis was a major contributing factor in the development of morbidity and mortality in neonates with surgical procedures.⁴ Another study showed that surgical site infections are a frequent and significant problem in infants operated on for abdominal birth defects, and related to morbidity and mortality.⁵ The aim of this study was to describe the incidence of neonatal surgical conditions and report the outcomes, including neonatal infection and mortality. To the best of our knowledge, this is the first study to identify outcomes of neonatal infection and mortality following abdominal surgical procedures in Indonesia.

Methods

A retrospective cohort study of all neonates who underwent abdominal surgical procedures at the Neonatology Department, Dr. Saiful Anwar Hospital, Malang, East Java, from January 2021 to August 2022 was done. The medical record information extracted were age at presentation/referral, gestational age, birth weight, sex, diagnosis, associated congenital anomalies, and pre-operative conditions. These parameters were compared to the main outcomes of incidence of infection and mortality.

All patients who underwent surgery for gastrointestinal or abdominal wall conditions were included if they were under 28 days of age for full term infants or under 40 weeks corrected gestational age for premature neonates. The following diagnoses for neonatal congenital gastrointestinal conditions were evaluated: anorectal malformation (ARM), biliary atresia (BA), spontaneous intestinal perforation (SIP), Hirschsprung's disease (HD), inguinal hernia (IH), malrotation with volvulus (MV), necrotizing enterocolitis (NEC), esophageal atresia +/- tracheoesophageal fistula (OA ± TOF), omphalocele (OMPH), gastroschisis (GS), hypertrophic pyloric stenosis (HPS), and jejunoileal atresia (IA). Patients

with incomplete medical record data, who died prior to receiving surgery, or had undergone surgery outside the neonatal period or at another hospital were excluded.

The incidence of infection and outcome within 30 days of admission were reported, including neonatal infection and mortality. Sepsis was defined as systemic inflammatory response syndrome (SIRS) in the presence of suspected or proven infection. SIRS is a widespread inflammatory response that may or may not be associated with infection. Thus, two or more of the criteria in the definition.⁶ must have been met, with one being abnormal temperature or leukocyte count, to diagnose sepsis.

The study protocol was approved by the Institutional Ethics Committee of Saiful Anwar Hospital. Results were expressed as means/medians, ranges, and percentages. Analyses were conducted using SPSS version 23 for Windows (SPSS Inc., Chicago, IL, USA) software. Results with P values <0.05 were considered to be statistically significant.

Results

Fifty-four neonates underwent abdominal surgery and met the inclusion criteria during the study period. There were 32 males and 22 females, with a male to female ratio of 1.4:1. The mean gestational age was 38.5 (SD 7.2) weeks and mean birth weight was 2,350 (SD 892) g. The median age at presentation was 2 (IQR 1-5) days. Almost all subjects were referral patients born elsewhere and referred to our hospital (87%). The most common neonatal abdominal surgical conditions were ARM, followed by NEC and HD. The characteristics of subjects and their presenting surgical diagnoses are described in **Table 1**.

The outcomes of patients at 30 days were recorded (**Table 2**). Twenty-six patients died during the 30 days after surgical procedures. The most common reported cause of death was sepsis. Twenty-three patients were discharged without morbidity (11 subjects) or while awaiting the next surgical plan (12 subjects). There were two patients who underwent repeat surgery, including repair of breakdown of anastomosis and stoma, related to surgical site infections.

Factors potentially associated with 30-day

mortality in neonates with abdominal surgical procedure were analyzed by logistic regression test. Sepsis, both pre- and post-operative, and pre-operative respiratory failure/hemodynamic instability were significantly correlated with mortality (OR 2.129; 95%CI 1.039 to 3.126; $P < 0.001$ and OR 0.778; 95%CI 0.233 to 1.167; $P = 0.041$, respectively). Other factors such as age at presentation, gender, gestational age, birth weight, referral or inborn patients, associated congenital anomaly, and emergency procedures were not significantly associated with mortality within 30 days of admission ($P > 0.05$) (Table 3).

Univariate analysis of time of referral, reported sepsis, and mortality revealed that the mean age at referral was 4.04 (SD 3.33) days, with a range of 1-17

days. Delayed referral (more than 5 days) was not associated with sepsis (OR 0.295; 95%CI 0.074 to 1.177, $P = 0.048$).

The survival rates of the sepsis and non-sepsis groups were analyzed by Kaplan-Meier (Figure 1). The survival time in the sepsis group was significantly lower than in the non-sepsis group ($P = 0.001$), with median survival time of 17.30 (1.68-13.98) days and 25.95 (1.63-22.76) days, respectively.

Discussion

Here we report the prevalence of neonates undergoing surgical procedures and analyze risk factors associated with sepsis and mortality. The most common abdominal surgical conditions were ARM, followed by NEC and HD, which were comparable to that of two neonatal surgical units at hospitals in Egypt (ARM, followed by esophageal atresia/tracheoesophageal fistula and HD).⁷ Anorectal malformation is a common cause of neonatal intestinal obstruction, with clinical manifestation of abdominal distension. Necrotizing enterocolitis, especially with gastrointestinal perforation, shows increased odds of mortality. More than 90% of patients with HD were diagnosed during the neonatal period because of increased awareness and improved diagnostic methods.⁷

Neonatal surgical cases require care in specialized centers offering high-risk neonatal support, with neonatology and pediatric surgical specialties. Neonates who are ill and have other risk factors such as preterm birth, low birth weight, chromosomal defects, genetic syndromes, or congenital anomalies, require management in highly dedicated neonatal intensive care units.⁸ However, studies that assessed for risk factors or predictors of mortality in neonates undergoing surgical procedures have been limited.

Table 1. Clinical characteristics and demographic data

Characteristics	(N=54)
Median age at presentation (IQR), days	2 (1-5)
Gender, n (%)	
Male	32 (59)
Female	22 (41)
Mean gestational age (SD), weeks	38.5 (7.2)
Gestational age, n (%)	
Preterm	12 (22.2)
Term	42 (77.8)
Mean birth weight (SD), g	2,350 (892)
Admission status, n (%)	
Born at Saiful Anwar Hospital	7 (13)
Outside referrals	47 (87)
Associated congenital anomaly, n (%)	22 (41)
Presenting surgical diagnosis, n (%)	
Necrotising enterocolitis	9 (16)
Gastroschisis	4 (7)
Omphalocele	5 (9)
Hirschsprung's disease	8 (15)
Anorectal malformation	28 (52)
Tracheo-esophageal atresia	2 (3)
Duodenal atresia	3 (5)
Jejunioileal atresia	2 (3)
Malrotation ± midgut volvulus	1 (2)

Table 2. Surgical neonates' outcomes at 30 days

Outcomes, n (%)	(N=54)
Discharged, without morbidity	11 (21)
Discharged, awaiting results and/or primary surgery	12 (23)
Repeat surgery	2 (3)
Not yet discharged	3 (5)
Died	26 (48)

Table 3. Risk factors associated with mortality within 30 days of admission

Risk factors	OR	95%CI	P value
Preterm	0.325	0.025 to 0.987	0.889
Low birth weight	0.667	0.127 to 1.021	0.755
Male	0.117	0.038 to 0.725	0.519
Referral	0.398	0.098 to 1.572	0.405
Associated congenital anomaly	0.445	0.076 to 1.066	0.123
Emergency procedure	0.235	0.077 to 0.975	0.569
Pre-operative respiratory failure/hemodynamic instability	0.778	0.233 to 1.867	0.041*
Sepsis	2.129	1.039 to 3.126	0.001*
Delayed referral (>5 days)	0.295	0.074 to 1.177	0.048*

*P values < 0.05 were statistically significant

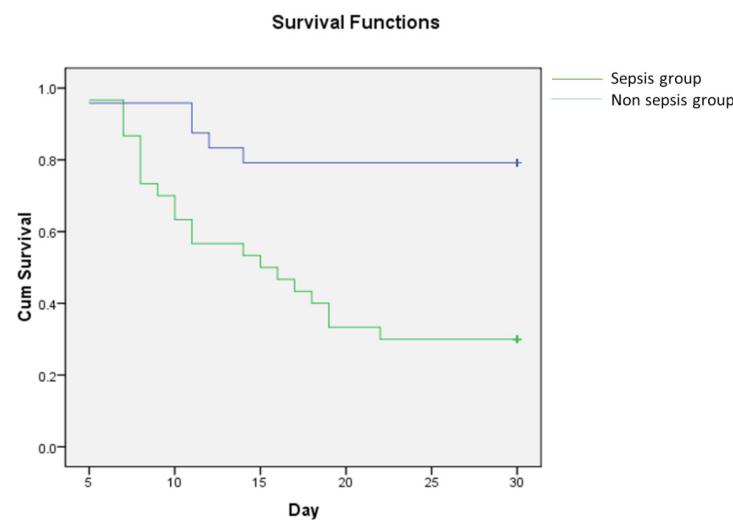


Figure 1. Kaplan-Meier survival estimates of sepsis and non-sepsis groups

Many possible factors are responsible for mortality in neonates. Factors that impact neonatal surgical outcomes can be grouped as pre-operative, intra-operative, and post-operative. Prematurity and low birth weight are associated with poor prognosis in neonates.⁹ A multivariate analysis showed gestational age and birth weight to be significant independent predictors of mortality, owing to immature immune and organ system function in preterm neonates.¹⁰ In our study, we reported outcomes of neonatal surgery at 30 days after surgical procedures. The incidence of mortality was 48%, with sepsis as the most common reported cause of death. A retrospective descriptive study of neonates who underwent emergency surgery in Uyo, Nigeria reported an overall mortality following surgery of 62.2%. Case fatality rates ranged from 0% for HD to 100% for tracheo-oesophageal fistule.¹¹

Another study conducted in Coimbra, Portugal reported overall in-hospital mortality of 6.4%, with causes of death including multiple organ dysfunction and preterm-related factors. Screening analyses of adverse outcomes showed that the presence of preterm birth (under 37 week gestation), very preterm (under 32 week gestation), low birth weight (under 2,500 g), very low birth weight (< 1,500 g), large for gestational age, acquired surgical indication, *American Society of Anesthesiologists* (ASA) physical status score 3 or above in at least one procedure, abdominal surgery, necrotizing enterocolitis, and the need for intraoperative cardiopulmonary resuscitation maneuvers were each significantly associated with higher risk of mortality.³ Preterm and low birth weight infants had increased risk of sepsis due to immature immune systems, potentially due to impaired innate

immune function. Prematurity increases morbidity and mortality amongst neonates undergoing surgery,¹² with identified risks including systemic sepsis, septic shock, pneumonia, unplanned intubation, and bleeding/transfusions as the most common postoperative complications.¹³

In our study, risk factors such as age at presentation, gender, gestational age, low birth weight, and associated congenital anomalies were not significantly associated with mortality within 30 days after surgery. Among our subjects, the proportion of very premature infants who underwent abdominal surgery was low compared to full term infants. Overall, the survival time in the sepsis group was significantly lower than in the non-sepsis group, with median survival times of 17.30 (range 1.68-13.98) days and 25.95 (range 1.63-22.76) days, respectively.

In our study, pre-operative respiratory failure/hemodynamic instability is not a factor for mortality. However, a study in Tunisia reported high overall mortality in infants undergoing neonatal surgery, with independent risk factors including the duration of surgery and the necessity of preoperative intubation.¹⁴

Delayed presentation has been reported to be a risk factor for mortality in neonatal surgical emergencies in developing countries. A study in Kenya reported that a median age of 3 days at presentation was correlated with higher mortality,¹⁵ while another study in Nigeria reported that the 65.5% mortality in neonatal surgical cases was associated with delayed presentation, of which 7.5% were ill on arrival and died during resuscitation. They attributed the delay to late diagnosis financial constraint, lack of adequate means of transportation, among others.¹⁶ We also analyzed time of referral with outcomes of sepsis and mortality. Delayed referral (more than 5 days) significantly correlated with mortality within 30 days, but not with sepsis. However, we did not evaluate the underlying reasons for delayed referrals. Some unorthodox practices such as inadequate neonatal resuscitation, instability during transport, and delayed referral were reported to be associated with higher mortality.¹⁷ Finally, the training of birth attendants in the recognition of neonatal surgical emergencies and having an efficient emergency transport system especially in rural areas for immediate referral has been suggested to curtail delayed referral and possibly improve outcomes.

In conclusion, mortality rate following neonatal abdominal surgery is high in Dr. Saiful Anwar Hospital, Malang, East Java. The factor associated with mortality is sepsis; pre-operative respiratory failure/hemodynamic instability and delayed referral are not correlated with mortality within 30 days after surgical procedure. Identification of this risk factor and early preventive measures are important in future strategic planning to improve the outcomes of neonates following abdominal surgery in this unit.

Conflict of interest

None declared.

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