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Epidemiologic factors associated with neonatal bowel perforations in Uganda: experience from a single tertiary referral hospital

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Abstract

Background Neonatal bowel perforations pose a significant disease burden for pediatric surgeons around the world. However, very little is known about these perforations in low-income settings. This study aims to investigate the epidemiology of neonatal perforations at a tertiary hospital in Uganda.

Results Twenty neonates with bowel perforation who were admitted to a single national referral hospital from May 2020 to April 2021 were included. Fifty-five percent ($n = 11$) of the neonates in this cohort were male, and 16 were term with birth weight above 2.5 kg. Thirteen were below 1 week of age and all maternal ages were less than 40 years. Pneumoperitoneum was the most common finding on erect abdominal X-ray and colon was the frequent site of perforation. Forty percent of the babies in this cohort had blood group O+. Fifty-five percent of our patients died before discharge.

Conclusion Outcomes for neonatal bowel perforations are still dismal. Health workers taking care of neonates should have a high index of suspicion for neonatal gastrointestinal perforations.

Keywords Neonatal bowel perforations, Low-income country, Epidemiology, Neonates

Background

Neonatal bowel perforations are a major cause of morbidity and mortality for infants with surgical disease worldwide and are especially common in very low birth weight (VLBW) and extremely low birth weight (ELBW) infants [1, 2]. In an African systematic review including

4849 neonates, emergent neonatal surgery involving bowel perforation incurred the highest mortality out of all surgical conditions [3].

The two most common causes of neonatal bowel perforations are necrotizing enterocolitis (NEC) and spontaneous intestinal perforation (SIP) [4]. Distinguishing the cause of bowel perforation is important as the management is different [5]. In contrast to NEC, SIP is usually focally isolated in the ileum and presents with free abdominal air without pneumatosis intestinalis [6]. The incidence of NEC in preterm infants is from 2 to 7% and up to 22% in ELBW infants, with death occurring in about a third of surgical NEC [7, 8]. Meanwhile, the incidence of neonatal SIP in VLBW infants in the USA is 1.6%, and 90% of cases presented at 28 weeks

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of gestation or under [9]. However, data from low-middle income countries on neonatal bowel perforations is sparse, and not much is known about the epidemiology of the disease.

While prematurity is the only known risk factor of neonatal bowel perforations, the primary etiology of and risk factors for both NEC and SIP is largely unknown, especially in low-income settings. Prenatal exposures may be a primary risk factor, including medications such as indomethacin, steroids, or pregnancy complications such as chorioamnionitis, bacterial or fungal infections, and the lack of enteric muscle coat [10, 11]. In extremely low birth weight infants, many believe that such perforations occur spontaneously [1].

A major barrier to understanding this disease is the bias of information arising from high-income countries (HICs) without commiserate information from low- and middle-income countries (LMICs) [8, 9]. This imbalance creates a skew in the epidemiologic data about a highly morbid disease and results that are poorly generalizable to the LMIC setting. Reporting LMIC data may also help improve the global understanding of the risk factors and potential underlying biology that puts infants at risk for spontaneous perforations.

We evaluated the epidemiology of infants and mothers presenting to our tertiary referral hospital to better understand the risk factors for neonatal perforation in our setting.

Methods

We conducted a retrospective review of all patients who were admitted for neonatal bowel perforation from May 2020 to April 2021. All records were collected from the prospectively created database of pediatric surgical admissions maintained by the pediatric surgery unit at our tertiary referral hospital. Approval for data collection and analysis was obtained from the Hospital Research and Ethics Committee (MREC 464) and all patients' caretakers and parents completed consent forms prior to surgery.

All patients that were admitted for neonatal bowel perforation were included in our study. Neonatal was defined as admission within the first 30 days of life. The diagnosis of bowel perforation was made based on clinical presentation and correlated with findings on erect abdominal radiographs (X-ray). Any record with significant missing data, as record of admission by minimal entry in the database, was excluded from the study.

Descriptive analyses were performed of the patient demographics, maternal and prenatal factors, and

clinical course. All analyses were performed using STATA 17.0.

Results

Demographics

In total, 23 neonates were admitted with neonatal bowel perforation from May 1, 2020 to April 30, 2021. Three babies were excluded due to significant missing data, resulting in a population of 20 infants included in the analysis.

Of these, 11 (55%) of the neonates were male, with the majority born at term (80%). The majority of neonates (85%) were normal weight for gestational age, with a median birth weight of 3.6 kg (IQR 2.9–3.6). Typically, at presentation these neonates were 4 days old; however, there was a large range of presentation—anywhere from 1 to 28 days of life. Eight of these neonates had O+ blood type and were either the first-born child or \geq fourth-born. Congenital anomalies were rare, affecting only 5% of the population and almost all neonates (70%) were breast fed (Table 1).

Table 1 Demographics

Gender (n, %)		
Male	11	55.0%
Female	9	45.0%
Gestational age (n, %)		
Preterm	4	20.0%
Term	16	80.0%
Birth weight (kilograms, M, IQR)	3.2	2.9–3.6
Age at presentation (days) (M, IQR)	4	3.5–13
Blood group		
O+	8	40.0%
O–	2	10.0%
A+	3	15.0%
B+	1	5.0%
Unknown	6	30.0%
Birth order (n, %)		
First	6	30%
Second	2	10%
Third	2	10%
\geq Fourth	8	40%
Missing	2	10%
Congenital anomaly (n, %)		
Present	1	5.0%
Absent	16	80.0%
Missing	3	15.0%
Breast fed (n, %)		
Yes	14	70%
No	4	20%
Missing	2	10%

Maternal factors

The median maternal age was 30 years old, and approximately 20% of the mothers were of advanced maternal age (age ≥ 35), with no mothers ≥40. All mothers had received antenatal care and ≥95% took prenatal vitamins (folic acid). A small number of mothers experienced complications during pregnancy—one mother who was diagnosed with hypertension and preeclampsia, three with malaria, one who experienced a threatened abortion, and one with arm prolapse. Only 20% of mothers used any medication during pregnancy—which primarily was prescribed for hypertension and malaria (Table 2).

Clinical course

While majority of infants who were admitted with neonatal bowel perforation had pneumoperitoneum on X-ray (60%), a quarter of infants had other findings including dilated bowel, ascites, complete whiteout with gasless abdomen, ground glass opacities, and calcifications. Only one infant had no abnormalities on X-ray. Those without pneumoperitoneum on X-ray underwent surgical operations based on presentations and clinical assessment findings. Almost all infants (75%) required a transfusion during their course (Table 3).

While colon was the most common part of the intestine perforated (30% colon, 15% cecum), the ileum was perforated in 25% of the neonates (Fig. 1). The patients who had perforations on the ileum or colon had a stoma placed by exteriorizing the perforation. All the patients who had a cecal perforation had biopsies taken and these were positive for Hirschsprung disease. Of the neonates that got post-operation complications, three had local wound sepsis while one developed anemia, but these

Table 3 Clinical course of the babies

X-ray findings (n, %)		
No abnormalities	1	5%
Pneumoperitoneum	12	60%
Dilated bowel	2	10%
Other abnormality	3	15%
Missing	2	10%
Received transfusion (n, %)		
Yes	14	75%
No	5	25%
Missing	1	5%
Outcome (n, %)		
Died	11	55%
Discharged	9	45%

recovered while on the unit and were among those who were discharged home. Fifty-five percent of the patients in this cohort died.

Discussion

Neonatal bowel perforations are a large contributor to the surgical disease burden among children and have a high fatality rate, but little information is known about its presentation in low- and middle-income countries. This is one of the first studies to describe the epidemiology of neonatal bowel perforation from a tertiary hospital in Uganda.

We found a small male predominance, though there is no statistical difference between male and female as per this cohort. This is comparable to other gastrointestinal perforation studies done elsewhere [12, 13]. Of note, a

Table 2 Maternal factors

Maternal age (M, IQR)	30	24–33
Received antenatal care (n, %)		
Yes	20	100%
No	0	0%
Prenatal folic acid (n, %)		
Yes	19	95%
No	0	0%
Missing	1	5%
Prenatal medication use (n, %)		
Yes	4	20%
No	16	80%
Intra-partum complications (n, %)		
None	14	70%
Malaria	3	15%
Other	3	15%

Location of Perforation

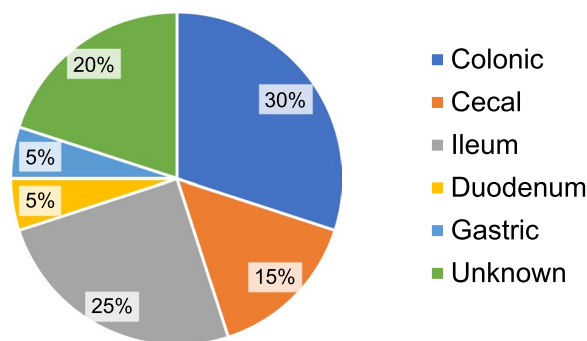


Fig. 1 Location of the bowel perforation. The figure shows the location of the bowel perforation as identified during the surgical operation of the baby. The colon was the most commonly identified perforation site. There were other perforations (unknown) that could not be identified, and this was either because the patient died before laparotomy or at operation there was a frozen abdomen

majority (80%) of our patients were term neonates, which seems to be contrary to the risk profile, as both SIP and NEC causing perforations appear to be more common in preterm neonates [1]. The higher prevalence of term neonates may be due to the higher likelihood of survival to presentation, as frequently these patients have to travel long distances in order to reach the tertiary health facility. Nevertheless, almost all of the patients were referred in from peripheral health facilities soon after birth, which could explain the early presentation at less than 7 days of life. The average age at diagnosis has been recorded to be 5 days in different studies [2]; however, the mean age at diagnosis for this cohort was 7.85 days. The mean age of presentation is skewed due to the few that arrived when they are many days old, with one even coming at 28 days of age.

Most patients had a birth weight above 2.5 kg, which was consistent with the fact that our cohort had many more term babies than preterm babies. This finding is similar to other studies that have shown significantly more babies with normal birth weight developing bowel perforations than those of low birth weight [13]. This could be because in our low resource setting, term babies are more likely to survive the neonatal period than preterm newborns. Pneumoperitoneum occurred in an average 60% of cases, which corroborated other reports suggesting 80% of cases [1, 12]. The next common finding in our cohort was dilated bowel. There were also instances of having no identifiable radiological findings on abdominal plain film, and this has been documented in other studies [13].

As with prior literature, the most common site of perforation is the colon [1]. There are also reports that document equal occurrence of perforations on ileum and colon [14], and with others showing a higher occurrence in the ileum [2]. In our setting as we report, the colon was the most common site for the perforations. However, perforation anatomic location was diverse ranging from gastric to rectal perforations, which may be explained by the mixed etiology and sites of perforation.

All mothers had access to antenatal care, and almost all mothers (95%) were able to receive folic acid. Only a minority of mothers took medications during pregnancy and 15% received treatment for malaria in the perinatal period. This finding suggests that maternal health may not be a large contributing factor to the likelihood of developing neonatal bowel perforation.

Majority of our babies with bowel perforations had blood group O+, suggesting the need for further research to study the relation between blood group and disease states in the neonatal period.

Outcome of mortality has been reported to be as high as 70% in some studies [12]. In our study, the mortality

rate was still high at 55%. This is likely exacerbated by lack of resources and human capital to provide the neonatal intensive care that these patients needed. Furthermore, the lack of parenteral nutrition severely lowered the chances of survival while awaiting bowel function to recover.

Limitations of this study include the single-center nature which may reduce generalizability. Nevertheless, cases are referred from across the country to this national referral center, so a representative sample of the nation's disease burden is still likely. The small number of cases also reduces the power to discern differences between groups and to make substantial associations. Furthermore, the retrospective observational design does not allow for prospective collection of data, which limits the type of clinical data that could be collected. Relatedly, missing data from chart review opened the potential for selection bias.

Conclusion

Outcomes of bowel perforations among neonates are still dismal. Published information on neonatal bowel perforations in our low-resource setting is modest. Cognizant of the findings with many term babies and no evidence of perforation on X-ray, health workers taking care of newborns should maintain a high index of suspicion for gastrointestinal injuries and also refer these patients to a tertiary health facility at the earliest opportunity as this will likely improve outcomes.

Abbreviations

VLBW	Very low birth weight
ELBW	Extremely low birth weight
NEC	Necrotizing enterocolitis
SIP	Spontaneous intestinal perforation
HIC	High-income countries
LMIC	Low- and middle-income countries
MREC	Mulago Hospital Research and Ethics Committee

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Authors' contributions

IO came up with the idea for this study. IO, RN, and SN collected the data for this study. IO and CS completed data analysis. IO, CS, JS, AW, PK, and NK proofread the manuscript for publication. All authors have read and approved the manuscript.

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Availability of data and materials

Data is available from the hospital pediatric database and the hospital record registry.

Declarations

Ethics approval and consent to participate

Approval was from Hospital Research and Ethics Committee through the Pediatric Surgery database approval. The database is approved for data collection and publication (MREC 464).

Consent for publication

Not applicable.

Competing interests

No author has any competing interest or conflict of interest to declare.

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