Original Article

The Incidence and Outcomes of Neonatal Intestinal Obstruction at Princess Marina Hospital Botswana

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Abstract

Background: Neonatal intestinal obstruction (NIO) is a surgical condition with good outcomes in well-resourced health facilities. In Botswana, there are no data on NIO. During the study, all NIO cases across the country were treated at Princess Marina Hospital (PMH), the nation's largest referral hospital. For NIO in Botswana. **Aim:** to determine the incidence, spectrum, outcomes and factors associated with mortality. **Methods:** A retrospective descriptive case series of neonates admitted between January 2010 and December 2012 to PMH with NIO. Data were collected from medical and surgical records. All cases under one month of age at admission were included. The incidence was calculated using national birth statistics and risk factors for mortality were explored using univariable and multivariable regression. **Results:** Seventy-nine NIO patients had a median age at admission of 3 days (IQR: 2-6), 49% were male, and median time from birth to surgery was 5 days (IQR: 3-6). The incidence of NIO was 5.96 per 10,000 live births. The most common diagnosis was jejunal obstruction (35%). In-hospital case fatality rate was 37%. In a multivariable model that included birth weight, time to surgery and maternal HIV status, only birth weight of >2500g was significantly associated with survival (OR=25.7, 95% CI 2.71-243.1; p<0.01). **Conclusion:** In Botswana, the incidence of NIO is similar to that in other settings. Overall mortality is high and low birth weight confers risk for mortality. This study provides a platform for further research to study the trends of NIO and explore other factors that affect outcomes.

Keywords: Neonates, Atresia, Intestinal Obstruction, Birth Weight, Congenital

Introduction

In high income countries (HICs), NIO is often correctable with surgery. Outcomes of neonates requiring surgery have improved over recent decades due to advances in understanding neonatal physiology, electrolyte, fluid, and nutritional management, timely surgical interventions, improved anaesthetic care, and better intensive care facilities.[4,5] Mortality from NIO in HICs is below 15%, while in low- and middle-income countries (LMICs) mortality remains as high as 40%.[4] In Africa, the high mortality rate has been attributed to late presentation for medical care, limited access to specialized neonatal intensive care unit (NICU) equipment, and fewer NICU staff.[6]

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Botswana is an upper middle-income, politically stable country in Southern Africa. The health care system is based on a primary health care model with most of the population living within 8km of a health facility. Princess Marina Hospital (PMH), one of the two tertiary hospitals in the country, is a 530-bed facility in the capital city, Gaborone. To date, there are no studies on the incidence or outcomes of NIO in Botswana. Until the end of 2012, PMH was the only hospital in the country with specialized paediatric surgery services. Neonates with symptoms of bowel obstruction, such as bilious vomiting, abdominal distension, or failure to pass meconium,

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were admitted to the PMH neonatal unit from private clinics and public hospitals across the country. Thus, all cases of NIO in Botswana were referred to PMH, thereby providing a unique opportunity to investigate this condition on a national level. By reviewing all cases of neonates admitted to PMH with confirmed or suspected NIO, the aim of this study was to estimate, for the first time, the burden and clinical outcomes of NIO in Botswana. In particular, we describe the causes of neonatal intestinal obstruction by post-surgical diagnosis, length of stay, case fatality rate, and factors associated with survival. Then, using national birth cohort statistics, we estimate the national incidence of NIO per 10,000 live births.

Methods

This was a retrospective descriptive case series of intestinal obstruction in the neonatal unit of PMH between 1st January, 2010 and 31st December, 2012. Retrospective data were collected from operating theatre logbooks, neonatal ward admission records, and death registers. Patients were included if they were aged ≤ 28 days at admission and were admitted for suspected intestinal obstruction due to presenting with bilious emesis, abdominal distension, or failure to pass meconium. Patients with a diagnosis of paralytic ileus or necrotizing enterocolitis were excluded from the study.

Data collection forms were completed to obtain variables such as age, gender, gestation, birth weight, maternal HIV status, place of referral, date of admission, date of discharge, and time from birth to surgery. Maternal HIV status was routinely included in neonatal admission records based on verbal report and antenatal records. Outcomes, namely discharge from hospital or death before discharge, were also recorded. For those who had surgery, dates of surgery and intraoperative diagnosis were recorded. When patients' medical files were not available, ward mortality registers and operating theatre logbooks were used to provide additional information. The data were recorded in a de-identified excel spreadsheet. Baseline characteristics were summarized using standard descriptive statistics. Continuous data were expressed as mean ± standard deviation (SD) when data were normal in distribution and median with interquartile range (IQR) when data were not normally distributed. Categorical data were reported using percentages. Data were analyzed using STATA version 12.0 (College Station, TX) with a p value of <0.05 deemed significant. Uni-variable and multi-variable analysis assessed the potential impact on survival of factors such as time to surgery from birth, birth weight, gestation, and maternal HIV status. The incidence of NIO per 10,000 live births was calculated using the total number of NIO cases born in a year and the total number of live births in Botswana during the same year. The live birth data were obtained from Botswana's National Statistics Office.[7] In-hospital case fatality rate (CFR) was calculated using the total NIO deaths and the total NIO admissions during the same period. Ethical approval was obtained from institutional review boards at the Botswana Ministry of Health, PMH, and the University of Botswana.

Results

Overall, 126 patient records were screened for enrollment into the study. Of these, 93 patients had NIO and 79 met the study eligibility criteria. Reasons for exclusion are summarized in Figure 1. Of the 79 patients, complete medical records were found for 55 (70%) and unit registers provided basic outcome data for the remaining (30%). The demographic data of the 79 patients are summarized in Tables 1A and 1B. There was no significant gender difference, with 39 (49%) being males. Of the patients whose birth weight was known, 32 (41%) had normal birth weight and, where HIV status was known, 27 (34%) were HIV exposed

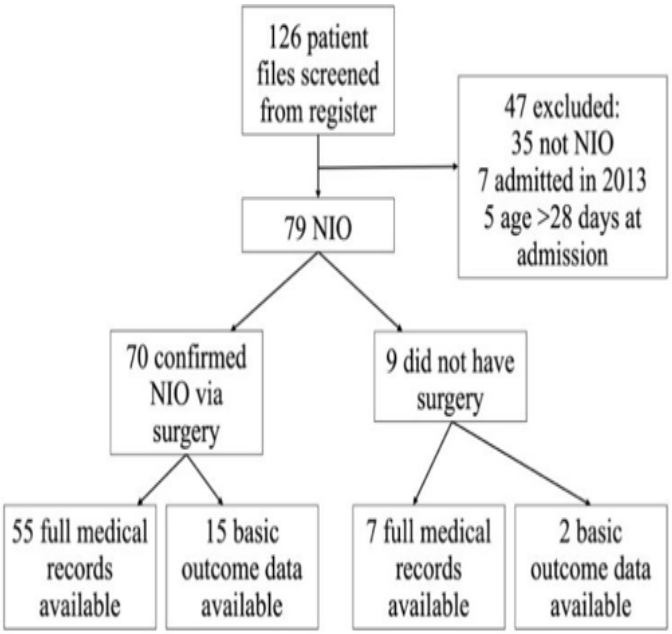


Figure 1. Study flow diagram showing enrolment of patients with suspected NIO

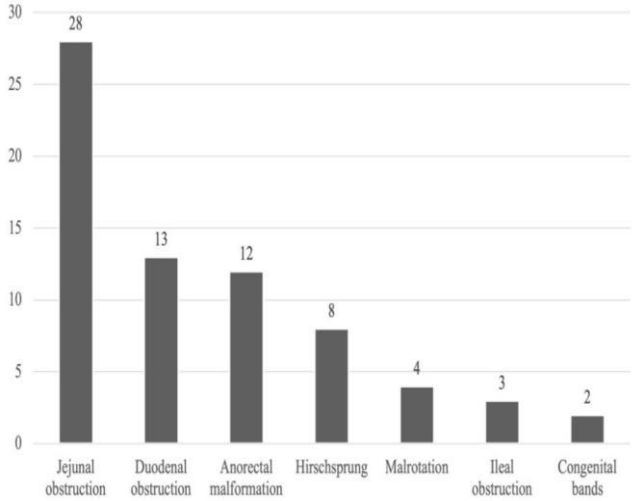


Figure 2. Pie chart demonstrating the frequency of the different diagnoses (n=70).

Table 1: Characteristics of a cohort of neonates with intestinal obstruction at Princess Marina Hospital, 2010-2012.

Variable	Category	Frequency n=79 (%)[2]	Summary statistics
Gender	Male/female	39 (49) / 40 (51)	
Birth weight (g)			
Median (IQR)	-	-	2559 (2015-3110)
Birth weight category	<2500	32 (41)	
	≥2500	32 (41)	
	Unknown	15 (19)	
Age at PMH presentation			
Median (days - IQR)	-	-	3 (2-6)
Age category (days)	≤3	49 (62)	
	>3	27 (34)	
	Unknown	3 (4)	
Had surgery	Yes	70 (89)	
	No	9 (11)	
Age on surgery day (n=69)			
Median (day - IQR)	-	-	5 (3-9)
Age category (days)	≤3	19 (24)	
	>3-≤7	31 (39)	
	>7	19 (24)	
	Unknown	10 (13)	
Days from admit-surgery			
Median (IQR) n=65	-	-	2 (1-5)
Time category (days)	≤3	46 (58)	
	>3 to ≤7	16 (20)	
	>7	4 (5)	
	Unknown	4 (5)	
	No surgery done	9 (11)	
Length of stay (days)			
Median (IQR), n=64	-	-	23 (13-36)
LOS category (weeks)	≤1	10 (13)	
	>1 to ≤2	11 (14)	
	>2 to ≤4	18 (23)	
	>4	25 (32)	
	Unknown	15 (19)	
Maternal HIV status	Positive	27 (34)	
	Negative	35 (44)	
	Unknown	17 (22)	

PMH: Princess Marina Hospital, NRH: Nyangabgwe Referral Hospital, IQR: Interquartile range, LOS: length of stay, g: gram.

Table 2. Diagnostic types, length of stay and survival outcomes of NIO (n=79).

Diagnosis	n	Median length of stay in days (IQR)	Mean length of stay in days (SD)	Case fatality rates n (%)
Cohort overall		23 (13-37)	25 (19)	29 (37)
By diagnosis:				
Jejunal obstruction	28	31 (12-38) *	31 (21) *	14 (50)
Duodenal obstruction	13	38 (20-57) *	36 (19) *	5 (38)
ARM	12	23 (15-41) *	27 (19) *	2 (17)
Hirschsprung	8	18 (14-28)	22 (13)	1 (13)
Malrotation	4	15 (14-18)	16 (3)	0
Ileal obstruction	3	31(21-41) *	31 (14) *	0
Congenital bands	2	17 (8-25)	17 (12)	0
Did not have surgery	9	0 (0-1)	0	7 (78)

IQR: interquartile range, SD: standard deviation, ARM: anorectal malformation. Note: *excludes unknown LOS: 3 in duodenal obstruction, 6 in jejunal obstruction, 1 in ileal obstruction, 3 in ARM and 2 in those who did not have surgery

Table 3. Incidence of neonatal intestinal obstruction in Botswana from 2010 to 2012

Year	**Number of NIO cases**	**Birth cohort**	**Estimated incidence of NIO per 10 000 live births**
2010	21	52 628	3.99
2011	28	39 168	7.15
2012	30	40 856	7.34
Total	79	132 652	5.96

Table 4. Univariate and multivariate summary of factors potentially associated with survival

Risk factors	**Univariate**		**Multivariate**	
	Odds ratio (95% CI)	p-value	Odds ratio (95% CI)	p-value
Birth weight (grams)				
< 2500g	1		1	
≥ 2500g	9.00 (2.73, 29.67)	<0.01	25.67 (2.71, 243.06)	<0.01
Time to surgery from birth (hours)				
≤72	3.27 (0.84, 12.72)	0.09	1.22 (0.15, 10.08)	0.86
>72	1		1	
Maternal HIV status				
Positive	0.32 (0.11, 0.94)	0.04	0.59 (0.14, 2.54)	0.48
Negative	1		1	

Note: All 3 variables (birth weight, time to surgery and maternal HIV status) were included in the multivariate model.

A total of 38 (48%) patients were from the PMH catchment area of southern Botswana, with 13 (16%) born at PMH. The most common diagnosis was jejunal obstruction in 28 (35%), followed by duodenal obstruction in 13 (16%) and anorectal malformation in 12 (15%, Figure 2). For the cohort overall, the median age at presentation to the PMH neonatal unit was 3 days (IQR 2-6, Table 1). The median age at presentation was older for malrotation with a median of 21 days (IQR 12-26) and congenital bands with a median of 26 days (IQR 25-26). The overall median age at surgery was 5 days (IQR 3-6). To estimate incidence, we used national annual birth data with a range of 39168 to 52628 births per year between 2010 and 2012.[7] During the same three-year time period, 79 of these births had NIO. The annual incidence of neonatal intestinal obstruction was therefore 3.99 to 7.34 per 100 000 (Table 2). For clinical outcomes, length of stay and survival were assessed in all 79 subjects (Table 3). The median length of stay was 23 days (IQR 13-26). Patients with duodenal obstruction had the longest median length of stay, at 38 days (IQR 20-57). Twenty-nine patients died before discharge, yielding an overall case fatality rate (CFR) of 37%. The CFR for those who had surgery was 31% (22/70) compared to 78% for those who did not. As illustrated in Table 3, all patients with malrotation, ileal obstruction, and congenital bands survived. The CFRs for duodenal obstruction, ARM and Hirschsprung's disease were 38, 17 and 13% respectively. For the patients who had surgery, the highest CFRs were seen in patients with jejunal obstruction (50%).

The seven patients who did not have surgery died within 24 hours of admission. Three were resuscitated unsuccessfully upon arrival in the neonatal unit, three were too unstable for surgery and one patient died in the operating theatre before surgery was initiated. Four of the seven patients were more than three days old at admission, 4/7 were referred from Nyangabgwe Referral Hospital, which serves as the referral center for Northern Botswana, 3/7 were male, had low birth weight (defined as <2500g), and 5/7 were HIV exposed.

Using univariate analysis, there was a strong correlation between birth weight and survival for this cohort of patients with NIO (Table 4). There was a 38% survival rate in those with birth weight <2500g as compared to 84% in those with birth weight ≥2500g. The odds ratio (OR) of survival was 9-fold higher (OR=9.0, 95% confidence interval [CI] 2.73-29.67) in patients with a birth weight ≥2500g. HIV exposed patients had less chance of survival compared to HIV unexposed patients (OR 0.32, 95% CI 0.11-0.94). When using a 72-hour cut point, there was an inverse relationship between time from birth to surgery and survival, but it was not statistically significant (p=0.09). Multivariable analysis including birth weight, time from birth to surgery and HIV exposure in the model showed that birth weight ≥2500g was a significant predictor of survival (OR=25.67; 95% CI 2.71, 243.06).

Discussion

This is the first study investigating NIO in Botswana. Unlike other institution-based studies,[7-10] we were able to extrapolate the findings of this single centre to the national level because all national cases were referred to PMH. The estimated overall national incidence of NIO during the study period was 5.96 per 10,000 live births. In sub-Saharan Africa, there is a paucity of research and literature on neonatal surgical conditions and most countries in this region do not have national registries for congenital abnormalities.[4] The reported incidence of 5.96 per 10,000 live births falls comfortably within the world-wide reported range of 1.3 to 19 per 10,000 infants per year as reported in a review by Stewart *et al*.[8] The incidence of NIO in Botswana is higher than the 2.9 per 10 000 reported in an Australian population-based study of more than one million births, though that study excluded all large bowel obstruction.[9]

With regards to the demographics of our study cohort, 49% were male, which is in contrast to a slight male preponderance reported in some studies.[10,11,12] The median birth weight was 2.6 kg, which is similar to studies in India where the median birth weight was 2.5 to 2.6 kg.[13,14] The median age of presentation of 3 days reported in our Botswana study is earlier than those reported in other studies done in LMIC, where the median age of presentation varied between 4 and 6 days of life, speaking perhaps to a more effective national referral system in Botswana than in these other countries.[10,14] While there is no previous study that reported the relationship between HIV status and NIO, in this study 34% of NIO cases were exposed to HIV, which was consistent with Botswana's HIV prevalence of around 30% among pregnant women between 2010-2012.[15]

Regarding the aetiologies of NIO, the most common lesion in this study was jejunal atresia (35%), which was also the lesion with the highest case fatality rate of 50%. Jejunal atresia is postulated to occur as a result of an intrauterine ischemic insult and is less commonly associated with other congenital abnormalities.[16] The second most common cause of NIO in this Botswana series was duodenal atresia, which accounted for 16% of cases. Duodenal atresia is thought to be caused by failure of recanalization of the solid cord stage of the duodenum at the end of the first trimester, and greater than half are born with other major congenital anomalies.[17] Associated congenital abnormalities were not documented in this Botswana study but it would be important to assess them in future studies. In contrast to our findings, most studies have shown that ARM is the most common etiology, accounting for 27 to 69% of NIO cases.[10,12,18,19,20] ARM accounted for 15% of NIO cases in this study. Similarly, several studies from Nigeria and Bangladesh showed that Hirschsprung's disease was the second most common lesion, but it accounted for only 10% of cases in this study.[11, 19, 20, 21]

The mortality rate in this study was high at 37%. This is similar to some institution-based studies in Nigeria, which also reported mortality greater than 30%.[14,19] However, it is higher than most studies, which have reported a CFR under 30%.[3,5,20,22] Early prenatal diagnosis and planned delivery of neonates with NIO in a fully equipped paediatric centre has improved survival in HIC.[23] In contrast, Botswana, like many countries in Africa, faces a lack of skilled manpower, equipment, and facilities, which may result in later diagnosis and poorer surgical outcomes.[4]

In this study, maternal HIV status, time to surgery, and birth weight were associated with mortality in univariate analysis. No prior studies in the literature have assessed HIV as a potential factor affecting outcomes of NIO. The literature is inconclusive about whether there is a high prevalence of birth defects among HIV exposed infants.[24] In our study, data about maternal antiretroviral drugs were not collected, limiting our ability to assess this possible correlation. Despite the median age of presentation to PMH being 3 days, the median age at surgery was 5 days. This delay could be attributed to the need to stabilize patients, the low number of paediatric surgeons at PMH, and the availability of theatre time. In this cohort, 84% of patients were not born at PMH and thus had to be transported from other facilities that may have lacked the expertise to stabilize sick neonates.

Low birth weight was the only significant factor in multivariable analysis. Similar associations between NIO mortality and low birth weight have been reported in the literature from Australia, the USA and India.[5,9,22] Low birth weight can be due to prematurity or intrauterine growth restriction and is often associated with congenital abnormalities. In this study, neither gestational age nor associated congenital abnormalities was assessed due to inconsistent recording. These factors should be collected in future studies on NIO in Botswana.

This study had the inherent limitations of a retrospective study, which included incomplete data sources and missing records. Due to incomplete records and inconsistent recording of data, factors such as severe dehydration, severe anaemia, and sepsis could not be analysed. Other important factors that could have affected outcomes such as the length of stay in the intensive care unit, duration of ventilation, other congenital abnormalities, co-morbidities and post-operative complications were not captured in this study. Maternal HIV status was obtained antenatally, and hence the lack of postnatal testing could have underestimated the prevalence of HIV-exposed babies. Furthermore, we could not account for cases of NIO that did not reach PMH; thus, our reported incidence might be an underestimation.

Conclusion

This study provides an overview of the magnitude of NIO in Botswana and highlights the challenges that are contributing to poor outcomes. These challenges are not unique to NIO but can be extrapolated to other neonatal surgical and non-surgical conditions. The incidence of NIO in our institution and nationally is comparable to that reported in other institutions and countries. The mortality is as high as in other African countries. Low birth weight is a significant factor affecting outcome. This study provides a platform for further research to study the trends of NIO and explore other factors that affect outcome.

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Conflicts of interest

There are no conflicts of interest.

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