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Neural tube defects in Uganda: follow-up outcomes from a national referral hospital

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OBJECTIVE Children with neural tube defects (NTDs) require timely surgical intervention coupled with long-term management by multiple highly trained specialty healthcare teams. In resource-limited settings, outcomes are greatly affected by the lack of coordinated care. The purpose of this study was to characterize outcomes of spina bifida patients treated at Mulago National Referral Hospital (MNRH) through follow-up phone surveys.

METHODS All children presenting to MNRH with NTDs between January 1, 2014, and August 31, 2015, were eligible for this study. For those with a documented telephone number, follow-up phone surveys were conducted with the children's caregivers to assess mortality, morbidity, follow-up healthcare, and access to medical resources.

RESULTS Of the 201 patients, the vast majority (n = 185, 92%) were diagnosed with myelomeningocele. The median age at presentation was 6 days, the median length of stay was 20 days, and the median time to surgery was 10 days. Half of the patients had documented surgeries, with 5% receiving multiple procedures (n = 102, 51%): 80 defect closures (40%), 32 ventriculoperitoneal shunts (15%), and 1 endoscopic third ventriculostomy (0.5%). Phone surveys were completed for 53 patients with a median time to follow-up of 1.5 years. There were no statistically significant differences in demographics between the surveyed and nonrespondent groups. The 1-year mortality rate was 34% (n = 18). At the time of survey, 91% of the survivors (n = 30) have received healthcare since their initial discharge from MNRH, with 67% (n = 22) returning to MNRH. Hydrocephalus was diagnosed in 29 patients (88%). Caregivers reported physical deficits in 39% of patients (n = 13), clubfoot in 18% (n = 6), and bowel or bladder incontinence in 12% (n = 4). The surgical complication rate was 2.5%. Glasgow Outcome Scale–Extended pediatric revision scores were correlated with upper good recovery in 58% (n = 19) of patients, lower good recovery in 30% (n = 10), and moderate disability in 12% of patients (n = 4). Only 5 patients (15%) reported access to home health resources postdischarge.

CONCLUSIONS This study is the first to characterize the outcomes of children with NTDs that were treated at Uganda's national referral hospital. There is a great need for improved access to and coordination of care in antenatal, perioperative, and long-term settings to improve morbidity and mortality.

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KEYWORDS follow-up; LMIC; low-middle-income countries; myelomeningocele; neural tube defects; Uganda

Spina bifida or myelomeningocele describes a class of neural tube defects (NTDs) that are caused by incomplete neural tube closure during the 4th week of pregnancy and result in various levels of neurological deficit. Adequate folic acid consumption during early pregnancy prevents the occurrence of NTDs. However, because the neural tube closes by week 4 of fetal development, early access to antenatal care (ANC) is crucial in the prevention or early detection of NTDs.[8] In Uganda, 4 routine ANC visits are recommended as part of the national clinical guidelines, with the first occurring between weeks 10 and 20 of gestation.[11] Findings from the 2016

ABBREVIATIONS ANC = antenatal care; GOS-E Peds = pediatric revision of the Glasgow Outcome Scale–Extended; MNRH = Mulago National Referral Hospital; NTD = neural tube defect; SSA = sub-Saharan Africa; VP = ventriculoperitoneal.

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Uganda Demographic and Health Survey indicated that while 97% of Ugandan women accessed ANC at least once, only 60% completed the recommended 4 visits. The reasons for not attending visits included not knowing when to obtain ANC, believing ANC is unnecessary, and financial burden of transport.[7] Because the neural tube closes by week 4 of fetal development, there is no clinical or educational infrastructure in place in Uganda for the prevention and/or early detection of NTDs. This likely contributes to the trend toward a higher incidence of NTDs in sub-Saharan Africa, although published data remain limited.[4,15,18]

The severity of NTDs depends on the level and degree of spinal cord exposure, with symptoms ranging from mild cosmetic symptoms, such as dimples or tufts of hair on the lower back in the case of spina bifida occulta, to severe paralysis, chronic infections, incontinence or retention, and paralysis in the case of rachischisis. Patients are also at increased risk for complications such as hydrocephalus, with the majority of patients with open spina bifida developing hydrocephalus that requires ventriculoperitoneal (VP) shunts.[5,14] In an attempt to mitigate the complications associated with open spina bifida, the standard of care in upper-middle-income countries in the acute phase includes diagnosis in utero, cesarean section rather than vaginal birth to avoid infection, surgical closure of the open lesion within 24 hours, and continued monitoring for the development of hydrocephalus, with surgical intervention as needed. Moreover, due to the complexity of their diagnoses, patients in upper-middle-income countries are monitored by multiple highly trained specialty healthcare teams (e.g., neurosurgery, urology, orthopedics, pediatrics, physical therapy). In resource-limited settings, outcomes are greatly affected by the lack of coordinated care.

Outcomes research on pediatric spina bifida in sub-Saharan Africa (SSA) remains limited. A 2011 study in Eastern Uganda found the regional under-five mortality rate to be 37% for infants with treated spina bifida.[15] Of note, this rate was in a setting where medical care for spina bifida is relatively more accessible due to the presence of a regional pediatric hospital. Given that outcomes are known to greatly improve with initial survival and community-based support, it is realistic to estimate that other districts of Uganda with even less access to community-based rehabilitation most likely have higher associated mortality.

In a 10-year survival study of Ugandan infants following myelomeningocele closure, Sims-Williams et al. found that most deaths were not directly related to myelomeningocele, but rather to infection and neglect.[10] Furthermore, posthospitalization complications arise in SSA due to cultural beliefs or poverty, resulting in improper or altogether lack of treatment.[3] Stigmas surrounding medical disabilities and birth defects further complicate spina bifida treatment and outcomes and severely impact the lives of patients and their caregivers, particularly those from lower socioeconomic backgrounds.[6,13] However, there is evidence that community-based support and follow-up for patients and their families significantly improve patient survival after surgical management.[1] The outcomes of pediatric spina bifida in Uganda have yet to be elucidated at a national level.

In the present study, we sought to assess the mortality and quality of life of pediatric spina bifida patients presenting to Mulago National Referral Hospital (MNRH) in Uganda through a quick and affordable phone follow-up survey.

Methods

Patient Population and Study Setting

As the sole national referral hospital, MNRH serves as a tertiary referral hospital for the entire country, with most patients reporting low socioeconomic status. MNRH is located in Kampala, the capital of Uganda, in the central region. All patients presenting with spina bifida between January 1, 2014, and August 31, 2015, were entered into a database along with demographic information (age, sex, district of origin, telephone number), dates of admission, surgery, and discharge, diagnosis, treatment, and outcome.

Ethics Approval

Ethics approval was provided by the Stanford University IRB in the United States and the Makerere University IRB in Uganda.

Data Collection

Data collection was completed as described by Xu et al.[17] Briefly, phone surveys were developed after reviewing the literature and survey designs, consulting a content expert, and performing a Ugandan collaborator review for adaptation to this setting. Surveys inquired about caregiver demographics, follow-up healthcare, morbidity and mortality, quality of life, and access to home health resources. Calls were conducted in the participant's language by Ugandan research staff.

Statistical Analysis

Data analysis was completed using Microsoft Excel 2013. Descriptive statistics were calculated for demographics, mortality, and follow-up healthcare (Tables 1–3). Chi-square statistics were calculated between surveyed and nonrespondent groups; $p < 0.05$ was considered significant. Functional outcomes were assessed using the Glasgow Outcome Scale—Extended pediatric version (GOS-E Peds).[2]

Results

Inpatient Demographics

During the study period, 201 spina bifida patients (77 females, 38%) presented to MNRH with a median age of 6 days (Table 1). The median length of stay was 20 days. Ninety-two percent of patients (n = 185) had a myelomeningocele, with 87 patients (43%) presenting with concurrent myelomeningocele and hydrocephalus; 9 patients presented with an encephalocele (4%), 3 with cranium bifidum (1%), 2 with spina bifida occulta (1%), and 2 with anencephaly (1%).

One-hundred six patients (53%) were born at term, 2 were born prematurely (1%), and 93 (46%) did not have a documented gestation age. Similarly, 96 patients were

TABLE 1. Inpatient demographics

	Value*	Percentage
Patient demographics		
No. of patients treated	201	
Female	77	38%
Male	124	62%
Median age, days	6	
Discharged w/ documented phone no.	78	
Median length of stay, days	20	
Diagnosis category		
MMC	185	92%
MMC & hydrocephalus†	87	43%
Encephalocele	9	4%
Cranium bifidum	3	1.5%
Spina bifida occulta	2	1%
Anencephaly	2	1%
Gestation age		
Term	106	53%
Premature	2	1%
Not specified	93	46%
Mode of delivery		
Spontaneous vaginal delivery	96	48%
Cesarean section	8	4%
Not specified	97	48%
Treatment‡		
Surgical intervention	102	51%
Defect closure‡	80	40%
VP shunt‡	32	15%
ETV	1	0.5%
Not specified	99	49%
Outcome		
Died	4	2%
Discharged	103	51%
Unknown	94	47%

ETV = endoscopic third ventriculostomy; MMC = myelomeningocele.
* Values are presented as the number of patients unless specified otherwise.
† A subset of patients with myelomeningocele was concurrently diagnosed with hydrocephalus.
‡ A subset of patients underwent both defect closure and VP shunt placement during hospitalization (11, 5%).

TABLE 2. Patient demographics at follow-up

	Value*	Percentage
Patient demographics		
No. of patients w/ survey results	53	
Female	17	32%
Male	36	68%
Median age, yrs	1.76	
Median time to follow-up, yrs	1.51	
Diagnosis category		
Myelomeningocele (MM)	39	74%
MM & hydrocephalus	10	19%
Encephalocele	3	6%
Cranium bifidum	0	0%
Spina bifida occulta	1	2%
Anencephaly	0	0%
Region of residence		
Central	38	72%
Western	13	25%
Eastern	1	2%
Northern	1	2%
Caregiver religion		
Christian	8	15%
Muslim	45	85%
Caregiver education		
None	2	4%
Primary	18	34%
Secondary	27	51%
Diploma/certificate	6	11%
Caregiver occupation		
Business	21	40%
Farmer	16	30%
Salaried worker	7	13%
Skilled worker	1	2%
Unemployed	8	15%

* Values are presented as the number of patients unless stated otherwise.

born via spontaneous vaginal delivery (48%) and 8 via cesarean section (4%); the delivery method was not specified for 97 children (48%).

A total of 113 procedures were performed in 102 patients, accounting for over half of the patients admitted for spina bifida (n = 102, 51%): 80 defect closures (40%), 32 ventriculoperitoneal (VP) shunts (15%), and 1 endoscopic third ventriculostomy (0.5%). Time-to-surgery data were available for 30 patients (15%), with a median time of 10 days to surgery (range 1–33 days).

Four (2%) patients died in the hospital, 103 (51%) were discharged, and 94 were not specified (47%). Of those who survived their hospital stay, 78 had a phone number on file.

TABLE 3. Mortality

	Value*	Percentage
Follow-up mortality		
Overall mortality	20	38%
30-day mortality	12	23%
1-yr mortality	18	34%
Median discharge to death, days	20	
Cause of death		
Spina bifida complications	14	70%
Surgical site infection	3	15%
Other infection	2	10%
Intestinal complications	1	5%

* Values are presented as the number of patients unless stated otherwise.

Follow-Up Demographics

A total of 53 patients (17 female, 32%) were surveyed with a median time to follow-up of 1.51 years (Table 2). Of these patients, 49 (92%) were diagnosed with a myelomeningocele, of whom 10 (19%) had concurrent myelomeningocele and hydrocephalus. Three patients (6%) were diagnosed with an encephalocele, and one (2%) with spina bifida occulta. Three-quarters of patients (n = 40) had surgical intervention: 35 (66%) defect closures and 11 (21%) VP shunts, with 6 (11%) of those patients undergoing both defect closure and VP shunt placement.

Most patients (72%, n = 38) resided in the central region, where MNRH is located, with 25% (n = 13) in the western region and 2% each in the eastern and northern regions (n = 1 each). The mother was the primary caregiver for 92% of patients (n = 49), followed by the father for 8% of patients (n = 4). Eighty-five percent (n = 45) of caregivers had either primary or secondary education, 11% (n = 6) had a diploma or certificate, and 4% (n = 2) had no formal education. The most common caregiver occupations were business (40%, n = 21) and farming (30%, n = 16), followed by salaried work (13%, n = 7) and skilled work (2%, n = 1); 15% of caregivers (n = 8) were unemployed. There were no statistically significant differences between the surveyed and nonrespondent group demographics.

Mortality

At follow-up, 20 (38%) patients had died; the 30-day mortality rate was 23% (n = 12), and the 1-year mortality rate was 34% (n = 18; Table 3). The median time from discharge to death was 20 days. The leading cause of death reported was complications of the disease or surgical intervention (n = 17, 85%), with surgical site infections reported in 3 patients. Two patients died of other infections, and 1 died of intestinal complications.

There was no statistically significant difference in mortality between patients who underwent surgery (n = 40; 38% mortality) and those who did not (n = 13; 38% mortality) (p = 0.95). Similarly, there was no statistically significant difference in mortality between females (n = 17, 53% mortality) and males (n = 36; 31% mortality) (p = 0.12).

Follow-Up Healthcare

Of survivors, 91% (n = 30) have received healthcare since their initial discharge from MNRH: 27 caregivers (82%) reported a clinic visit, and 3 (9%) patients were readmitted (Table 4). Two of the readmitted patients received a VP shunt, and 1 (originally managed nonoperatively) underwent a myelomeningocele closure at a regional hospital. Three patients (9%) did not receive healthcare postdischarge. Two-thirds of patients (n = 22) returned to MNRH for their care, and 82% (n = 27) reported spina bifida as the reason for their visit. Caregivers of 2 patients (6%) cited hydrocephalus and 1 cited (3%) malaria as the reason for their visit.

Quality of Life Measures

At the time of follow-up, the average patient age was 1.76 years (range 1.19–3.23 years). Caregivers reported that 13 (39%) patients developed a physical movement problem. Fourteen (42%) patients were able to follow commands, and 30 (91%) could speak. With respect to psychosocial function, all patients (n = 33) were reportedly friendly, 30 (91%) played every day, 27 (82%) behaved well with parents, and 15 (45%) behaved well with siblings. GOS-E Peds scores were correlated with upper good recovery in 58% (n = 19) of patients, lower good recovery in 30% (n = 10), upper moderate disability in 9% (n = 3), and lower moderate disability in 3% (n = 1) of patients (Tables 4 and 5).

TABLE 4. Follow-up healthcare

	No. of Patients	Percentage
Follow-up healthcare		
Received healthcare	30	91%
Hospital admission	3	9%
Clinic visit	27	82%
Did not receive healthcare	3	9%
Returned to MNRH	22	67%
Reason for care		
Spina bifida	27	82%
Hydrocephalus	2	6%
Malaria	1	3%

Associated Conditions and Complications

Hydrocephalus was diagnosed in 29 (88%) patients, with 8 (24%) patients reporting increased head circumference at follow-up (Table 5). Six (18%) patients were found to have clubfoot, and scoliosis was reported in 1 (3%) patient. Bowel or bladder incontinence was present in 4 (12%) patients. Of the 40 patients who underwent surgery, 1 patient developed wound dehiscence and a CSF leak, resulting in a surgical complication rate of 2.5%.

Access to Home Health Resources

Of the 33 survivors, 5 patients (15%) reported access to home health resources postdischarge. Four patients received clubfoot braces: 3 at MNRH and 1 at Kalangala Medical Center. The patient who underwent surgery at the Mbale CURE regional hospital received monthly home visits.

Discussion

Our findings show that the availability of medical resources and documentation for spina bifida patients in Kampala, Uganda, is very limited, and that, unsurprisingly, the lack of resources and infrastructure translates to poor patient outcomes. Nearly half of our spina bifida patients were delivered vaginally, demonstrating a lack of antenatal care and counseling that these children should be delivered via cesarean section. The 1-year mortality rate for spina bifida patients at MNRH was 34%. This is moderately higher than that reported in similar studies, e.g., 29% in rural northern Tanzania and 27% in southern Nigeria, but far greater than that of high-income countries.

TABLE 5. Quality of life measures and associated conditions

	Percentage of Patients
Psychosocial function	
Friendly	
Plays every day	100%
Behaves w/ parents	91%
Behaves w/ siblings	82%
Neurological function	45%
Physical movement deficit	
Can follow commands	39%
Can say words	42%
Associated conditions	91%
Hydrocephalus diagnosis	
Increased head circumference	88%
Clubfoot	24%
Bowel or bladder incontinence	18%
CSF leak	12%
Wound dehiscence	6%
Seizures	6%
Scoliosis	6%

For comparison, a 2012 study in the United States reported a 1-year mortality rate of 6.4% in infants born with spina bifida between 1998 and 2002.[9,12,16] Interestingly, the mortality rate in the MNRH cohort is nearly 2-fold (34% vs 19%, respectively) that reported in recent studies from a regional pediatric neurosurgical center in Eastern Uganda where patients usually undergo surgery within 48 hours, are closely monitored for hydrocephalus, and have access to routine follow-up healthcare.[10] The marked difference in mortality between these 2 cohorts highlights the opportunity to better outcomes at a national level by improving coordination of care and timely access to surgery.

The leading cause of death in spina bifida patients at MNRH was reported to be spina bifida complications or surgical site infections (85%). Forty-three percent of patients at hospital admission were noted to have hydrocephalus, but at follow-up the eventual percentage of associated hydrocephalus was 88%. As only 15% received shunts at MNRH prior to discharge, with little clinical care received after discharge, compared to 97% of patients in the aforementioned Eastern Uganda study who underwent surgery for hydrocephalus, it is possible that the high mortality could be related to undiagnosed hydrocephalus.[10] For patients who did survive, although 39% of caretakers reported physical disabilities, only 4 patients total received assistive braces and only 15% had access to home health resources after discharge. This disparity emphasizes the dramatic unmet need for this population of patients.

GOS-E Peds scores fell in a bimodal distribution, with the majority of patients either dead at the time of follow-up or having mild disability and good recovery, with only 12% of caregivers reporting moderate disability and none reporting severe disability. This distribution suggests that within 1 year of discharge, patients either progress to death or recover many functions, with few patients able to continue living with moderate to severe disability in the community.

While it is encouraging that the majority of caregivers reported normal cognitive and social development in patient survivors, one of the key limitations to our study is that it is dependent on anecdotal reports of subjective interpretations by caregivers. Therefore, we were unable to obtain reliable, standardized neurological assessments of patients during follow-up. Moreover, due to the self-reported nature of the questionnaire, we were unable to reliably assess for patient neglect by the family or caregiver.

Many patients were discharged against medical advice and prior to receiving treatment. In our study, 48% had no documented disposition, either discharge or death. The lack of documented disposition mostly reflects the frequency of patients leaving the hospital against medical advice. Several factors can contribute to this phenomenon. One factor is pressure on mothers to return to their homes and families as they are typically the primary caretaker for other members of the family. Another significant factor can be financial limitation. Although evaluation and admission to the hospital is free, before surgery can be undertaken, the families had to gather money to pay for laboratory tests, CT scans, and purchase shunts, which may have become impossible for some families. These factors are further exacerbated by extraordinarily long wait times for surgery. Patients in this cohort waited a median time of 10 days to surgery, with some patients waiting over a month for surgical intervention. This delay likely contributed to the number of family members that chose to take their children home rather than to continue to wait for intervention. Since documentation was inconsistent, we cannot be certain that all 48% without documentation reflected families that left without medical treatment. Our results found that medical records at MNRH were not consistently implemented or maintained. These alarming results accentuate the need for proper medical record infrastructure as the basis for delivering care to low-middle-income countries. Proper training of medical professionals is important, but without transparent documentation of patient data and follow-up care, it is exceedingly difficult to identify problem areas to raise the standard of care meaningfully and consistently.

Conclusions

Patients with spina bifida in Uganda experience a lack of coordinated care prior to, during, and after birth, lack of timely access to surgery and longitudinal medical resources after discharge, and inconsistent medical documentation throughout. This shortfall culminates in a higher 1-year mortality compared with upper-middle-income countries and demonstrates the greater need for improved care in antenatal, perinatal, and long-term settings.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Grant, Xu, Vaca, Nalwanga, C Muhumuza, Kiryabwire, Ssenyonjo, Mukasa, M Muhumuza. Acquisition of data: Grant, Vaca, Nalwanga, C Muhumuza, Kiryabwire, Ssenyonjo, Mukasa, M Muhumuza. Analysis and interpretation of data: Xu, Vaca, He. Drafting the article: Xu, Vaca, He. Critically revising the article: Grant, Xu, Nalwanga, C Muhumuza, Kiryabwire, Ssenyonjo, Mukasa, M Muhumuza. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Grant. Administrative/technical/material support: C Muhumuza. Study supervision: Grant, Xu.

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