

Demographics, referral patterns and outcome of neural tube defect patients in Southwestern Uganda

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Abstract

Purpose

In Uganda, the burden of neural tube defects (NTDs) poses a serious neurosurgical and public health challenge; however, published data on this patient population is lacking. We sought to characterize the NTD patient population, maternal characteristics, referral patterns of these patients, and quantify the burden of NTDs in Southwestern Uganda.

Methods

A retrospective neurosurgical database at a referral hospital was reviewed to identify all patients with neural tube defects treated between 08/2016 and 05/2022. Descriptive statistics were used to characterize the patient population and maternal risk factors.

Results

232 patients were identified (121 male, 52.2%). Median age at presentation was 2 days (IQR: 1–8). 86.8% of NTD patients presented with spina bifida (n = 204) and 31 with encephalocele (13.2%). The most common location of dysraphism was lumbosacral (n = 180, 88%). Median length of stay was 12 days (IQR: 7–19). One-third of all patients presented from Isingiro, Mbarara, and Kasese. The median maternal age was 26 years (IQR: 22–30). The majority of mothers received only primary education (n = 100, 43.7%). The majority of mothers reported prenatal folate use (n = 158, 67.2%) and regular antenatal care (ANC) (n = 220, 93.6%), although only 23.4% underwent an antenatal ultrasound (n = 55). Of all patients, 80% were delivered vaginally (n = 188). Overall, 67.4% of patients were discharged (n = 157) and 10% died (n = 23).

Conclusions

This is the first study to describe the NTD patient and maternal population in Southwestern Uganda. A prospective case-control study is necessary to identify unique demographic and genetic risk factors associated with NTDs in this region.

Introduction

Neural tube defects (NTDs) are a class of birth defects caused by the incomplete closure of the neural tube between days 24 to 28 of development, at a time when most women are still unaware of their pregnancy [1]. The severity of neurological deficits and patient presentation associated with NTDs depends on the lesion level and the degree of spinal cord exposure. Symptoms of NTDs can range from

mild cutaneous stigmata in spina bifida occulta to paralysis, bladder/bowel dysfunction, hydrocephalus in open myelomeningocele [1].

It is estimated that globally 300,000 neonates are born with NTDs per year at a rate of 18.6 per 10,000 live births, with approximately 190,000 occurring in low-and-middle-income countries [2–5]. The prevalence of NTDs in Uganda has not been measured in a national study, but various hospital based surveillance studies have estimated it to range between 9.8 and 39.8 per 10,000 births [6–11]. Because spina bifida is a chronic condition, all affected infants require lifelong monitoring and management [4]. This results in a significant financial burden given the average cost of spina bifida over a child's lifetime is approximately \$791,000, including caregiver costs [12].

Since the 1960s, the prevalence of neural tube defects has declined significantly in some high-income countries (HICs), likely due to both an increase in folic acid supplementation, early detection via alpha-fetoprotein measurements and ultrasonography and subsequent increase in pregnancy terminations [13, 14]. In fact, in a model proposed by Blencowe et al., approximately half of the cases of NTDs in 2015 ended in elective termination for fetal anomalies [5]. These trends have not been witnessed at the same rates in low-and-middle-income countries (LMICs) in part due to lack of access to antenatal care (ANC), early prenatal diagnosis, and safe pregnancy termination.

The cause of NTDs is not completely understood, but studies have suggested environmental and genetic factors may play a role. Folic acid deficiency is one well-known risk factor associated with the development of NTDs, which has prompted the U.S. Public Health Service to recommend folic acid supplementation for all women capable of becoming pregnant [15, 16]. Other maternal risk factors for developing NTDs include smoking, obesity, various medications, lower socioeconomic status, micronutrient deficiency, environmental exposures, and history of children with NTD [4, 13, 17].

Although we have come a long way in understanding NTDs globally, there remains a paucity of data characterizing patients in LMICs. Since 2008, Duke Department of Neurosurgery has worked in Uganda to improve care for neurosurgical patients. In 2014, Duke established the Duke Global Neurosurgery and Neurology (DGNN) and formalized the educational partnership with Mbarara Regional Referral Hospital (MRRH). Since then there has been an effort to quantify the scope of neurosurgical disease in Southwestern Uganda and to standardize the treatment of neurosurgical patients via establishment of databases focused on various neurosurgical pathologies treated at MRRH. Given the lack of published data on NTDs in Uganda, our study aimed to describe the NTD population and their mothers in Southwestern Uganda over the past 5 years.

Methods

Setting

MRRH is a referral hospital for Western region of Uganda, with a catchment area of four million people [18–20]. It is a publicly funded hospital that is part of Uganda's decentralized, tiered public sector health

system consisting of health centers, district hospitals, regional and national referral hospital [18]. The most recent study calculated the hospital has a capacity of 600 hospital beds, 8 ICU beds and 8 operating theaters and has a surgical volume of 8515 operations per year [19]. The neurosurgery department was established in 2012, and currently consists of 2 neurosurgeons, 2 neurosurgical residents who rotate through MRRH, which is a College of East, Central, and Southern Africa (COSECSA) training site, 1 medical officer, and several nurses [21, 22]. Duke Division of Global Neurosurgery and Neurology established an academic partnership with MRRH in 2014 and established a prospective electronic neurosurgical database in 2016.

Data Collection

The DGNN/MRRH prospective neurosurgical database was reviewed to identify all patients with neural tube defects treated between 08/2016 and 05/2022. Information on patient demographics including referral location, neonatal delivery method, NTD clinical characteristics, neonatal clinical course, maternal characteristics were abstracted. Our main outcomes of interest were discharge disposition and length of stay. Descriptive statistics were used to characterize the patient and maternal population. Tableau used to perform geographic analyses of referral patterns.

Ethical Approval

Ethical approval was obtained from Mbarara University of Science and Technology Research Ethics Committee, Duke University Health System Institutional Review Board and the Uganda National Council of Science and Technology.

Results

Patient Demographics

232 patients with NTDs were treated at MRRH between August 2016 and May 2022, of which 121 were male (52.2%) (Table 1). Of all NTD patients, 86.8% presented with spina bifida (n = 204), while 31 patients presented with encephalocele (13.2%). Median age at presentation was 2 days (IQR: 1–8) for the entire patient cohort; median age at presentation for spina bifida and encephalocele was 2 days (IQR: 1–7) and 1 day (IQR: 0–24), respectively. The most common location of dysraphism was lumbosacral (n = 180, 88%), followed by thoracic (n = 13, 6%) (Fig. 1).

Referral Patterns

Patient were referred from a total of 33 districts in Southwestern Uganda and one patient presented from East Demographic Republic of Congo (Fig. 2). The most common referral district was Isingiro (n = 32, 13.9%), followed closely by Mbarara (n = 30, 13%) and Kasese (n = 24, 10.4%), and one third of all patients presented from one of these districts.

Maternal Characteristics

The median maternal age was 26 years (IQR: 22–30). The majority of mothers received only primary education (n = 100, 43.7%) while 5.7% of mothers had a college education (n = 13) (Table 1). Education level data was missing for 31.9% of mothers (n = 73). The median household size was 5 (IQR: 3–6). The majority of mothers reported prenatal folate use (n = 158, 67.2%) and regular ANC (n = 220, 93.6%), although only 23.4% underwent an antenatal ultrasound (US) (n = 55) (Fig. 3). In total, 17% (n = 30) and 12.3% (n = 29) of mothers reported prenatal malaria and HIV infections, respectively. Anti-epileptic medication use (n = 1, 0.4%) was uncommon in the maternal population.

Patient Outcomes

Eighty percent of patients were delivered vaginally (n = 188), 18.3% delivered via cesarean section (n = 32), and 1 patient had an unknown delivery method. Overall, 67.4% of patients were discharged (n = 157), 12.9% absconded (n = 30), 4.7% were transferred (n = 11), and 10% died (n = 23) (Table 2). Median length of stay was 12 days (IQR: 7–19). In regards to post-delivery management, 12 patients required a blood transfusion (n = 5.1%) and 22 required oxygen supplementation (n = 9.4%).

Discussion

There is limited published data on epidemiology of neural tube defects patients and maternal characteristics in rural Uganda. Since 2014, Duke Department of Neurosurgery has had a long-standing educational partnership with the Neurosurgery Department at MRRH. We have maintained a prospectively collected database of all patients treated by the department since 2016, including both adult and pediatric patients. This is the first study to describe the demographics, referral patterns and maternal characteristics of patients presenting with neural tube defects to MRRH in Uganda.

Our study is the first to describe referral patterns of NTD patients presenting for treatment in detail, with specific focus on referral locations as well as rate of referrals from each district. To this date, there is only one published study looking at referral locations of surgical patients presenting to MRRH. In that study, Kayima et al. described referral patterns of patients with anorectal malformation and discovered that most patients presented from the Southwestern Region, although there were several from Rwanda, Tanzania and even Central Uganda.[20] However, there was no reported referral rate per district. Similarly, all but one of our patients presented from SW Uganda, and the remaining patient was referred from Eastern DRC. We noted highest referrals from the most populous districts in the Western region, including Mbarara, Isingiro and Kasese.

Maternal characteristics of patients with NTDs have rarely been described in the literature although several researchers had previously analyzed these characteristics in a group of Ugandan patients with all congenital birth defects, including NTDs. While young maternal age is common in Uganda, with 1 in 4 adolescent women age 15–19 already mothering or pregnant with their first child, the majority of mothers are in their 20s [23]. In one study, the average maternal age at the time of delivery in Kampala was found

to be 25 years, which is in line with a birth defect surveillance study that noted that 63% of mothers of patients with birth defects were in their 20s, similar to findings in our study [10, 24].

Utilization of ANC is necessary in order to make a prenatal diagnosis of spina bifida. More than 90% of mothers in our study attended at least one ANC visit at some point during their pregnancy, which is similar to previously published estimates [9]. However, while 4 ANC visits are recommended in Uganda, the Ugandan Demographic and Health Survey found that less than 2/3rds of pregnant women completed all 4 visits, and it was unclear what was the average gestational age during first visit [25]. In their study of children with congenital birth defects, Barlow-Mosha et al found that 44.6% of mothers had their first ANC visit during the second trimester and 47.5% during the third trimester [9]. Utilization of antenatal US for diagnosis is limited in Uganda; in fact, in our patient population, only 23% of mothers underwent screening. Vaginal delivery was 80% in our patient population, similar to previously published estimates of vaginal delivery rates of children with congenital defects [9, 10]. Early presentation to ANC and consistent utilization of antenatal US is necessary to provide earlier NTD diagnosis, and allow time to prepare the mothers for delivery and postnatal long term management of this condition.

Although this study was not designed to assess specific maternal risk factors associated with NTD, we noted several trends. The rate of HIV among mothers was 12%, slightly above previously described rates of 8.8% and 9.6% [9, 10]. Meanwhile, prenatal malaria was slightly less common at 17% compared to the rate of 25% described among mothers of NTD patients in Sudan [26]. Perhaps most importantly, although folic acid is provided and recommended to women presenting to ANC in Uganda, its use was not universal [9]. In our patient population, 67% of mothers reported prenatal folate use. Perhaps even more significantly, from anecdotal experience we note that most mothers do not start folate supplementation until after their first ANC visit. Similarly, in a population in Sudan, Sadik et al found that although 69% of mothers of patients with NTD took folate, its use was not regular [26]. Folate is the most well researched risk factors for NTDs, and consistent pre-conception use is necessary in order to prevent NTDs, since the neural tube closes at 28 days of development, prior to when most women are aware of their pregnancy [1]. Current advocacy effort to require universal folate fortification are necessary in order to reduce the burden of NTDs worldwide [27, 28]. Among the leaders of this movement is the Global Alliance for Prevention of Spina Bifida F (GAPSBiF), a coalition of individuals and organizations, co-founded by the G4 Alliance, currently working to introduce a World Health Assembly Resolution on folate fortification for prevention of spinal dysraphism in children [29].

In-hospital mortality for NTD patients in Kampala was previously reported to be 2%, although in that patient cohort 47% of patient had missing discharge disposition [25]. Our in-hospital mortality rate was slightly higher at 10% and 5% of patients had a missing discharge disposition. Long-term mortality is high in this patient population given patients with NTDs require lifelong management and are prone to complications due to infection and hydrocephalus [30]. While our study was not designed to assess long-term mortality, long term mortality rate of children with myelomeningocele has been reported to range between 38–55% in Uganda [25, 30]. In Sub-Saharan Africa, NTDs are estimated to be responsible for a under-5 mortality rate of 8 per 10,000 live births [5]. Prevalence reduction is necessary for societal benefit.

One study estimated that mandatory universal fortification would result in a societal cost of just \$957 per death averted and an incremental cost-effectiveness ratio (ICER) of \$15 per disability-adjusted life year [31]. Traditionally, if ICER of an intervention is equal to or less than one GDP per capita per DALY averted, then the intervention is deemed highly cost effective [32]. Thus, in Uganda where the GDP per capita in 2021 was \$883.90, mandatory folic acid supplementation would be highly cost-effective to society [33].

There are several limitations to our study. Although our data was collected prospectively while patients were still admitted at the hospital for their initial surgery, most information was obtained from medical records. Additionally, since this was a hospital based surveillance system, it has limitations in generalizability to more rural populations. Furthermore, given we did not include a cohort of mothers of patients without NTDs, study was not designed to assess risk factors associated with this pathology. Finally, given this was a database based study, long-term follow up post hospital discharge was limited.

Conclusions

This is the first study to describe the demographics, referral patterns and maternal characteristics of patients presenting with neural tube defects to Mbarara Regional Referral Hospital in Uganda. Additionally, this study captures one of the longest treatment periods for this patient population in a low-income setting. Further prospective case-control studies are necessary to better characterize this patient population, provide an accurate calculation of prevalence and most importantly identify region specific risk factors among mothers of NTD patients.

Declarations

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Disclosures

The authors have no financial disclosures.

Competing Interests

The authors have no competing financial or non-financial interests.

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Author Contributions

Josephine Najjuma, Zaina Nakaziba, Amos Kasoba collected data. Maria Punchak, Josephine Najjuma analyzed data. Maria Punchak prepared figures and tables. Maria Punchak, Shahaan Razak wrote the main manuscript. Michael Haglund, Anthony Fuller, David Kitya conceptualized the study. All authors reviewed the final manuscript.

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Tables

Table 1
Demographics of neural tube defects patients presenting to
MRRH, 2018–2022 (n = 232).

	Total (n = 232) n (%)
Presentation Age, days (median [IQR])	2 [1–8]
Gender	
Female	111 (47.8%)
Male	121 (52.2%)
Type of NTD	
Spina Bifida	204 (86.8%)
Encephalocele	31 (13.2%)
Maternal Age, years (median [IQR])	26 [22–30]
Education Level	
None	12 (5.2%)
Primary	100 (43.7%)
Secondary	31 (13.5%)
College/University	13 (5.7%)
Missing Data	73 (31.9%)

Table 2
 Management of NTD patients presenting to MRRH,
 2018–2022 (n = 232).

	Total n (%)
Delivery Method	
Vaginal	188 (80.0%)
C-section	43 (18.3%)
Received Blood Transfusion	12 (5.1%)
Received O2 Supplementation	22 (9.4%)
Outcome	
Discharged	157 (67.4%)
Transferred	11 (4.7%)
Absconded	30 (12.9%)
Died	23 (9.9%)
Missing Data	12 (5.2%)
Length of Stay, days (median [IQR])	12 [7–19]

Figures

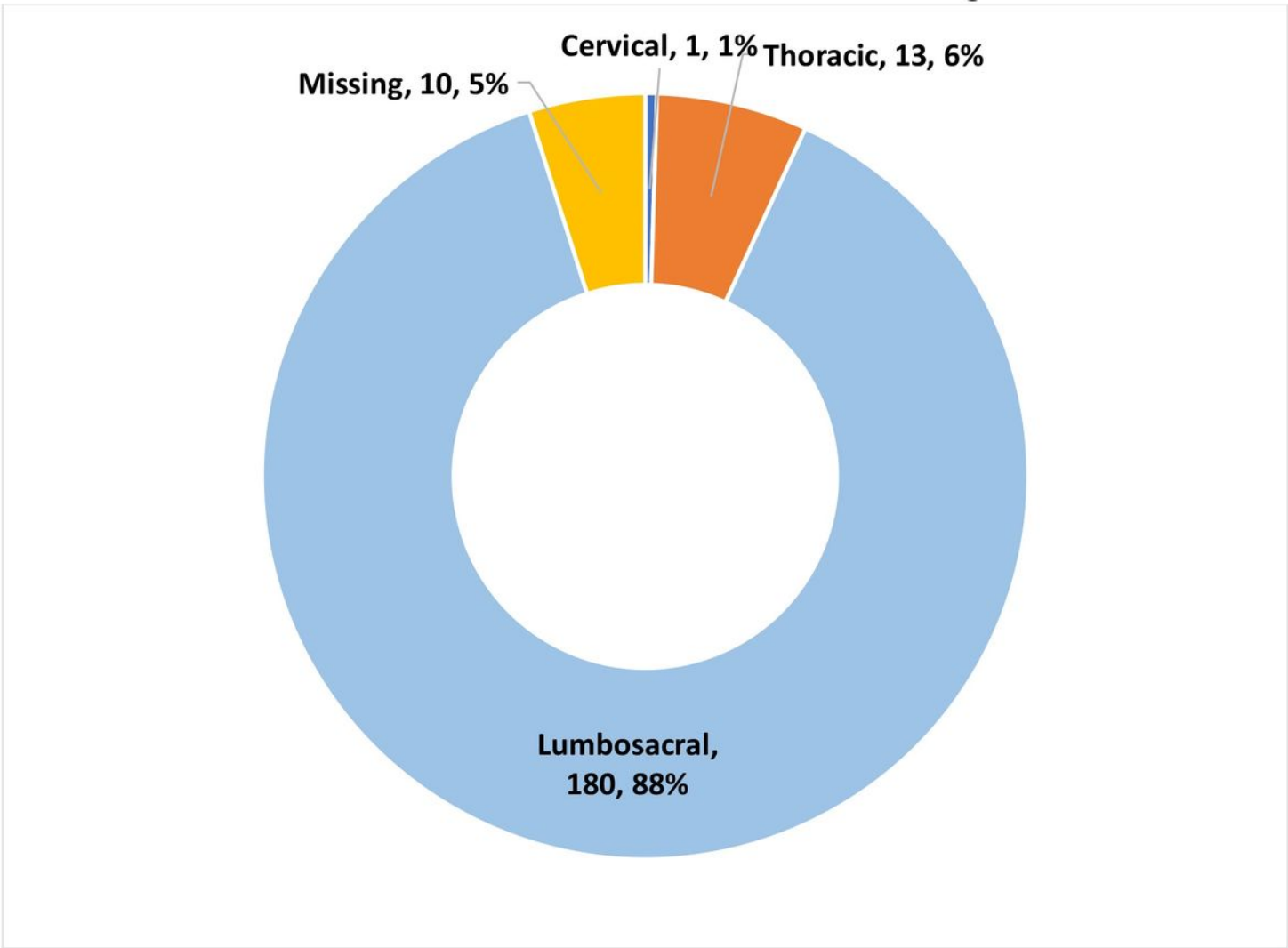


Figure 1

Dysraphism location in spina bifida patients in Southwestern Uganda.

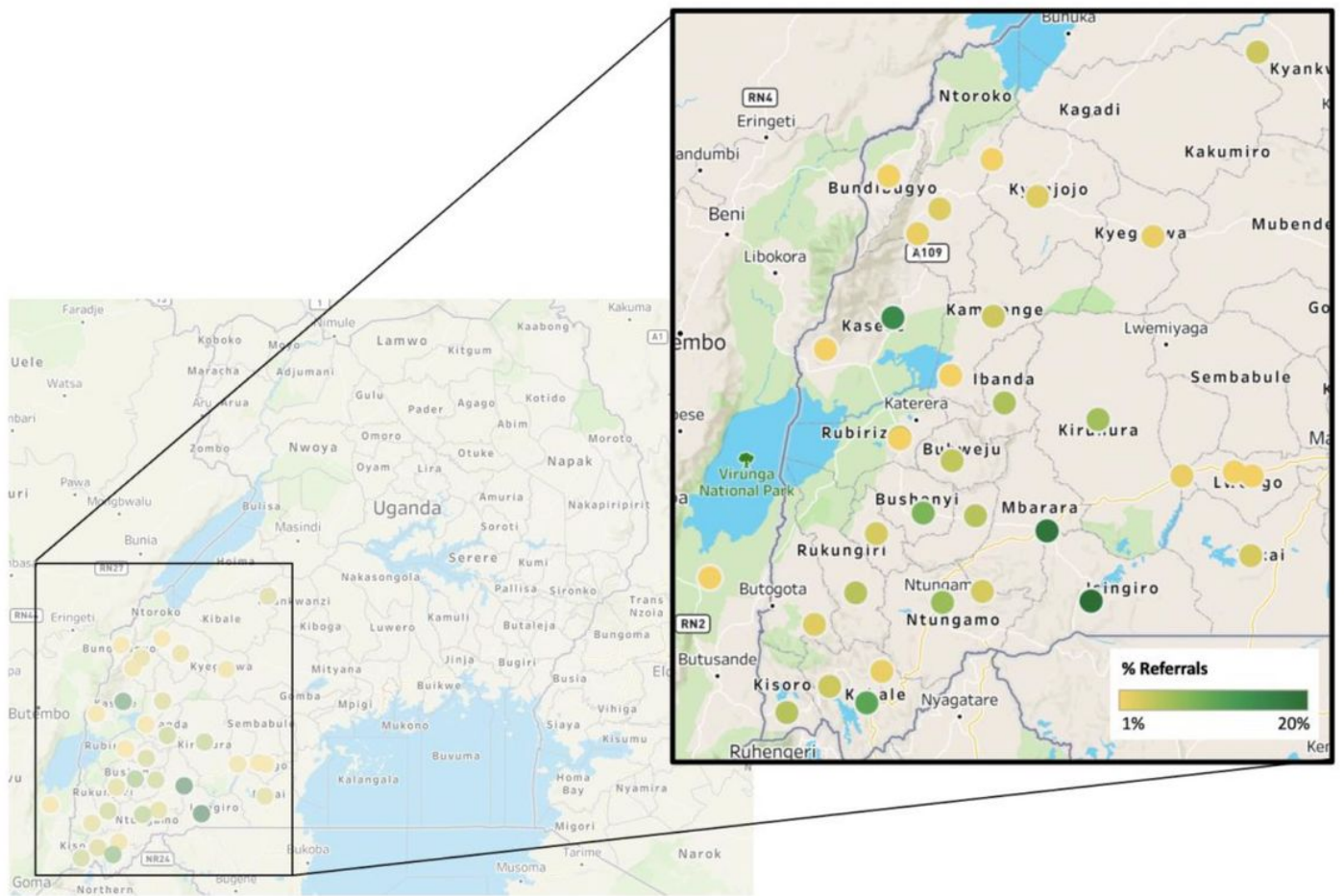


Figure 2

Referral patterns of neural tube defect patients presenting to Mbarara Regional Referral Hospital.

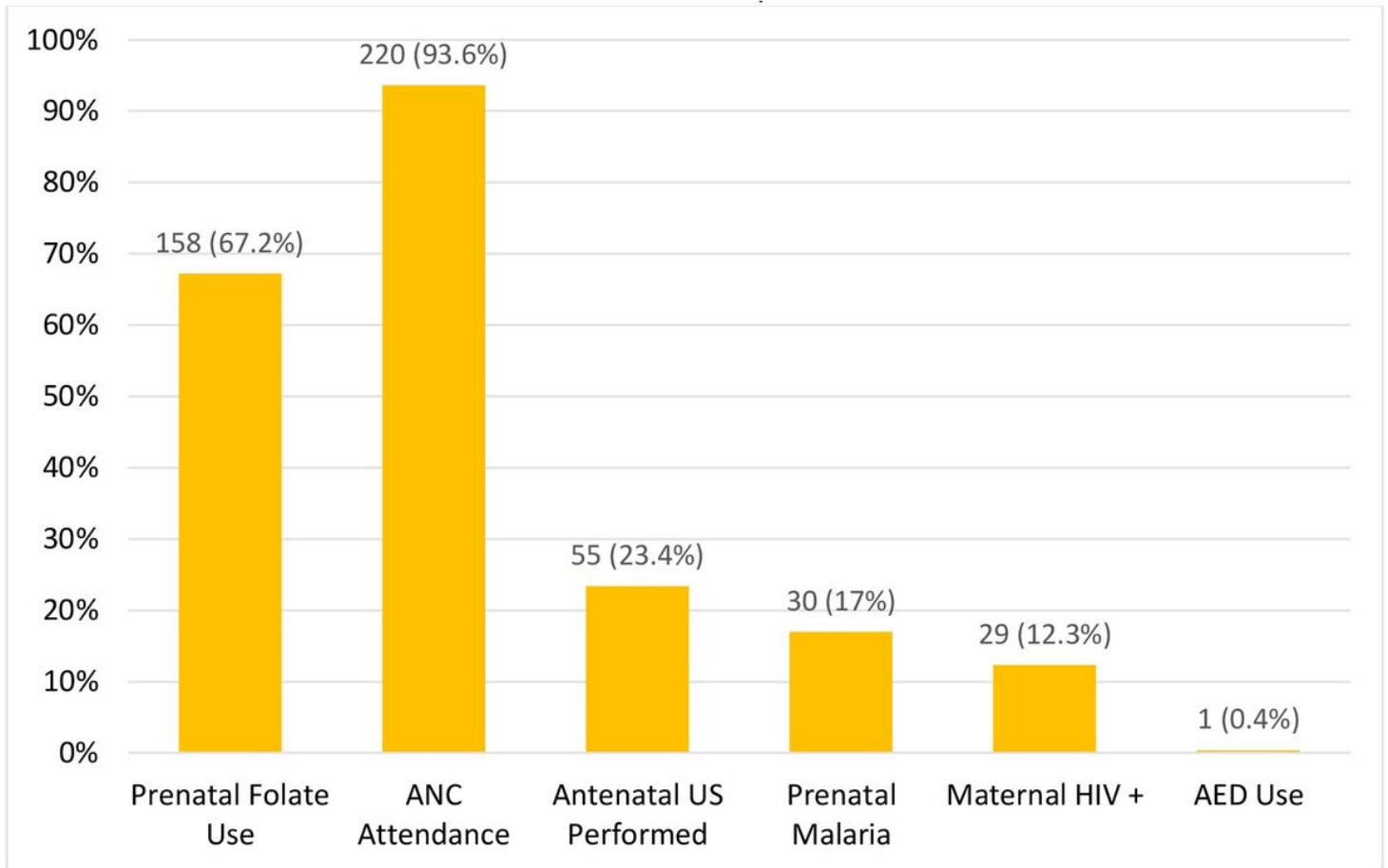


Figure 3

Prenatal characteristics of mothers of NTD patients.