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Single surgeon case series of myelomeningocele repairs in a developing world setting: Challenges and lessons

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ABSTRACT

Purpose: Neural Tube Defects are the second most common group of birth malformations following congenital heart anomalies, with myelomeningoceles being the most severe manifestation (MMC). They require expedited surgical repair, preferably within 72 h of birth. In low- and middle-income countries (LMIC) where resources are limited, timing to MMC repair is not optimal and leads to undesirable outcomes. The purpose of this study was to determine whether a proactive approach in a setting from a LMIC could achieve repair within 72 h.

Methods: A concerted effort to expedite repair of all neonates referred with a MMC was undertaken from 01 January 2014 to 1 August 2015. A consensus was reached between neonatologists and neurosurgeons that neonates born or admitted with a MMC are referred immediately to surgeons and that repair will be performed within 72 h of birth. Hospital records of neonates who had MMC repaired during this period were reviewed for infant characteristics and hospital outcomes.

Results: 24 patients with a MMC were operated upon by the senior author (CP) during the study period. Only 13 of these patients were born at the treating institution and 11 were referred from outside hospitals. Most MMCs were in the lumbosacral region and mean MMC surface area was 19.4 cm^2. Mean time to repair for the entire series was 13.6 days. Patients born at the treating institution has a mean time to repair of 10.5 days and patients referred from outside had a mean time to repair of 17.3 days. Series wide, only 21% of neonates were operated upon in less than 72 h.

Conclusion: Despite a pro-active commitment to repairing MMCs within 72 h for the duration of this series, satisfactory time to repair was not achieved. Late referral, referral from outside hospitals and operating theatre availability were the predominant factors leading to delay in MMC repair. Nevertheless, time to repair in our series was significantly shorter than that reported in MMC repair series based in similar environments. This suggests that even if the gold-standard of a 72-h window cannot be achieved, neonates benefit from much quicker repair when a concerted effort to minimise repair time is employed. This study also highlights the urgent need to address health care constraints in LMIC to improve outcomes for this vulnerable group.

1. Introduction

Neural Tube Defects are the second most common group of birth malformations following congenital heart anomalies, with myelomeningoceles being the most severe manifestation (MMC).[1] The incidence of MMCs varies and according to geographical location ranges between 1 per 200 live births and 1 per 10 000 live births.[2] The incidence in South Africa has been reported as 0.63–1.74 per 1000 live births.[3] Mothers that have conceived a child with a MMC have a 3% risk in subsequent pregnancies and mothers that have conceived two children with a MMC have a 10% subsequent risk.[2] Folate deficiency is a well-known cause for MMC development and folate supplementation has received considerable attentions as preventative treatment.[4] Anti-epileptic medications increases

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Abbreviation list

CHBAH	Chris Hani Baragwanath Academic Hospital
CSF	Cerebrospinal Fluid
HIV	Human Immunodeficiency virus
LMIC	Low and Middle Income Countries
MMC	Myelomeningocele
NICU	Neonatal Intensive Care Unit
NTD	Neural Tube Defect
NVD	Normal Vaginal Delivery
VP	Ventriculoperitoneal

the risk of MMCs with sodium valproate increasing the risk 20-fold.[5] Other factors thought to increase the risk of MMCs include diabetes, obesity, heat exposure, fever, alcohol, tobacco and illicit substances.[6]

Survival rate for neonates born with a MMC before the 1960's was between 10 and 12%.[7] Treatment was typically postponed until the age of 2 years and survival was based on a self-selected cohort. Antibiotic availability, development of the ventriculoperitoneal (VP) shunt and neuropathic bladder management drastically improved survival in neonates born with MMCs and led to a paradigm shift that advocated MMC repair within 48–72 h.[7] In fact, Pinto et al demonstrated that repair immediately after birth, termed "time zero repair" yields even better long-term results.[8] Based on this paradigm shift, at least 75% of children born with MMCs can be expected to reach early adulthood.[7]

Unfortunately, the low- and middle-income countries (LMIC) do not have adequate resources required for aggressive early surgery and yet are faced with a large burden of MMC. It is well known that within a developing world setting that timing to MMC repair is not optimal and leads to undesirable outcomes. As such, it is imperative that treatment of MMCs is analysed critically within existing healthcare frameworks with the aim of improving health systems and thereby patient outcomes. One study from a LMIC reported that average age of infants at time of MMC repair was 4.7 months.[9] The aim of the current series was to determine characteristics, age at repair and outcomes of neonates who had MMC, in a setting from a LMIC where there are resource constraints.

2. Methods

2.1. Study design

This study is a consecutive single surgeon, single centre, retrospective review of case series of neonatal myelomeningoceles repaired at a tertiary hospital in Johannesburg, South Africa. This study was approved by the Human Research Ethics Committee (Medical) at the University of the Witwatersrand with clearance certificate number M151101. A proactive approach was used in which neurosurgery, neonatology and anaesthesia worked together in prioritising the transfer of infants with MMC's to our institute and improve access to theatre and post operative high care.

2.2. Study settings

This study was conducted at Chris Hani Baragwanath Academic Hospital (CHBAH). CHBAH is a public, tertiary hospital in Soweto, Johannesburg, South Africa. The hospital conducts about 20 000 births per year and is a referral centre for about 13 000 births from local and district hospitals. It is also a referral centre for surgical service for southern Gauteng and North West provinces. All neonatal surgical patients are admitted to a neonatal unit which has 185 neonatal beds, of which 42 are high care beds and 18 are neonatal intensive care unit (NICU) beds. Since 2003 the National Food fortification program began fortifying maize meal and bread flour with micronutrients including folate which resulted in a 41.6% decline in the rate of spina bifida.[10]

2.3. Study population

Neonates with MMCs that presented following birth or were referred to CHBAH for repair from 1 January 2014 and 31 July 2015 had their hospital records reviewed for demographics, clinical presentation, surgical management, and hospital outcomes.

2.4. Pre-surgical preparation for MMC repair

Neonates referred with a MMC were assessed and dressed with an occlusive paraffin gauze dressing to avoid contamination. They were assessed for associated conditions such as lower limb function, congenital hip dysplasia and bladder function. Pre-operative antibiotics were not routinely instituted. Neonates were cross-matched and surgical repair was planned at the next available neonatal theatre list.

2.5. Surgical repair procedure

The neonatal theatre temperature was maintained at 28 °C. Neonates were proned onto a warming pad with pressure point management and had their head and limbs covered with cotton rolls and aluminium foil. Surgical repair was undertaken with loupe 2.5X magnification in the standard fashion. Large dorsal defects following MMC reconstruction were treated with local flaps. There were variations in MMC size, location and patient characteristics which naturally led to disparities in cases including the need for local flaps in some patients.

2.6. Operator details and quality control

All cases were performed by the senior author (CP). At the time of the series, the surgeon had been trained by a consultant to perform the procedure independently and had performed 15 MMC repairs before. All operations were performed in the same theatre. Standard technique as described above was used in all cases.

2.7. Post-operative care and follow-up

Neonates were extubated in theatre and were transferred to the neonatal high care or NICU for monitoring. Wounds were dressed with an occlusive dressing and neonates were nursed prone for seven to ten days until the skin was healed and sutures removed. Dressings were checked and changed daily. Head circumference and fontanelles were assessed daily. If development of hydrocephalus was suspected a Computed Tomography brain scan was undertaken and neonates had cerebrospinal fluid (CSF) diversion with a ventriculo-peritoneal (VP) shunt. Follow up was undertaken until 1 January 2016. Patients were seen on an outpatient basis and assessed clinically.

2.8. Data analysis

Factors that may have contributed to post-operative complications were statistically analysed. Cross tabulation between variables of interest was performed. Association between continuous data variables was tested with an unpaired student *t* test. Categorical data variables had a low frequency of events and as such, a Fischer's exact test was used to assess statistical significance. Statistical significance was considered significant when a *p*-value was less than 0.05. This case series has been reported in line with the PROCESS Guideline.[11]

3. Results

A total of 24 patients (8 females and 16 males) presented with a MMC between January 2014 and August 2015. Demographic and birthing details are outlined in Table 1. Gestational period ranged from 35 to 40 weeks. Six of the infants were recorded as being in breech position and there was one set of twins, whereby only one of the infants was affected

Table 1
Demographic and birthing details.

MEAN GESTATION PERIOD (weeks)	38.1
Gender	
Male	67% (n = 16)
Female	33% (n = 8)
Mode of delivery	
Natural vaginal delivery	54% (n = 13)
Caesarean section	46% (n = 11)
MEAN WEIGHT (grams)	2821
MEAN LENGTH (cm)	47.8
MEAN HEAD CIRCUMFERENCE (cm)	34.9
Mean 1 min apgar score	7.8
Mean 5 min apgar score	9.4
Referral route	
In hospital	53% (n = 13)
Referring hospital	47% (n = 11)

by a MMC. The lightest neonate was 2300 g and the heaviest 3600 g. Head circumference ranged from 31 to 37 cm at birth. There was a slight preponderance of patients born with MMCs at our tertiary hospital (n = 13) as opposed to being referred from a referring hospital (n = 11). Maternal characteristics are presented in Table 2. Five mothers were positive for human immunodeficiency virus (HIV) infection. Four of the mothers were aware of their HIV status prior to pregnancy and one was diagnosed following birth of her child. The 2 mothers on anti-epileptics were on sodium valproate.

MMC characteristics are detailed in Table 3. The smallest MMC had a surface area of 3 cm^2 and the largest had a surface area of 36 cm^2. Half (n = 12) of the neonates had a CSF leak on presentation and one third (n = 8) had an associated kyphotic abnormality. Table 4 presents neurological abnormalities that were present in this series of MMC neonates and Table 5 presents associated non-neurological abnormalities. There were two cutaneous abnormalities, both of which were located over the lower back in the vicinity of the MMC; one was a capillary haemangioma and the other was a fawn's tail – a hairy patch. Other congenital abnormalities that were identified within the series were a horseshoe kidney and rectal prolapse. One neonate also had bilateral femur fractures (see Fig. 1).

Notes pertaining to detailed pre-operative assessment could only be retrieved for 17 of the 24 neonates. There were no deviations from the initial management plan. Mean time to MMC repair was 13.6 days. Five neonates had their repairs performed within 72 h of birth. Fig. 2 presents the timing of MMC repairs within our series. Mean time to repair for the patients born at CHBAH was 10.5 days and mean time to repair for patients born at referring institutions was 17.3 days. Comparison between the two groups was not significant ($p = 0.14$). Other reasons for delay to surgery was medical workup including for renal dysfunction, respiratory distress and cardiac workup for murmurs and availability of theatre.

Four patients within the series required a local flap for closure of a large skin defect. Two neonates had a Limberg flap and the other two had a reading man flap.

Twelve neonates within series (50%), required a VP shunt for hydrocephalus. One of the neonates with hydrocephalus demised and did not have a VP shunt inserted due to CSF infection. None of the neonates demonstrated a latex allergy. Strict measures restricting latex exposure were not undertaken in this series.

Table 2
Maternal parameters.

HIV infection status	
Yes	21% (n = 5)
No	50% (n = 12)
Unknown	29% (n = 7)
Pregnancy antiepileptic use	
Yes	8% (n = 2)
No	66% (n = 16)
Unknown	625% (n = 6)

Table 3
MMC characteristics.

MMC region	
Cervical	0% (n = 0)
Thoracic	4% (n = 1)
Lumbar	58% (n = 14)
Sacral	38% (n = 9)
MEAN MMC SURFACE AREA (cm^2)	19.4 ± 9.7
Csf leak on presentation	
Yes	50% (n = 12)
No	50% (n = 12)
Kyphotic deformity	
Yes	33% (n = 8)
No	67% (n = 16)

Table 4
Associated neurological abnormalities.

VARIABLE	
LOWER LIMB NEUROLOGY	
Lower Limbs Intact	29% (n = 5)
No Movement below Ankle	0% (n = 0)
No Movement below Knee	13% (n = 2)
No Movement below Hip	6% (n = 1)
Complete Paralysis	53% (n = 9)
CLINICAL ASPIRATION/DYSPHAGIA	
Yes	13% (n = 2)
No	87% (n = 15)
RADIOLOGICAL CHIARI TYPE II MALFORMATION	
Yes	94% (n = 16)
No	6% (n = 1)
HYDROCEPHALUS	
Yes	54% (n = 13)
No	46% (n = 11)

Table 5
Associated non-neurological abnormalities.

VARIABLE	RESULT
CLUBFOOT	
Yes	71% (n = 12)
No	29% (n = 5)
CONGENITAL HIP DYSPLASIA	
Yes	24% (n = 4)
No	76% (n = 13)
NEUROGENIC BLADDER	
Yes	41% (n = 7)
No	59% (n = 10)
CUTANEOUS ABNORMALITY	
Yes	12% (n = 2)
No	88% (n = 15)

Mean Pre-operative haemoglobin was 14.3 g/dL and mean post-operative haemoglobin was 12.7 g/dL. The largest haemoglobin drop was 5.5 g/dL from 17.5 g/dL to 12 g/dL. Mean transfusion volume was 41 mls.

Table 6 presents post-operative complications arising from this series. Of the six infections that arose, five were CSF infections and one was a superficial wound infection. One infection was in a patient repaired within 72 h and the other 5 were in patients repaired after 72 h ($p = 0.77$). Wound dehiscence was minor in three of the cases. All three of the patients with a CSF leak went on to complicate with both wound dehiscence and CSF infection. Reoperation to address complications was performed for two of the five patients with wound dehiscence and two of the three patients with CSF leak.

No significant relationship was found between gestational age and wound dehiscence ($p = 0.58$), between birth weight and wound dehiscence ($p = 0.10$) or between maternal HIV status and wound dehiscence ($p = 0.54$).

There was no significant relationship between CSF infection and time

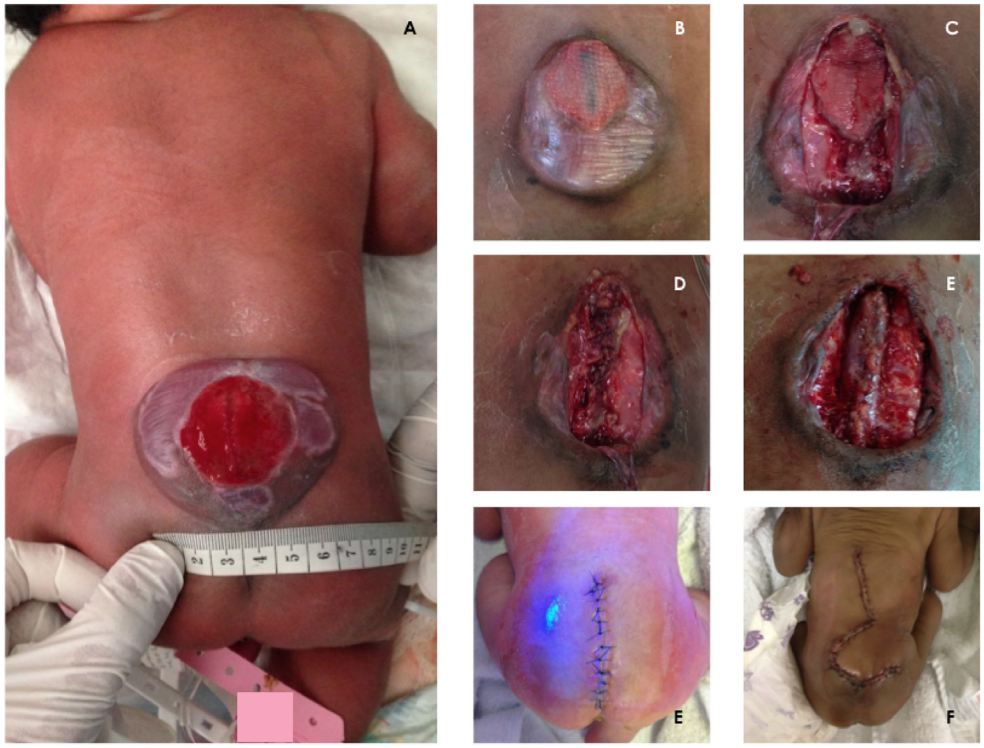

Fig. 1. **A** Neonate with typical Myelomeningocele (MMC) from series. **B** MMC placode and surrounding membrane with dysplastic skin. **C** Placode freed from surrounding dysplastic skin. **D** Reconstruction of placode into neural tube. **E** Dura was dissected off MMC cavity and closed primarily over the reconstructed placode. **F** Primary closure of MMC skin defect. **G** Author elected to utilise a Limberg flap as defect was large.

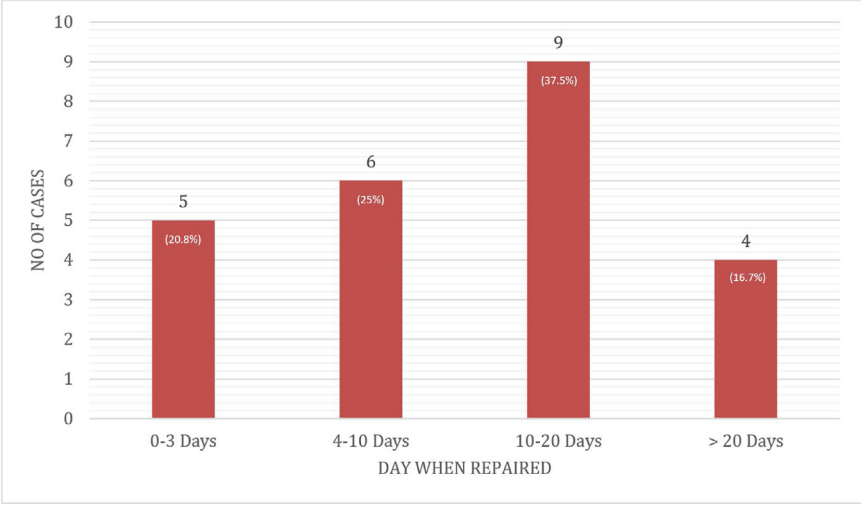

Fig. 2. Frequency Distribution of days from birth to Neural Tube Defect Repair in original case series.

Table 6
Postoperative complications.

VARIABLE	RESULT
WOUND DEHISCENCE	
Yes	21% (n = 5)
No	79% (n = 19)
CSF LEAK	
Yes	12.5% (n = 3)
No	87.5% (n = 21)
INFECTION	
Yes	25% (n = 6)
No	75% (n = 18)

to surgery ($p = 0.15$), CSF infection and gestational age ($p = 0.87$), CSF infection and birth weight ($p = 0.76$), CSF infection and maternal HIV status ($p = 0.11$).

There were two mortalities within this series. One was a neonate with a large MMC requiring a flap for closure. This was complicated by wound dehiscence, CSF leak and infection leading to systemic sepsis. The other was a neonate with episodes of apnoea, stridor, aspiration, and dysphagia related to Chiari Type II malformation.

4. Discussion

Management of MMCs provides a formidable challenge in LMIC.

Although, expedient closure of MMCs, preferrable within 72 h, is a well-accepted standard of care, health system challenges often prevent attainment of this well-accepted standard. In developed countries a target of closure within 48 h is used. Current guidelines have found insufficient evidence that this reduces rates of infection or ventriculitis but do recommend prophylactic antibiotics if closure is delayed beyond 48 h[12] In realising this short-coming, a concerted effort was made between the neurosurgical and neonatal team to expedite time to MMC repair. Efforts centred around creating awareness to expedite referrals and motivating for extra theatre lists to accommodate neonates with MMCs.

Mean time to MMC repair within our series was 13.6 days, with only five of the 24 patients operated within 72 h.

The delay in MMC repair is the result of several factors. An important factor was delay in the transfer of patients from outside hospitals. Patients born at the treating institution had a mean time to repair of 10.5 days and patients referred from outside had a mean time to repair of 17.3 days. A limiting factor in patient transfer was availability of high-care beds. A second stumbling block to delayed repair was availability of theatre time. A single neonatal emergency list exists and is shared between paediatric surgery and all the sub-specialities – opening up extra lists was rarely possible. This unfortunately impacted negatively toward repairing MMCs in a timely fashion. Delay based on medical grounds, for medical optimisation prior to surgery did affect several patients but was not the most common reason for delay.

In the current series there were 4 neonates that were repaired beyond 20 days, which increased mean time to repair significantly. Although timing to repair in the current series is not ideal, it is interesting to note, that Attenello et al from the United States reported that 19% of MMC repairs occur outside the 48 h mark based on countrywide database analysis.[13] Their results regarding timing are superior to the results from the current series, however they do demonstrate that even in a highly developed setting it is not easy to repair all MMCs within the first few days of life. By comparison, Mnguni et al presented their large collective experience of 309 children treated with MMCs in a similar developing world setting.[9] Due to constrained healthcare resources average age of MMC repair in their series was 4.7 months. Given that our series was undertaken within a similar environment, with similar health constraints, our time to surgery of 13.6 days demonstrates that a concerted effort to minimise time to MMC repair can be beneficial in expediting surgery. This study will hopefully provide impetus, in a developing world setting, to bring down times to MMC repair even further. To compare our current practice, in the last year 2022 a total of 10 MMCs were repaired with a mean time to surgery of 17.1 days with only 2 being repaired within 72 h and 4 being repaired beyond 20 days (see Fig. 3). This is unfortunately due to limited theatre availability as well as ongoing delays with referrals. We now have a dedicated weekly Wednesday elective list for repair of MMC's which has improved our problem of theatre availability however does not help for babies born on Thursday to Sunday.

Our series unfortunately illustrates that MMCs, in our developing world setting, provide a significant burden of disease when compared to developed nations. Within a 19-month period, we had 24 MMCs presenting to our service. By comparison, the MOMS trial, which was a multicentre trial between three centres, had 183 patients included in the trial from February 2003 to December 2010.[14] This disparity, at a local level, highlights the need for review of our current strategies employed to reduce the risk of MMCs. Gender distribution was skewed toward male neonates at 67%, which may have been the result of a small series and is not in-line with the reported female preponderance. Most births were via natural vaginal delivery (NVD) at 56% and not via C-section. This is the result of predominant postnatal as opposed to prenatal diagnosis of MMCs in our developing world setting.

The majority of MMCs in our series were lumbar in nature. This is comparable to other large series. CSF leak at birth was present in 50% of neonates in this series. In comparison to the series by Sattar et al from Pakistan, who reported a rate of 3.8%, this is quite a high rate.[15] The high rate may be explained by the low rate of C-section delivery in this series leading to birth trauma of the MMC sac via NVD. Finally, the rate of kyphosis in the current series was 33.33%. This is higher than the rate of 15% quoted in the literature and is possibly the result of a small sample.[16]

HIV prevalence in our local community is as high as 30%. In-line with this, at least 21% of the mothers in our series were positive for HIV. Two mothers within the series were using sodium valproate as epileptic treatment during their pregnancy. This reflects problems with patient education on perinatal anti-epileptic use and is a known problem of poor maternal awareness of perinatal MMC risk factors in our region.[17,18]

Within the current series there was a 21% rate of wound dehiscence. This amounted to 5 cases of which the dehiscence in 3 of the patients was minor, with skin edge necrosis that was treated conservatively. If this is considered, the rate is modified to 8.3%. Comparatively, Chand et al had a wound dehiscence rate of 5.4% and Lee et al had a rate of 10%.[19,20] CSF leak rate within the series was at 12.5%. This is in-line with other series. Chand et al had a CSF leak rate of 8.1% and Ghani et al had a CSF leak rate of 12.5%.[19,21] It has been found that performing simultaneous shunting while repairing the MMCs has led to significantly reduced rates of CSF leak as well as shorter lengths of hospital stay.[22]

Infection occurred in 25% of the patients within the series. Of the 6 infections within series 5 were CSF infections, giving the series a CSF infection rate of 21%. This is a high rate. Comparatively, Demir et al had a CSF infection rate of 16.4% and Attenello et al in their nation-wide United States study had an 18% infection rate.[22,13] Due to the busy nature of our neonatal service and constant shortage of beds, infection

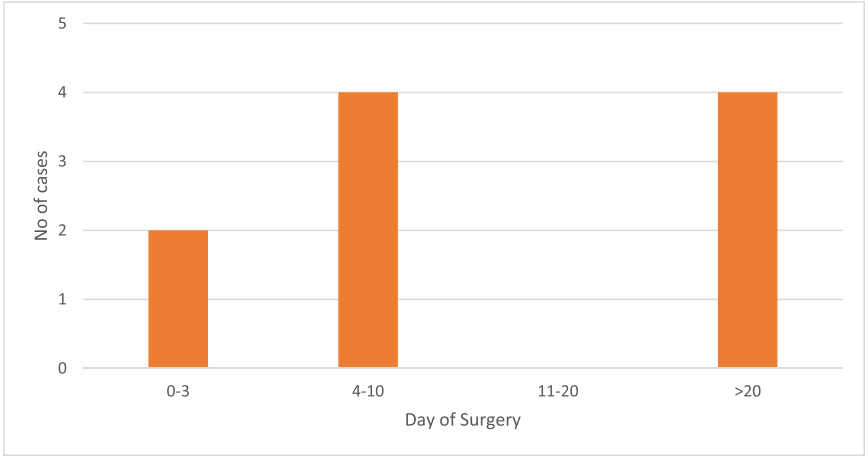

Fig. 3. Frequency Distribution of days from birth to Neural Tube Defect Repair for 2022.

control measures can at times be less than ideal. Furthermore, in our setting we do not have access to antibiotic impregnated VP Shunts, which has clearly been shown in the BASICS trial to decrease CSF infection rate.[23] As expected, the three patients that had a CSF leak went on to also complicate with wound dehiscence and CSF infection. This is well recognised and has been reported in other operative MMC series as well.[20,24,25]

No statistical significance was reached on investigation of parameters that could have influenced complications in this series. The small sample size of 24 neonate in the current series was a limitation.

5. Conclusions

We present our consecutive series of 24 MMCs repaired by a single surgeon in a developing world setting. The premise of this study was a realisation that expedient closure of MMCs in our environment is challenging and that a concerted effort by a motivated paediatric and neurosurgical team could reduce time to MMC repair. We achieved a mean time to repair of 13.6 days. While not ideal, it does represent a significant improvement in our LMIC setting. Our series results and complication profile were comparable to other reported series. The current study highlights the formidable management challenge MMCs pose in a limited resource environment and highlights the need for health system reform when addressing challenges posed by complex congenital disease. Within our local setting, we hope that this study inspires further efforts to reduce time to MMC repair. We continue to work closely with our paediatric colleagues and referral hospitals to encourage early referral and transfer of all MMCs.

CRediT authorship contribution statement

Denver Naicker: Writing – original draft, Writing – review & editing. **Keletso Leola:** Data curation. **Mlamuli Mzamo Mkhaliphi:** Data curation. **Morena Nthuse Mpanza:** Investigation. **John Ouma:** Supervision, Writing – review & editing. **Firdose Lambey Nakwa:** Investigation. **Sithembiso Velaphi:** Supervision, Writing – review & editing. **Christos Profyris:** Investigation, Methodology, Project administration.

Declaration of competing interest

The authors have no competing interests to declare that are relevant to the content of this article.

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