

## Description and early clinical outcome of patients with omphalocele admitted to a tertiary hospital in Kigali, Rwanda over a three-year period – a cross-sectional study

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### ABSTRACT

**BACKGROUND:** Studies suggest that patients with omphalocele have poor outcomes which are associated with the high rate of associated congenital abnormalities. A variety of surgical management techniques have been described, with some requiring equipment not available in resource-limited countries.

**OBJECTIVES:** This study aimed to describe associated abnormalities, management and early hospital outcomes of patients with omphalocele.

**METHODS:** A retrospective study of newborns diagnosed with omphalocele hospitalized from January 2014 to December 2016 at a tertiary level facility, the University Hospital of Kigali (CHUK) in Kigali, Rwanda. Case-file review of included newborns and analysis of the data collected was performed with SPSS version 16.0.

**RESULTS:** Thirty-one patients were hospitalized with omphalocele during the three-year study period. A limited number of investigations were done to diagnose possible associated congenital abnormalities. Three patients (9.7%) were found to have cardiac abnormalities, nine (27.0%) had suspected genetic abnormalities including Trisomy 13, 18 and Beckwith Wiedemann Syndrome. In terms of management, ten patients (32.3%) underwent primary closure. Sixteen patients (51.6%) developed sepsis during hospitalization. Of the thirty-one patients hospitalized, nine (27.0%) died in the hospital. The only factor found to be associated with increased mortality was the size of the omphalocele, with small omphaloceles associated with lower mortality than large omphaloceles (OR 0.909, P-value 0.028).

**CONCLUSION:** Mortality of these patients is significant and slightly higher in patients with larger omphalocele. Newborns with omphalocele should receive appropriate investigations to diagnose associated congenital abnormalities and have early recognition and prompt management of complications, especially sepsis. The results are limited by the small sample size and limited investigations performed to detect associated abnormalities.

**Keywords (MeSH):** Omphalocele; abdominal wall defect, congenital abnormalities, early mortality.

### INTRODUCTION

Patients with omphaloceles have higher mortality than patients with gastroschisis, as they are more likely to have associated congenital abnormalities, including cardiac, gastrointestinal, neurologic, pulmonary, genetic and renal abnormalities [1]–[6]. The treatment options of patients with omphaloceles will vary according to the size of the omphalocele. Small omphaloceles (defined as omphaloceles <5cm) are usually treated by primary closure, and large/giant omphaloceles (those >5cm or that

contains the liver in the sac) are typically managed by staged or delayed closure [7]–[10]. In unusual cases of an extremely large (>10 cm) omphalocele or in a premature newborn having respiratory difficulties, some studies show that a topical sclerosing agent (half strength Povidone-Iodine with or without associated powdered antibiotic combination) can be used as a bridge to delayed fascia closure [11], [12]. In high-resource settings, this medical treatment is used as a temporary measure while waiting for definitive management which consists of a staged closure.

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Neonatal morbidity and mortality of patients with omphaloceles have been directly associated with the presence or absence of associated anatomical and chromosomal abnormalities and their severity [2], [5], [13]–[16]. The size of the defect has also been shown in some studies to be associated with the outcomes with major omphalocele having higher mortality than minor omphalocele [9]. Studies have shown that the early mortality of newborns with omphalocele can be between 8-34% [4], [17]

Despite the fact that every year, newborns are referred to the University Teaching Hospital of Kigali (CHUK) from health facilities all over the country, there are no local guidelines developed for management of patients with omphalocele. Screening for associated congenital abnormalities is not always possible and therefore variable, and the outcome of these patients is unknown.

**Aims:** to identify associated congenital abnormalities, describe management and early hospital outcomes in newborns presenting with omphalocele at CHUK, Kigali, Rwanda.

## METHODS

**Study design:** Retrospective cross-sectional study

**Source/location of the population:** The study included all newborns with omphalocele admitted to the Departments of Pediatrics and Surgery at CHUK from January 2014 to December 2016

**Study setting and location:** CHUK is the main tertiary-level referral teaching hospital, located in Kigali, Rwanda, with a catchment area of approximately seven-million people.

**Participants/subjects:** All newborns admitted for the first time at CHUK with a diagnosis of omphalocele and whose medical file was available were included.

**Variables and outcomes:** The primary objective of this study was to describe the early hospital outcome of these newborns with omphalocele. Early hospital outcome was defined as either death in hospital or discharge purpose and facilities (continued care at home or in other health facilities, palliative care at home or in other facilities). The secondary objectives were to determine what types of associated congenital abnormalities found in these patients and to determine which treatment they received.

**Measurement of outcome/definition of variables:** A medical file review was undertaken. The treatment variable as well as the diagnostic criteria were defined according to documentation by the clinical team in the medical file.

**Sample size (power calculation):** All newborns who were admitted for the first time at CHUK were enrolled and all data was analyzed. Therefore, no sample size calculation was necessary for the descriptive part of the study.

**Data sources and measurement:** Identification of eligible patients was done by searching the registries of the Pediatric Emergency

room (ER), Neonatal unit (NICU) and surgery wards and the hospital electronic statistics with the admitting diagnosis of 'Abdominal wall defect', 'Omphalocele', 'gastroschisis', 'umbilical hernia'. All files of patients with these diagnostic categories were retrieved and only the newborns who were found to have omphalocele documented as a final diagnosis were included in the study. All data was obtained from patient's medical files from the archives of CHUK.

**Data Management and Statistical analysis:** The questionnaire (data-collection tool) was explicitly designed for this study. The data was collected using a paper questionnaire. The collected data was entered into a password protected Epi-data sheet and then exported to Statistical Package for the Social Sciences (SPSS) version 16.0 for analysis. Univariate analysis was performed to calculate the proportion of newborns in each category and bivariate analysis using Chi-square and Fisher's exact test were performed to test for associations between these categorical variables and the primary outcome (early hospital mortality).

## ETHICS/STUDY OVERSIGHT:

**Risk to subjects:** No physical, social, emotional, legal and/or financial risks were identified.

**Institutional review board (IRB):** The research protocol was reviewed and approved by the Ethics committee of CHUK (Ref: EC/CHUK/291/2017) on 24 February 2017.

**Confidentiality:** Personal data was not used in the analysis. Each patient was assigned a unique study identifier number. A password protected linking study ID, and personal identifier (name, hospital ID) was kept separately by the principal investigator (PI). Only the researcher and the research team had access to the study data and information.

**Informed consent:** Only patient files were consulted. Therefore no informed consent was sought for this study

**Funding & Sponsors:** No funding has been sought or gained for this project.

**Potential conflict of interest:** The first authors of this study was a student at the University of Rwanda, and the research was a part of her requirements to be awarded a bachelor's degree in medicine and surgery. All authors were part of the clinical team at CHUK who had taken care of these patients. However, the authors of this study declare no potential conflict of interest.

**Incentives for subjects:** There were no incentives offered to patients whose data was used in this study.

## RESULTS

**Patient description:** Thirty-one patients with omphalocele were hospitalized at CHUK between 1<sup>st</sup> Jan 2014 and 31<sup>st</sup> Dec 2016. Seventeen (54.8%) were females, 13 (41.9%) were males, and one baby had ambiguous genitalia. Twenty-one patients (67.7%) were born at term, two (6.5%) were preterm, and eight (25.8%) patients had no documentation of gestational age. Five (16.1%) newborns had low birth weight (birth weight <2.5 kg) and seven newborns had no documentation of birth weight. Maternal age, previously described as being a risk factor for omphalocele, was not documented in any of the patients' files. Only one patient had

documentation of prenatal ultrasound which was reported to be normal at six months of gestation [11], [18].

The mean age at admission was 2.8-days-of-life and a median of 2-days-of-life, with 25 (80%) being admitted between 24 hours

and seven days of age. Seven (22.6%) newborns had no documentation of omphalocele size, while 11 (35.5%) were found to have an omphalocele < 5 cm and 13 (41.9%) >5cm. The membrane was ruptured in 5 (16%) newborns and intact in 26 (84%) newborns (Table 1).

**Table 1: Associated congenital abnormalities found on physical examination and investigations performed on admission.**

Associated congenital documented	N	%
No associated congenital suspected on physical exam	15	48.3%
Clinical features of Trisomy 13	4	12.9%
Clinical features of Trisomy 18	3	9.7%
Clinical features of Beckwith Wiederman Syndrome	2	6.5%
Suspected cardiac abnormalities (by clinical exam)	5	16.1%
Confirmed cardiac abnormalities (by heart echocardiogram)	3*	9.7%
Associated GIT abnormalities*	6	19.4%
CNS abnormalities**	4	12.9%
Other associated abnormalities	6	19.4%
<b>Investigations performed</b>		
Cardiac Ultrasound	4	12.9%
Abdominal Ultrasound	10	32.3%

\*GIT abnormalities: 2 imperforated anus, 1 cleft lip and palate, 1 malrotation and jejunal atresia, 1 left kidney hydronephrosis and right kidney atresia, and 1 right kidney cystic lesion. \*\*CNS abnormalities: 3 patients with microcephaly and 1 with craniosynostosis.

Five patients were suspected to have a cardiac anomaly by clinical exam, but among these patients, only one had a cardiac ultrasound undertaken which revealed Tetralogy of Fallot (TOF). Meanwhile out of the remaining patients (26) who were not suspected to have any cardiac abnormalities, three had a cardiac screening ultrasound performed, of which one patient was normal, one patient had a small patent foramen ovale (PFO), and one patient had a patent ductus arteriosus (PDA) and a PFO.

We found that there was a non-statistically significant trend for an association between larger omphaloceles and increased risk of rupture (OR 2.67, CI: 0.21-34.2, p=0.58). Of note, two of the patients with ruptured membrane did not have documentation of omphalocele size and were not included.

In our patient population, larger omphaloceles were not associated with the presence of suspected genetic syndrome (when combining suspected Trisomy 18, Trisomy 13 and Beckwith Wiedemann Syndrome) (OR 0.8438, CI 0.14-4.97, p=0.604).

**Patient management and complications:** None of the patients underwent a staged closure with an application of a tissue expander such as a Dacron-reinforced Silastic silo. Ten (32.3%) underwent primary closure, while 17 (54.8%) underwent conservative management.

The patients' conservative management included normal saline dressing in the majority of the cases (n=23) while two were

dressed with fusidic acid creme dressings, three dressed with silver sulfadiazine dressings and two dressed with Vaseline dressing. One patient did not have documentation of dressing type.

Of note, of the non-operative patients, four were judged to have poor outcomes and therefore were not offered surgical management, but were sent home or to district hospital for palliative care. There is a non-statistically significant trend for patients with smaller omphalocele to undergo surgical management (OR=2.5, CI of 0.34– 18.33, p= 0.34).

Complications were common in our patient population. Three (9.7%) had an infection of the omphalocele, five (16.1%) had a ruptured omphalocele at admission, and two (6.5%) had a ruptured omphalocele during hospitalization. Sixteen of the patients (51.6%) were also diagnosed with sepsis; one (3.2%) had jaundice. Nine (29.9%) had no complications.

**Early Hospital Outcome - Hospital mortality:** Nine (29%) patients died in hospital, and most deaths occurred early, with six (19.4%) dying before ten-days-of-life. Mean age of death was 13.6 days. In the 22 surviving infants, the mean length of stay was 13.9 days (Range 1-40 days). The early (hospital) mortality rate of the patients was 29%, with 71% of patients being discharged alive (Table 2).

Table 2. Early hospital outcome

	Frequency	Percent
Death in hospital	9	29.0%
Discharged home	11	35.5%
Counter referral to DH for further care	7	22.6%
Sent home or to DH for palliative care	4	12.9%
<b>Total</b>	<b>31</b>	<b>100.0%</b>

Factors associated with survival to discharge: The only factor that was found to be significantly associated with survival was the size of the omphalocele, with omphaloceles <5cm being associated with a significantly lower odds of mortality (OR 0.0909, CI of 0.0091-0.9064,  $p=0.028$ ). The presence of sepsis, having a

suspected genetic syndrome and being treated with conservative management were all associated with increased odds of hospital mortality, but none of these factors were found to be statistically significant (Table 3).

Table 3. Bivariate analysis of factors associated with death during hospitalization

	Odds Ratio (OR)	95% CI	P-value
Omphalocele size <5cm	0.09	0.009-0.91	$p=0.028$
Omphalocele size > 5cm			
Sepsis	5.06	0.85- 30.18	$p=0.069$
No Sepsis			
Suspected genetic syndrome	5.07	0.84- 30.41	$p=0.085$
No suspicion of a genetic syndrome			
Non-operative management	5.54	0.59-52.33	$p=0.116$
Surgical			

## DISCUSSION

This study aimed to describe the associated abnormalities, management and early hospital outcome of patients admitted to CHUK with omphalocele during a three-year period. In our study, we found that patients with omphalocele have high mortality with almost a third of our patients with early hospital death. This is concerning, especially given the fact that this study only reflects early hospital mortality and that since some of the patients were referred to the District Hospitals or home were on palliative care, the overall mortality of patients with omphalocele is higher. The only factor significantly associated with mortality of these patients was the size of the omphalocele with larger omphaloceles having significantly higher mortality than smaller omphaloceles ( $p=0.028$ ). This result goes in line with previous studies suggesting that the size of the omphalocele affects the prognosis of these patients, with larger omphaloceles having a higher mortality rate compared to a smaller omphalocele [9]. Our study also showed that these patients had a high rate of sepsis with 16 (51.6%) of our patients developing sepsis during the hospital stay. Neonatal infections are the leading cause of death in newborns in low-income countries [19] and are well documented at CHUK [20], [21]. The observation that these newborns have a high rate of infection is not wholly unexpected and is multifactorial, including poor hygiene and transferring conditions, use of non-sterile materials and techniques in the dressing of the omphalocele, and also poor feeding conditions.

Interventions to reduce nosocomial infection and to improve early recognition and management of sepsis should be developed. This can include better-transferring conditions, availability of sterile dressing facilities, improved handwashing, and improved nutrition, etc.

Although documentation of omphalocele size was incomplete and although this was not statistically significant, our study suggests a trend for surgical management in smaller omphalocele (OR=2.5,  $p=0.34$ ), which is comparable with other studies describing primary closure as the mainstay of treatment for smaller omphaloceles [8]. This clearly could have played a role in the mortality of these patients, but our study does not allow us to conclude if those with larger omphalocele died because of the size of the omphalocele and associated congenital abnormalities or because they did not have access to these surgical techniques. At the time of the study, CHUK lacked most of the equipment needed and had no pediatric surgeon to perform the surgery in a timely fashion.

**Limitations:** This study had a small sample size as omphalocele is a rare condition, this resulted in reduced power and may mean that some of our "non-significant" results were Type-II errors. The results were based on a medical file review and there was incomplete documentation of some of the variables in the case files. There were also a minimal number of investigations done to screen for other associated congenital abnormalities, and as a

result we were not able to conclude whether these cardiac and genetic abnormalities could significantly impact the early outcome (mortality) of these patients, or whether their associations were also linked to the size of the omphalocele. Also, there was a lack of documentation of the reason for the surgeon's decision to manage conservatively or with a surgical approach. Finally, because there was no follow-up, the actual mortality of these patients may be much higher, as some patient who were classified as "discharge alive" were discharged for palliative care.

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