Published in final edited form as:
*Semin Pediatr Surg*. 2018 October 01; 27(5): 321–326. doi:10.1053/j.sempedsurg.2018.08.004.

# Care of Infants With Gastroschisis in Low-Resource Settings

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## Abstract

There is great global disparity in the outcome of infants born with gastroschisis. Mortality approaches 100% in many low income countries. Barriers to better outcomes include lack of antenatal diagnosis, deficient pre-hospital care, ineffective neonatal resuscitation and venous access, limited intensive care facilities, poor access to the operating theatre and safe neonatal anesthesia, and lack of neonatal parenteral nutrition. However, lessons can be learned from the evolution in management of gastroschisis in high-income countries, generic efforts to improve neonatal survival in low- and middle-income countries as well as specific gastroschisis management initiatives in low-resource settings. Micro and meso-level interventions include educational outreach programs, and pre and in hospital management protocols that focus on resuscitation and include the delay or avoidance of early neonatal anesthesia by using a preformed silo or equivalent. Furthermore, multidisciplinary team training, nurse empowerment, and the intentional involvement of mothers in monitoring and care provision may contribute to improving survival. Macro level interventions include the incorporation of ultrasound into World Health Organisation antenatal care guidelines to improve antenatal detection and the establishment of the infrastructure to enable parenteral nutrition provision for neonates in low- and middle-income countries. On a global level, gastroschisis has been suggested as a bellwether condition for evaluating access to and outcomes of neonatal surgical care provision.

### Keywords

gastroschisis; low-resource settings; low and middle-income countries; bellwether

## Introduction

The global disparity in the outcome of gastroschisis (GS) is glaring. Survival in high-income countries (HICs) has improved significantly over the last half century; from approximately 10% in the 1960's to current survival rates of over 95%[1,2]. Such improvements have not

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been duplicated in most low and lower middle-income countries with recently reported survival rates of 0-2% in Uganda, 0% in Cote d'Ivoire, and 16% in Zimbabwe[3–5]. In an international survey, two-thirds of paediatric surgery centres in sub-Saharan Africa reported a mortality rate from GS of between 75-100% and the remaining third between 50-75%[6]. Outcomes vary widely in middle-income countries globally with reported survival rates of 20% in Iran, 21% in Jamaica, 25% in Nigeria, 66% in Turkey, 35-71% in South Africa, 43-77% in China, 90% in Malaysia and 92% in Thailand[7–13].

It has been suggested by some that GS is a disease of HICs. However, the literature suggests a truly global congenital anomaly with a rising incidence[2,3,12,14–27]. In low- and middle-income countries (LMICs), the number of patients with GS presenting to a healthcare facility is increasing[15,28]. In Pretoria, there was a 35-fold increase in presenting cases between 1981 and 2001[15]. Indeed, GS is a condition regularly encountered by paediatric surgical teams in LMICs with, in one survey, an estimated 22 cases/ institution/ year in low-income countries and 12 cases/ institution/ year in middle-income countries[6]. The aetiology remains unknown[2]. The associated risk factors such as low maternal age, low body mass index, smoking, use of anti-depressants, exposure to contraceptive hormones during the first trimester, pre-gestational or gestational diabetes, alcohol, cocaine and other drugs have mostly been derived from HIC data[2,14,25,27,29–41]. Very little epidemiological data from LMICs is available. In a prospective cohort study in Uganda the majority of mothers were between 20-29 years of age despite a high proportion of teenage pregnancies in the country compared to HICs. Furthermore, mothers denied smoking or taking drugs[4]. Investigating risk factors for GS in different settings across the globe may provide fresh aetiological clues[4,42].

The paucity of data on GS from LMICs is reflected in studies investigating clinical management, interventional strategies and outcomes. This paper describes the particular challenges of managing infants with GS in the low-resource setting, potential solutions, and the use of GS as a bellwether procedure for global health evaluation and planning.

## Challenges of Managing Gastroschisis in Low-Resource Settings

The current successful management of GS in HICs results from a multi-faceted approach; antenatal diagnosis, planned delivery at a tertiary paediatric surgery centre or adequate pre-hospital management and safe transfer, pre-intervention resuscitation, bowel reduction and defect closure, and post-interventional neonatal care including the provision of parenteral nutrition until enteral feeding is established. Each component of this care package presents different challenges in the low-resource setting.

### Antenatal diagnosis and pre-hospital management

In LMICs, the majority of women now receive some antenatal care as per the World Health Organisation (WHO) guidelines[43]. However, the WHO does not currently recommend an ultrasound scan as part of that antenatal care package[43]. Antenatal ultrasound scans that do happen, are often performed in the private sector with varying levels of reliability[4]. In a prospective study of 42 neonates with GS in Kampala, 24% (n=10) of mothers had undergone an antenatal ultrasound scan, but only one had been given the correct diagnosis[4].

Hence, the majority of neonates with GS in low-resource settings are born outside of a tertiary paediatric surgery centre with no prior warning or advice regarding how to manage a neonate born with this condition[4,5,42]. Awareness and education in the community and district level hospitals regarding the pre-hospital management is commonly deficient. In Kampala, 81% of neonates with GS were born in a first or second level healthcare facility, but for most neonates, appropriate care was not initiated; 81% were without appropriate bowel coverage, 54% without intravenous (IV) access or IV fluids, 83% were without a nasogastric (NG) tube, 52% were breastfeeding and only 58% arrived within 12-hours of delivery[4]. Only 35% travelled by ambulance[4].

Delays in accessing neonatal surgical care and deficient pre-hospital management result in many neonates with gastroschisis presenting with hypothermia, hypovolaemia, coagulopathy and sepsis[4,5,9,42]. In addition, 25% present with complex GS. In some infants this may reflect postnatal factors such as bowel exposure, contamination, damage and/ or torsion of the vascular pedicle resulting in intestinal ischaemia and necrosis[44]. Even those with simple GS commonly present with very edematous and matted bowel, making reduction and closure even more challenging.

## Neonatal resuscitation and ward care

On arrival at the tertiary paediatric surgery centre, additional barriers to optimal care may exist; neonatal resuscitation may be delayed or ineffective. In many LMIC settings, newborns with GS are nursed on the general paediatric surgical ward rather than the neonatal unit, or neonatal intensive care unit (NICU) if one is available. This is often because they are considered ‘dirty’ and an infection risk to other patients. Severe shortages of the paediatric surgical workforce exist in most LMICs and hence a neonatologist, paediatric surgeon and trained neonatal nurse may be unavailable or significantly delayed following presentation[45]. In such settings, each nurse may have to care for many sick newborns and may intentionally focus time and energy caring for other infants considered more likely to survive[4]. Wesonga noted that nurses are used to sending these infants home to die suggesting that the mind-set of key members of the medical team may be a barrier to improved survival[4,6]. Similarly, newborns with GS are not prioritised for the limited operating theatre space in such settings, resulting in significantly delayed surgical care or no care even after arrival to a tertiary paediatric surgical care facility[4]. Finally, mothers are often separated from their infants negating the opportunity for them to contribute to their monitoring and basic care.

## Gastroschisis reduction and closure

The optimal method of gastroschisis reduction and closure in HICs remains controversial. The two most commonly utilised methods are primary closure under general anesthesia in the operating room or serial reductions using a preformed silo over a number of days followed by either bedside or operating room closure, with or without a general anesthetic[46,47]. Allotey compared 53 consecutive neonates that underwent either primary closure or preformed silo application and reported lower mean airway pressures and inspired oxygen requirement, higher urine output and no inotropic support in the latter group; 43% of those undergoing primary closure required inotropes[48]. A randomised controlled trial

comparing primary closure with preformed silo reported a lower requirement for ventilation in the silo group with no difference in other outcomes[49]. A meta-analysis comparing primary closure with all methods of staged closure also reported fewer ventilator days ($p<0.0001$), reduced time to first feed ($p=0.04$) and lower infection rates ($p=0.03$) in the latter group amongst studies with least selection bias[50]. Subsequently, a systematic review and metaanalysis comparing preformed silo with all alternative strategies reported lower ventilatory requirements with the former. Indeed, many neonates in the silo group required no ventilation[47]. These findings are consistent with a lower risk of abdominal compartment syndrome with use of the preformed silo.

In HICs the increased cardiorespiratory support required after primary closure can, typically, be provided in the context of a neonatal intensive care unit (NICU). This is often unavailable in LMICs; 36% availability in an international survey[6]. Furthermore, the very edematous and matted bowel that results from late presentations in LMICs may predispose to more severe abdominal compartment syndrome if primary closure is undertaken. This should mean that the preformed silo could result in improved outcomes through reduced NICU requirements. Reasons for the limited use of silos in LMICs include lack of availability, expertise and expense[6].

It is estimated that 63-79% of infants with GS in LMICs undergo general anesthesia for bowel reduction and abdominal wall closure[6]. Neonatal anesthesia can be life-threatening in this setting due to a lack of specialist training, resources and the higher American Association of Anaesthesiologists (ASA) score of the newborn at the time of surgery due to the limited pre-hospital management and in-hospital resuscitation[44,51]. In addition, neonates with GS are often born early; in Durban, South Africa 64% were preterm and 72% <2.5kg and in Harare, Zimbabwe 43% were preterm and 72% <2.5kg[5,42]. This increases the risk of neonatal anesthesia further[51].

## Intravenous access and parenteral nutrition

Maintaining consistent intravenous (IV) access in the newborn infant is challenging. In HICs, the challenge is usually overcome as a result of appropriately trained personnel that can be dedicated to the task, a wide range of central lines that can be inserted via peripheral and central veins. In addition, the deployment of specialist equipment such as ultrasound aids effective venous access[44]. Dedicated personnel such as nurse specialists, equipment such as mobile ultrasound machines and suitable consumables are often unavailable in low-resource settings. Where central venous lines are available, infection control practices may not be well established, resulting in a higher rates of sepsis. Writing from Durban, Sekabira noted that despite having access to NICU and PN, the mortality from gastroschisis was still 43% with central line sepsis being a leading cause of death[42].

For neonates with simple gastroschisis, the median duration of PN requirement in HICs is 23 days[1]. Despite PN being available for adults and older children in many tertiary level hospitals in LMICs, it is commonly unavailable for neonates. In an international survey, only 19% of tertiary paediatric surgery centres in LICs had access to PN[6]. The challenges for provision of PN to neonates in low-resources settings are two-fold. There is a lack of infrastructure and availability of neonatal specific PN bags, as well as difficulties in

achieving central IV access. The shorter bench-life of neonatal PN compared to adult PN as purchased by manufacturing companies in LMICs adds to the complexity in terms of transportation and risk of waste. In sub-Saharan Africa, South Africa manufactures neonatal PN and can transport it efficiently within the country and to adjacent countries. However, transportation further afield is not currently deemed feasible. Many other countries in sub-Saharan Africa do not have an in-country PN manufacturing company and do not have the inhospital facilities, equipment and training to prepare it locally.

## Strategies for Optimising Gastroschisis Outcomes in Low-Resource Settings

### Antenatal diagnosis and pre-hospital management

To achieve the consistent and accurate diagnosis of gastroschisis and other congenital anomalies in LMICs, WHO guidelines on antenatal care will need to be amended to include ultrasound scanning. This would lead to the incorporation of prenatal scans in national guidelines and protocols as part of routine antenatal care. Antenatal ultrasound scanning currently undertaken in the private sector varies considerably in reliability. This is related to the varying level of training undertaken by the providers and possibly the quality of the equipment available[4]. National standards for training and service provision for antenatal ultrasound scanning may help to improve diagnostic accuracy. Incorporating education regarding parental advice and referral when a congenital anomaly is detected is also vital. Consideration would have to be given to the ethical implications of antenatally diagnosed congenital anomalies and suitable guidelines and safeguards would be required.

In many LMICs stigma towards infants born with a congenital anomaly and indeed their families remains a problem. Consequently, at present it is likely that many neonates with gastroschisis or other congenital anomalies never reach a healthcare facility. Hence, community engagement and education regarding congenital anomalies and the availability of treatment is required. Improving pre-hospital care at first and second level healthcare facilitates and safe transfer for neonates with gastroschisis has the potential to make a significant impact on the outcomes[4,5]. Potential methods for achieving this include production of a pre-hospital management protocol to be distributed throughout such facilities, outreach training led by the tertiary paediatric surgical team, and/ or inviting district hospital care providers to a neonatal surgery study day held centrally at the tertiary paediatric surgery centre. This would have the added benefit of enhancing networking and communications between different members of the multi-disciplinary team at the different levels of healthcare. The protocol could be tailored to the local environment and may include the use of a clear plastic covering for the bowel, training on how to avoid torsion of the intestinal vessels and hence ischaemia, administration of IV fluids and NG tube insertion if available, kangaroo care, and safe, efficient transfer to the tertiary paediatric surgery centre.

### Neonatal resuscitation and ward care

There is evidence that implementation of protocols can improve care and outcomes of critically ill paediatric patients[52]. This would help to both standardise care, particularly for neonates with simple gastroschisis, and also help to gain a team consensus regarding the

roles of the various multidisciplinary team members in the patient's care. Establishing secure venous access should be an early priority to ensure effective resuscitation. Failure of venous access often precedes demise of the surgical newborn in LMICs[3]. To prevent this eventuality, medium term venous access options should be achieved early on, before peripheral veins are used up. These include percutaneous central venous access and possibly use of the umbilical vein for initial resuscitation.

Ekenze et al undertook a quality improvement (QI) project focussed on improving neonatal surgical outcomes in Nigeria through co-ordinated interdisciplinary collaboration[53]. This involved both individual specialist training and multidisciplinary team training between paediatric surgeons, anaesthetists and nurses. It resulted in a significant reduction in overall mortality from 48.9 to 22.7% ($p<0.05$)[53]. Khan et al undertook a QI project focused on reducing surgical site infection rates after congenital heart surgery in Pakistan[54]. Pivotal to their implementation strategy was nurse empowerment through appointment of a senior nurse to oversee the project, liaise with key stakeholders and train/ supervise local nurses on clinical skills, actively participate on ward rounds, and demonstrate assertive communication skills[54]. They reported a reduction in surgical site infection and bacterial sepsis from 30 to 1% ($p=0.0001$)[54].

Numerous studies focused on reducing neonatal mortality in LMICs have highlighted the benefit of involving mothers in the monitoring and basic care for their baby[55–57]. This is particularly important in low-resource settings where nursing staff are commonly overburdened[58–60]. Bhutta et al undertook a QI project in Pakistan utilising maternal training and empowerment; this reduced the LOS for their very low birth weight neonates from 34 to 16-days without increasing complications[57]. Although these strategies have been shown to improve outcomes in isolation, most successful initiatives for improving neonatal survival in LMICs involve a multi-faceted approach[55,57,61]. Agarwal et al implemented a simple bundle of interventions aimed at improving neonatal survival on a busy neonatal unit in Pakistan[55]. This included protocol-based management with abandonment of unnecessary interventions, nurse training and empowerment, training and utilisation of mothers as caregivers, aggressive enteral feeding, infection control measures, and rational use of antibiotics[55]. This resulted in a significant reduction in overall mortality from 29.3/1000 to 20.3/1000[55]. Another step towards improving outcomes for neonates with GS may be to move their primary care from the paediatric surgical ward to the neonatal care unit or NICU, if available. All these QI measures require whole team co-ordination, motivation and buy-in.

## Gastroschisis reduction and closure

As noted above, preformed silos have the potential for improving survival in neonates with gastroschisis in low-resource settings by minimising the risk of compartment syndrome and need for neonatal intensive care[47–50]. They also have the added benefit that they can be applied by a suitably trained medical officer / registrar or specialist nurse at the bedside, negating the need for an emergency theatre slot and consultant paediatric surgeon which may not be available[47]. In the United Kingdom, a pre-formed silo has been used routinely in many centres for sutureless closure of GS. These silos cost approximately $300 each, a price deemed by many as too expensive for the low-resource setting[6,62]. While it could be argued

that this option is still cheaper than surgery, cost-effectiveness studies are currently unavailable[62]. In some middle- and high-income countries including Mexico, Malaysia, France and Japan, the Alexis Wound Protector and Retractor (Applied Medical ®) has been used as an alternative (Figure 1). While this device has the potential disadvantage of an intra-abdominal ring which is stiffer than pre-formed silos manufactured specifically for abdominal wall defects, good outcomes have been reported in the limited studies available[63–66]. The Alexis wound protectors costs just $25-$30 each and hence are much more affordable[67]. A multi-centre interventional study using the Alexis device in LMICs would help to evaluate its effectiveness in this setting and promote its widespread use if found to be effective.

Several other strategies for gastroschisis reduction and closure have been trialled in low-resource settings. Du et al advocate for immediate reduction of the bowel and defect closure in an OR adjacent to the delivery room in those that are antenatally diagnosed[10]. Similarly, the Bianchi technique can be utilised with bedside reduction and closure of the defect immediately after resuscitation[68–70]. This technique has the benefit of avoiding neonatal anesthesia, however it may expose the neonate to an increased risk of abdominal compartment syndrome and need for intensive care. In order to minimise this risk, an umbilical flap or ‘turban’ can be utilised without closing the fascia defect underneath thus reducing the tension and intra-abdominal pressure[71–73].

## Parenteral nutrition and intravenous access

Provision of short-term PN can be life-saving for neonates with gastroschisis and other gastrointestinal congenital and acquired conditions requiring surgical intervention. Although deemed an expensive resource, PN can in fact be cost-effective in terms of disability-adjusted life years (DALYs) averted. This is particularly true for neonates with conditions such as gastroschisis, which can potentially be cured with the use of a short period of PN resulting in a full, normal life[74]. Urgent work is required to evaluate and develop existing supply chains so that PN can become available for neonates in LMICs. Such a venture would require collaboration between numerous stakeholders including manufacturing companies, paediatricians, gastroenterologists, nutritionists, laboratory team members, paediatric surgeons, hospital management and procurement teams. Collaboration with international partners could help to facilitate this. Similarly, an interventional study aimed at improving outcomes from gastroschisis that incorporated use of PN in the low-resource setting may provide the evidence and incentive required to get such a programme off the ground. At present, the majority of neonates with gastroschisis die within the first week of life, hence one might consider providing PN only to those who survive to 1-week to optimise resource allocation[75]. This would also be consistent with studies suggesting outcomes are better for children in intensive care if PN is started after a week rather than immediately when they are so sick during the first few days of admission[76].

In the immediate resuscitative period, studies have shown that umbilical vein catheterisation can be used successfully in neonates with gastroschisis[77]. In the longer term, provision of central lines for neonates requiring short-term PN has the potential to be life-saving. Again, studies proving that gastroschisis can be successfully managed in the low-resource setting

utilising these basic resources may be required to help incentivise local procurement and management teams to provide such resources. Such research is required to help overcome the current beliefs that gastroschisis is a futile condition not worthy of precious resource utilisation[4].

An early and aggressive enteral feeding program has the potential to minimise PN requirements. Earlier time to first enteral feed has been associated with a shorter duration of PN and length of hospital stay in both HIC and LMIC settings without increasing the risk of necrotizing enterocolitis[29,78,79]. When PN is not available, there may be the potential for some survivors without this resource[13]. Term neonates are estimated to have the ability to survive up to 1-month without nutrition[80]. Hence, those few who are delivered at term or close to, have simple gastroschisis, and do not succumb to sepsis have a chance of survival without PN. In Blantyre, Malawi, the mortality from gastroschisis is reported to be 60% without routine availability of PN[3]. Similarly, in Malaysia, Naidu reports some survivors without the use of PN[13].

## Gastroschisis as a Bellwether Condition

Bellwether surgical procedures were widely reported in The Lancet Commission on Global Surgery published in 2015[81]. These procedures can be seen as surrogates for the overall quality of healthcare and availability of resources. The three proposed procedures were laparotomy, caesarean section, and treatment of an open fracture. Following outcome analyses from a wider range of operations, these three were considered the best proxies for estimating the capacity of an institution to provide a broader range of surgical care. Hence, if an institution can provide these three procedures effectively, then it should also be able to manage a wide range of general surgical, obstetric and orthopaedic emergencies. However, the provision of surgical care for neonates or young children was not considered during this process and indeed provision of these three bellwether procedures provides little information about whether a centre has the capacity to provide neonatal surgical care.

The ability to assess institutional capacity and access to surgical services is vital for global health planning. The Lancet Commission bellwether procedures have been used to map 2-hour access to emergency and essential surgical care globally[82–85]. This helps to identify areas to prioritise global health funding and efforts to help reach the target of 80% coverage of essential surgical and anaesthetic care per country by 2030[81]. Such data is not available regarding access to neonatal or paediatric surgical care. Yet up to 50% of the population in LMICs are children[45]. Indeed congenital anomalies are a major global health problem, now listed as the 5$^{th}$ leading cause of death in children under 5-years of age globally[86]. The overwhelming majority (97%) of the deaths from congenital anomalies are in LMICs and it is estimated that up to two-thirds of the disability and deaths related to congenital anomalies could be averted through the provision of surgical care[87,88].

GS is one of the commonest congenital anomalies and has been suggested as a bellwether condition for assessing the capacity of an institution to provide neonatal surgical care[3,89]. This is because in most cases it is an isolated condition and caring for neonates with GS requires all the components of a neonatal surgical care system. Hence, if an institution is

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able to effectively care for neonates with GS, it is likely to have the skills and resources available to effectively manage a wide range of other neonatal surgical conditions. In order to ensure neonates are appropriately represented in plans to scale up access to surgical care globally, it will be vital to first map current access and outcomes; GS could be used as a proxy for this. In addition to the tertiary level care setting, GS tests the ability of first and second level care facilities to resuscitate, stabilise and safely transfer a surgical neonate.

## Conclusion

The current disparity in outcomes for GS between HICs and LMICs is glaring and reflects poorly on the global community. This paper outlines potential solutions including a practical bundle of intervention for use in LMICs. There is very limited published literature from LMICs using similar interventions and further research would be informative. In addition to GS service delivery, the results of such research could aid strategic planning for neonatal surgical services more widely as many of the recommended interventions may also help to improve outcomes for other neonatal surgical conditions. This is a neglected area on the global health agenda which should now be prioritised if neonatal and under-5 mortality targets set in the Sustainable Development Goals are to be met[90].

## Acknowledgements

We thank Dr. Alejandro A. Peñarrieta Daher, Dr. Eduardo Bracho Blanchet, Dr. Roberto Dávila Pérez and Dr. Cristian R. Zalles Vidal from Hospital Infantil de México Federico Gomez, México, for information provided. We also acknowledge Ms Kat Ford, Ms Sarah Bradley and Ms Kate Tavener for sharing information from fieldwork in Uganda.

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**Figure 1.**

A) Alexis WP&R in situ 3-days after application, B) Alexis WP&R being removed 24 hours after complete bowel reduction, C) Dressing applied following sutureless closure and left in situ for 14-days.



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