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Monika Uribe Leitz Date

The Impact of Infectious Complications in Gastroschisis

on Costs and Length of Stay

By

Monika Uribe Leitz
Master of Public Health

Global Health

_____

Mehul V. Raval, M.D., M.S.
Committee Chair

_____

Carlos Del Rio, M.D.
Committee Member

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By

Monika Uribe Leitz

M.D., Universidad Anahuac, 2012

Thesis Committee Chair: Mehul V. Raval, M.D., M.S.

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Abstract

The Impact of Infectious Complications in Gastroschisis on Costs and Length of Stay

By Monika Uribe Leitz

Purpose: Gastroschisis (GS) is the most common congenital abdominal wall defect and the incidence is rising. Management and outcomes for GS remain highly variable. Infectious complications have been shown to adversely impact the care of GS patients. Our objective was to provide estimates of the impact of infectious complications on length of stay (LOS) and costs.

Methods: Using an adminstrative national discharge database, 1,378 patients with GS were identified. Patient and hospital level characterisics were compared for patients with and without infectious complications. LOS and costs were evaluated using regression models controlling for patient and hospital level factors as well as for the type of infectious complication.

Results: Two-thirds of all GS patients had infectious complications. Infectious complications were common for both simple and complex GS (63.5%, 73.1%). After controlling for patient and hospital factors including simple versus complex GS, LOS in patients with infection was significantly higher than in patients with no infection (unadjusted 39 days vs. 32 days, p=<0.001, adjusted 4.5 day increased LOS, p=0.001). Specifically, sepsis was associated with increasing median LOS by 11 days (p=<0.0001), candida infection by 14 days (p=0.0004), and wound infection by 7 days (p=0.007). Although costs did not differ between patients with and without infection, on stratified analyses for specific infection type costs were elevated. Sepsis increased the median costs by $22,380 (95% Confidence Interval (CI):$14,372-$30,388;p=<0.0001), wound infection increased costs by $32,351 (95%CI:$17,221-$47,481;p=<0.0001), catheter-related infection (CRI) by $57,180 (95%CI:$12,834-$101,527;p=0.011), and candida infections by $24,500 (95%CI:$8,832-$40,167;p=0.002).

Conclusion: Infectious complications among GS patients are common and are important drivers of increased costs and prolonged LOS. We provide national estimates in terms of dollar figures and number of days increased by specific infectious complications that may help guide future investment toward quality improvement efforts.

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Table of Contents

Chapter 1: Introduction

The under-five mortality rate has decreased significantly in recent years. Neonatal deaths have had a slow decrease, and represent 44% of all deaths in this age group (Oza, Lawn, Hogan, Mathers, & Cousens, 2015). However, the majority of these deaths could have been prevented with optimal care, including the prevention of infection. Infections are one of the leading causes of death in children in the world. Specifically, neonates in the intensive care unit (NICU) are at a higher risk of acquiring nosocomial infections and other infections because of their immunological status and other comorbidities (Bucher et al., 2011).

Infectious complications are important comorbities in patients with gastroschisis; a congenital anomaly of the abdominal wall. Neonates with gastroschisis require a surgical intervention and are admitted to the NICU. Few studies have looked into the impact of SSI and specific infectious complications in this population and its outcomes (e.g., length of stay, costs and other comorbidities). Protocols and procedures have been difficult to standardize and report within the hospital setting and even more so at a national level. As a result the impact of specific infectious complications has been overlooked in gastroschisis newborns, because the main focus is to achieve a timely closure of the defect. Nevertheless, infections are a big driver of morbidity, increased length of stay and costs in these patients.

1.1 Epidemiology

Gastroschisis is a common congenital anomaly found in approximately five in every 10,000 births (Kunz, Tieder, Whitlock, Jackson, & Avansino, 2013). The incidence of this disease has increased over the years, but its mortality has declined, having a 90% survival rate (Kilby, 2006). It is usually an isolated anomaly, with no other chromosomal anomalies found,

although with high rates of intestinal atresia, necrotizing enterocolitis and intestinal malrotation. Often these patients with intestinal atresia, intestinal peforation, or other anomalies are considered complex gastroschisis. The intestinal length in patients with gastroschis can be short or dysmotile or both (Phillips, Raval, Redden, & Weiner, 2008).

Many studies have tried to identify the reason for the increase in the incidence in gastroschisis, finding that women under 20 years old (Holland, Walker, & Badawi, 2010) have a significant increase of pregnancies with gastroschisis (Minutillo, Rao, Pirie, McMichael, & Dickinson, 2013). Other associated factors could be maternal substance use, such as cocaine, marihuana and alcohol, which can be associated with early interruption of the fetal omphalomesenteric blood supply (Kilby, 2006). An accurate etiology has not been identified yet.

Despite high survival rates the complications of gastroschisis remain severe. Gastroschisis is one of the leading causes of short-bowel syndrome and one of the leading indications for small bowel transplantation (Lao, Larison, Garrison, Waldhausen, & Goldin, 2010).

1.2 Pathophysiology

Gastroschisis comes from the Greek "abdominal cleft." It is a paraumbilical defect in the abdominal wall, usually found to the right, allowing abdominal contents to herniate through the defect and to be in direct contact with the amniotic fluid (Cowan et al., 2012). Contrary to omphalocele, gastroschisis is not covered by the peritoneal membrane. The prolonged exposure of the intestine to the amniotic fluid causes an inflammatory response that can cause intestinal injury and in most cases ileus. The defect is usually small (<4 cm); and because it is

small, it is rare to find evisceration of solid organs such as the spleen, liver and kidneys. Usually hollow organs with positive intraluminal pressure are eviscerated, such as the small intestine (Castilla, Mastroiacovo, & Orioli, 2008).

1.3 Treatment

The treatment of pregnant mothers with a gastroschisis fetus is still in debate. There is no clear indication of whether a cesarean section or vaginal delivery is best in terms of outcomes for the newborn. Usually, babies with gastroschisis have intra-uterine growth restriction and are more likely to be born prematurely (Edward T. Bope MD, 2014).

To date, there is a large variation in management of patients with gastroschisis, as well as closure and repair techniques, which has made it hard to standardize the best treatment for this population, leading to a wide variety of short-term and long-term outcomes depending on the institution. Two main surgical techniques have been described: primary fascial closure and staged repair with a silo. Many studies have tried to describe the best method for clinical outcomes, but none has proved to be superior (Pastor et al., 2008). Furthermore, the difference in infectious complications in patients with primary closure versus secondary closure, which might lead to important recommendations in treatment and management of these patients, have not been studied. Likewise, the difference in patients with simple gastroschisis and complicated gastroschisis with and without infection has not been studied, making it difficult to improve quality of care in these patients and defining if infection really has an impact on the outcome of patients, in terms of length of stay, costs, and other comorbidities. The purpose of this study is to identify if infectious complications make a difference in these outcomes.

Chapter 2: Comprehensive Review of the Literature

Gastroschisis (GS) is the most common abdominal wall defect, and its incidence has been increasing worldwide, with an of incidence of 4-5 per 10,000 births in the last decade (Kilby, 2006). This trend has been seen globally as shown in Table 1 (Bermejo, Mendioroz, Cuevas, & Martinez-Frias, 2006). Thus, GS is not only a problem for newborns and their families, but a critical public health problem that needs to be addressed. Researchers believe that gastroschisis may be considered a pandemic, strongly associated with young maternal age (Castilla et al., 2008; Clark, Walker, & Gauderer, 2009).

Gastroschisis is not a fatal malformation, with a 90% survival rate (Fillingham & Rankin, 2008) and great long-term outcomes if treated appropriately.

Table 1: Trends of incidence increase of gastroschisis worldwide.

Rates of gastroschisis in 14 members' registries of International Clearinghouse for Birth Defects Surveillance and Research with significant temporal trend

Registry	Rate per 10 000		P trend (χ^2 test)
	First three years	Last three years	
Japan (1974-2003)	0.96	2.58	<0.01
Australia:			
Western Australia (1980-2003)	1.53	4.30	<0.01
Victoria (1983-2003)	0.71	2.44	<0.01
Canada Alberta (1980-2003)	1.57	3.53	<0.01
USA Atlanta (1974-2003)	0.85	2.48	<0.05
Mexico (RYVEMCE) (1980-2003)	1.44	5.11	<0.01
South America (ECLAMC) (1974-2003)	0.04	2.92	<0.01
Norway (1974-2003)	1.34	2.74	<0.01
Finland (1993-2003)	1.70	3.73	<0.01
Ireland Dublin (1980-2003)	0.13	2.05	<0.01
England and Wales (1995-2003)	1.52	2.05	<0.01
France:			
Paris (1981-2003)	0.18	3.44	<0.01
Central East (1978-2003)	0.42	1.60	<0.01
Slovak Republic (1995-2003)	0.55	1.10	<0.05

RYVEMCE=Mexican Registry and Epidemiological Surveillance of External Congenital Malformations. ECLAMC=Estudio Colaborativo Latino Americano de Malformaciones Congénitas.
The 11 registries with non-significant temporal trend (mean rate per 10 000 of the period): USA Texas 1996-2002 (3.85); Netherlands North 1981-2003 (0.81); Germany Saxony Anhalt 1987-2003 (1.54); Hungary 1982-2003 (0.38); Italy North-East 1981-2003 (0.51); Italy Emilia Romagna 1978-2003 (0.81); Italy Tuscany 1992-2003 (0.42), Italy Campania 1991-2003 (0.58); Malta 1993-2003 (1.02); Israel Birth Defects Monitoring System 1978-2003 (0.29); United Arab Emirates 1996-2003 (0.79).

The etiology of GS has not been clearly identified. The majority of the studies suggest an association between low maternal age (under 20 years of age) and maternal environmental

factors, such as drug consumption during pregnancy, which increase the risks of GS, as shown in Table 2 (Skarsgard et al., 2015).

Table 2: Risk factors of a gastroschisis pregnancy.

TABLE 3. *Bivariate, Age-Adjusted, and Multivariate Logistic Regression Models Evaluating Risk Factor Prediction of a Gastroschisis Pregnancy*

	Bivariate logistic gee model			Age-adjusted logistic GEE model			Multivariate logistic GEE model		
	OR	95% CI	*p*-value	OR	95% CI	*p*-value	OR	95% CI	*p*-value
Age (years)	0.84	0.83, 0.86	<0.0001	—	—	—	0.85	0.83, 0.87	<0.0001
Alcohol	1.65	1.20, 2.29	0.0023	1.67	1.22, 2.30	0.0016	0.82	0.57, 1.18	0.2885
Tobacco	3.32	2.77, 3.98	<0.0001	2.53	2.08, 3.06	<0.0001	2.86	2.22, 3.66	<0.0001
Marijuana	7.94	5.50, 11.48	<0.0001	4.58	3.05, 6.90	<0.0001	—	—	—
Cocaine	11.32	5.10, 25.13	<0.0001	8.02	3.41, 18.83	<0.0001	—	—	—
Methamphetamine	2.90	0.83, 10.15	0.0950	1.16	0.32, 4.21	0.8236	—	—	—
Heroin	10.05	1.88, 53.79	0.0070	5.39	0.73, 39.87	0.0990	—	—	—
Any illicit drug	9.24	6.47, 13.21	<0.0001	5.46	3.69, 8.07	<0.0001	3.54	2.22, 5.63	<0.0001
History diabetes	2.29	1.39, 3.78	0.0011	3.40	1.97, 5.88	<0.0001	2.81	1.42, 5.57	0.0031
Depression meds	4.69	2.60, 8.45	<0.0001	6.09	2.97, 12.49	<0.0001	4.04	1.38, 11.80	0.0108
Folic Acid	0.62	0.51, 0.76	<0.0001	0.95	0.77, 1.17	0.6448	0.88	0.69, 1.14	0.3514

—, not used in multivariate model, rather combined in composite "illicit drug" variable.
GEE, general estimating equation.

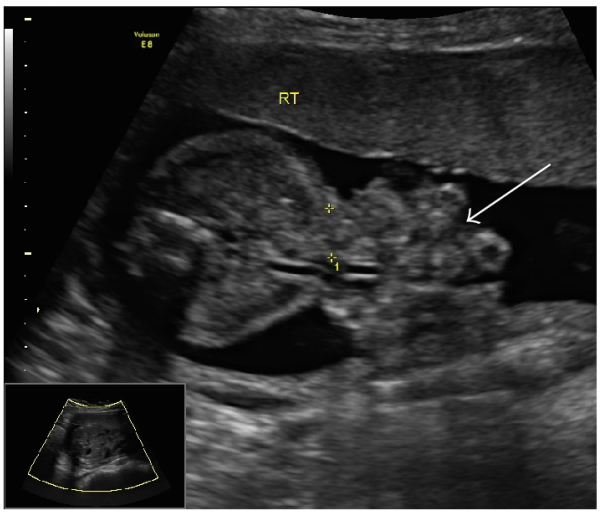
It is important to make the distinction between omphalocele and GS. Omphalocele is an abdominal wall defect in which the eviscerated organs are covered by a membrane, and do not come into direct contact with the amniotic fluid (Kelly & Ponsky, 2013). Omphalocele has a genetic predisposition, whereas GS is believed to be related to environmental factors (Henrich, Huemmer, Reingruber, & Weber, 2008). However, according to Feldkamp et al., gastroschisis may have a multifactorial model of inheritance (Feldkamp, Carey, Pimentel, Krikov, & Botto, 2011). They found a statistically significant risk of gastroschisis related to familial factors (Feldkamp et al., 2011). In terms of race and ethinicty, no associations between these factors and GS have been identified, although reported rates of GS in the U.S. have been higher in Caucasians compared to African-Americans (Abdullah et al., 2007) and

Orientals (Forrester & Merz, 1999). Other congenital anomalies are usually present in patients with omphalocele, such as Beckwith-Wiedemann syndrome, pentalogy of Cantrell, bladder/cloacal extrophy, and Down syndrome (Kelly & Ponsky, 2013), whereas patients with GS usually do not have other specific congenital anomalies associated.

Gastroschisis is also one of the most common congenital malformations that can be diagnosed prenatally with an ultrasound (Frybova, Vlk, Kokesova, & Rygl, 2015). The typical sonographic finding in patients with gastroschisis are multiple loops of bowel floating freely in the amniotic fluid (David, Tan, & Curry, 2008). Figure 1 shows the typical ultrasound finding (David et al., 2008). Gastroschisis can be diagnosed as early as in the first trimester, by the 11th week of pregnancy when the physiological deffect should have returned to the peritoneal cavity (Cullen et al., 1990). However, no standardized protocol of ultrasound timing in mothers pregnant with GS infants exists, nor are there specific ultrasound parameters that could help identify postnatal outcomes, since the management and treatment of expecting mothers varies significantly according to their attending physicians. Several studies have attempted to identify prognostic factors, but a consensus has not yet been reache. A study by Ghionzoli et al. sought to identify prognostic ultrasound factors that could help determine outcomes of patients with gastroschisis that could lead to postantal complications. For example, polyhydramnios has been associated with fetal bowel dilation (FBD) and atresia in this patient population. Patients with these findings have worse clinical outcomes, such as longer parenteral feeding, a need for greater bowel resection, and intestinal necrosis and sepsis, although these outcomes have no effect on mortality (Ghionzoli et al., 2012). These findings are important to mention because they impact the clinical outcome of the newborn, as well as their length of stay (LOS) and costs. The study by Ghionzoli et al. can be compared to the study by Fybrova et al., where they concluded that intra-abdominal

dilation is a strong predictor of intestinal atresia and therefore has a worse postnatal outcome. In the study by Fybrova, more than half of the women had olygohidramnios, and they correlated this with worse postnatal outcomes as well. Many others are skeptical about specific ultrasound parameters to determine outcomes in newborns with GS because one of the most studied parameters is bowel dilation, which is a very inaccurate parameter to measure. The parameter to measure results in many descrepancies because the definition of bowel dilation and the specificity of where the bowel is measured vary across institutions and sonographers. Bowel dilation can be identified by measuring small bowel, large bowel, luminal diameter, or outer bowel wall diameter, (Langer, Khanna, Caco, Dykes, & Nicolaides, 1993) which makes it very inaccurate and difficult to standardize. Such is the case of Badillo et al., where they didn't find any correlation betweeen the presence of additional gastrointestinal (GI) abnormalities found on the prenatal ultrasound and postnatal outcomes. They found that fetuses with abnormal GI findings in the prenatal ultrasound did not have a worse clinical outcome compared to those with normal GI findings. Further studies are needed to determine a gold standard for ultrasound parameters.

Figure 1: Ultrasound image showing small anterior wall defect beside umbilical cord insertion with small bowel herniation (arrow).



Based on these different parameters, many studies have tried to determine the best moment for delivery. Since the exposure of the intestines to the amniotic fluid causes more dilation and inflamation, many researchers believe that early delivery is preferred. However, the results have been mixed. Some studies suggest worse outcomes with early delivery, such as increased risk of infectious complications and worse long-term neurodevelopmental outcomes. A study conducted by Maramreddy found that patients that were delivered before 37 weeks of gestation had 14 times increased risk of morbidity, specially catheter related sepsis, which can be associated with the delay of full enteral feeds (Maramreddy, Fisher, Slim, Lagamma, & Parvez, 2009). These patients need a central catheter for a longer period of time, which leads to higher risk of infections. Other concerns about preterm delivery are longer days of stay, increased risk of hypothermia, hypoglycemia, hyperbilirubinemia, gastroesophageal reflux, abnormal intestinal motility, immature suck-swallow reflex, and pulmonary complications such as transient tachypnea and respiratory distress syndrome (Wang, Dorer, Fleming, & Catlin, 2004). A study conducted by Huang et al. concluded that term delivery is beneficial for the newborn with gastroschisis, with shorter LOS, earlier defect closures and shorter times to full feeds (Huang et al., 2002). Soares et al. Did not find any benefit of preterm delivery, because patients did not achieve full feeds faster (Soares et al., 2010). Other studies have focused on evaluating infectious complications and their association with gestational age. Baird et al., for example, found no association between infectious complications and preterm delivery (Baird, Puligandla, Skarsgard, & Laberge, 2012).

Gastroschisis management and treatment is complex and varies significantly from one hospital to an other and from physician to physician (Murthy et al., 2014). GS patients have many comorbidites due to the nature of the disease -- lacking an abdominal wall and with

their intestines and sometimes other abdominal viscera exposed. There is no gold standard in treatment and management for mothers expecting fetuses with GS, nor for the newborns. It is essential therefore, that these protocols are put into place to improve quality of care in newborns with gastroschisis.

For many years, an important topic of debate among healthcare providers has been infectious complications following surgical repair of GS. Many different treatment optionsare available for newborns with gastroschisis; they can have a primary surgical repair or a staged closure. Primary surgical repair is the method of preference by some surgeons, according to the latest surveys (Aldrink, Caniano, & Nwomeh, 2012). Primary repair consists of immediately closing the defect. In 1967, Schuster described sateged repair with visceroabdominal disproportion. Some studies have been conducted to assess which method is preferable, but much research is yet to be done. To date, very few studies have looked into infectious complications in patients with GS. This is a great concern because, although the survival rate is greater than 90%, imfectious complications contribute highly to patient morbidity (Henrich et al., 2008). In addition no guidelines exist regarding the duration and class of antibiotics to use in neonates with GS (Baird et al., 2012).

After researchers started recognizing differences in outcomes and mortality rates within their GS patients, they began to try to identify risk categories and understand what was happening. Amoury et al. found that newborns with atresias had a survival rate of 33%, whereas those without atresia had a survival rate of 66% (Amoury, Ashcraft, & Holder, 1977). Further studies have been conducted, leading to the risk categorization developed by Mollik et al., in which patients with bowel atresia, stenosis, perforation or ischemia are defined as having complex gastroschisis (CG) (Molik et al., 2001). Patients without these associated intestinal

abnormalities are considered to be simple gastroschisis (SG). Increased mortality and comorbidities, such as "longer duration of mechanical ventilation, extended period of adynamic ileus, and a longer time delay before tolerating full enteral feedings," have been seen in patients with CG (Molik et al., 2001). A study by Bergholz found "a strikingly increased mortality in newborns with complex compared to those with simple gastroschisis" (Bergholz, Boettcher, Reinshagen, & Wenke, 2014). It is not surprising that patients with CG have worse outcomes, as they have other GI abnormalities and comorbidities, but very few studies have been done to identify risk factors of infectious complications in newborns with GS independent of their risk categorization. Likewise, few studies have been conducted to identify which infectious complication leads to worse outcomes, higher LOS, and increased costs in newborns with GS. This study aims to identify these infectious complications, which will lead to quality improvement in healthcare.

A study conducted by Baird et al. using the Canadian Pediatric Surgery Network (CAPSNet) database to identify infectious complications depending on type of closure found that wound infections appeared to be more prevalent in high-volume centers, but the reason remains unclear (Baird et al., 2012). They also found that after an episode of catheter related infection (CRI), the risk of developing another CRI was higher, as was the LOS (Baird et al., 2012). According to Sydorak et al., the increase of costs in patients with GS is being driven by operative procedure, ventilatory days, male gender, and LOS (Sydorak et al., 2002). Almost half of the expenses (43%) were room expenses, physician fees (15%), respiratory and pulmonary care (10%), and supply and devices (10%), making up the majority of costs in their retrospective analysis of a single institution (Sydorak et al., 2002). Although this is a very useful study and one of the first in analyzing costs for GS, it is lacking very important variables of interest, such as classification of disease, other comorbidities and infectious

complications. These variables are essential because they can determine many clinical outcomes and therefore impact LOS and costs significantly. Infectious complications are associated with a significant proportion of deaths and LOS (Baird et al., 2012). In a study in Sweden with a study population of 96 patients, Kassa found that intestinal atresia, closed gastroschisis, secondary closure and sepsis were determinants of poor outcomes, as measured by LOS and duration of parenteral nutrition (Kassa & Lilja, 2011). Assumptions can be made in relating increased LOS with a proportional increase of costs, but the complications driving that increment have not yet been identified. If these complications could be identified, approaches to management and treatment of these patients could be improved, without necessarily increasing costs. With the recent changes in the healthcare industry and the integration of new policies into the U.S. healtchare system, it is essential that we take into consideration and acknowledge factors such as LOS and costs of the diseases that are being treated.

The results of all these studies are mixed and they depend mainly on the interest of the researchers or institutions. Many of the studies have focused on outcomes depending on mode of delivery and gestational age, and others have focused on mode of closure and timing; however, no study has taken all of these factors into consideration. An effort to standardize management of patients with GS must be made. It is imperative that the identification of infectious complications in newborns with GS is taken into account, and more efforts should be made to minimize these complications, since infectious complications, mainly sepsis, are still the leading cause of mortality in this patient population (Driver et al., 2000).

Gastroschisis has an important public health impact because it is a costly malformation and its incidence is increasing. This disease affects disproprotionately young women who,

because of social factors, may not seek healthcare and therefore have worse clinical outcomes. The medical technology to treat newborns with GS has improved over the past decades, and mortality has decreased. But as mortality has decreased, the costs have increased. According to Alvarez et al., the number of surgical repairs of GS doubled between 1996 and 2003 in the U.S. (Alvarez & Burd, 2007). As Mastroiacovo points out, this scenario calls for an increase in public health investment (Mastroiacovo, Lisi, & Castilla, 2006) that will improve surveillance in parts of the world where surveillance does not exist and enhance birth defect registries to allow for greater collaboration.

Chapter 3: Manuscript

"Journal of Pediatric Surgery"

a) Title Page for Manuscript

The impact of infectious complications in gastroschisis on costs and length of stay

b) Contribution of student

The Kids' Inpatient Database was provided to the student by Dr. Mehul V. Raval. It was analyzed using SAS by the student with help from Courtney McCracken and Curtis Travers from the Department of Pediatrics from Emory University. They also helped with the creation of tables and figures.

Dr. Raval was key in helping develop the concepts of the study, and the direction of the study.

The writing was done by the student, with input from Dr. Raval, and Courtney McCracken in the methods and results section.

c) Abstract

Purpose: Gastroschisis (GS) is the most common congenital abdominal wall defect and the incidence is rising. Management and outcomes for GS remain highly variable. Infectious complications have been shown to adversely impact the care of GS patients. Our objective was to provide estimates of the impact of infectious complications on length of stay (LOS) and costs.

Methods: Using an adminstrative national discharge database, 1,378 patients with GS were identified. Patient and hospital level characterisics were compared for patients with and without infectious complications. LOS and costs were evaluated using regression models controlling for patient and hospital level factors as well as for the type of infectious complication.

Results: Two-thirds of all GS patients had infectious complications. Infectious complications were common for both simple and complex GS (63.5%, 73.1%). After controlling for patient and hospital factors including simple versus complex GS, LOS in patients with infection was significantly higher than in patients with no infection (unadjusted 39 days vs. 32 days, p=<0.001, adjusted 4.5 day increased LOS, p=0.001). Specifically, sepsis was associated with increasing median LOS by 11 days (p=<0.0001), candida infection by 14 days (p=0.0004), and wound infection by 7 days (p=0.007). Although costs did not differ between patients with and without infection, on stratified analyses for specific infection type costs were elevated. Sepsis increased the median costs by $22,380 (95% Confidence Interval (CI):$14,372-$30,388;p=<0.0001), wound infection increased costs by $32,351 (95%CI:$17,221-$47,481;p=<0.0001), catheter-related infection (CRI) by $57,180 (95%CI:$12,834-$101,527;p=0.011), and candida infections by $24,500 (95%CI:$8,832-$40,167;p=0.002).

Conclusion: Infectious complications among GS patients are common and are important drivers of increased costs and prolonged LOS. We provide national estimates in terms of dollar figures and number of days increased by specific infectious complications that may help guide future investment toward quality improvement efforts.

d) Introduction

The under-five mortality rate has decreased significantly in recent years. Neonatal deaths have had a slow decrease, and represent 44% of all deaths in this age group (Oza et al., 2015). However, the majority of these deaths could have been prevented with optimal care, including the prevention of infection. Infections are one of the leading causes of death in children in the world. Specifically, neonates in the intensive care unit (NICU) are at a higher risk of acquiring nosocomial infections and other infections because of their immunological status and other comorbidities (Bucher et al., 2011).

Infectious complications are important comorbities in patients with gastroschisis; a congenital anomaly of the abdominal wall.

Neonates with gastroschisis require a surgical intervention and are admitted to the NICU. Few studies have looked into the impact of SSI and specific infectious complications in this population and its outcomes (e.g., length of stay, costs and other comorbidities). Protocols and procedures have been difficult to standardize and report within the hospital setting and even more so at a national level. As a result the impact of specific infectious complications has been overlooked in gastroschisis newborns, because the main focus is to achieve a timely closure of the defect. Nevertheless, infections are a big driver of morbidity, increased length of stay and costs in these patients.

To date, there is a large variation in management of patients with gastroschisis, as well as closure and repair techniques, which has made it hard to standardize the best treatment for this population, leading to a wide variety of short-term and long-term outcomes depending on the institution. Two main surgical techniques have been described: primary fascial closure and staged repair with a silo. Many studies have tried to describe the best method for clinical outcomes, but none has proved to be superior. Furthermore, the difference in infectious

complications in patients with primary closure versus secondary closure, which might lead to important recommendations in treatment and management of these patients, have not been studied. Likewise, the difference in patients with simple gastroschisis and complicated gastroschisis with and without infection has not been studied, making it difficult to improve quality of care in these patients and defining if infection really has an impact on the outcome of patients, in terms of length of stay, costs, and other comorbidities. The purpose of this study is to identify if infectious complications make a difference in these outcomes.

e) Methods

1.1 Overview

Data on patient encounters from the Agency for Healthcare Research and Quality – sponsored Healthcare Cost and Utilization Project Kids' Inpatient Database (KID) were analyzed (KID, 2012). The KID is an administrative data set of patients 21 years or younger and currently contains data on over 10 million hospitalizations from 44 states. The KID uses a sampling of pediatric discharges, and data are subsequently weighted to produce national estimates on outcomes of interest. The KID has a sample rate of 80% for all pediatric discharges and is estimated to capture 87% of the U.S. population (KID, 2012) .

Individual patients that are hospitalized multiple times in one year can be present in the KID multiple times, as it contains discharge-level records, not patient-level records (KID, 2012).

1.2 Study population

The dataset contains 3.2 million pediatric discharges and 255 variables. The International Classification of Diseases Codes 9th Revision (ICD-9-CM) code for gastroschisis 756.73 was used to identify the study population. Using this code 2,323 (7%) patients of the total sample where identified with gastroschisis.

Once the patients with gastroschisis were identified, further cleaning of the data was performed in order to maintain the most accurate number of patients who were born with gastroschisis, treated and discharged. Because the KID database only contains age in years, we limited the sample to those who had the "Age" variable of 0 years and patients who were discharged to their home or home healthcare. Patients who were transferred to another facility were not included, as this would not be an adequate estimate of length of stay (LOS) and costs. We also limited the sample to those patients who had a minimum of 15 days of LOS, in order to have accurate LOS and cost estimates. Additionally, patients who died; those who had omphalocele or another severe congenital anomaly, such as brain deformities, skull deformities, malposition of heart; and patients awaiting transplants and with "do not resuscitate" status were excluded from the study, because we considered that these patients did not represent the regular gastroschisis population and thus, could not be generalized.

After the final study population was defined, patients were divided into complex gastroschisis (CG) and simple gastroschisis (SG) groups. The simple gastroschisis group comprised patients with no other intestinal abnormality. In the complex gastroschisis group were patients with volvulus, intestinal atresia, stenosis, and necrosis (Molik et al., 2001); patients with gastrostomy and ileostomy complications were also categorized as complex. Later, the CG and SG groups were divided based on the presence of infection based on ICD-9-CM codes. Other variables were also created, such as other congenital anomalies, cardiac congenital anomalies, hepatic comorbidities, intestinal dysmotility and other comorbidities, which can be seen in further detail in Appendix 1.

1.3 Definition of variables

The variables were defined using ICD-9-CM codes, according to the "ICD-9-CM Official Guidelines for Coding and Reporting Effective October 1, 2011." All variables were created using the "DX" variable from the KID 2012. For further detail, please refer to Appendix 1.

- Infection: Infection codes were extracted from the "DX" variable, creating an "All infection variable." The following subgroups of infections were created: sepsis, urinary tract infection (UTI), respiratory infection, wound infection, candidiasis, intestinal infection, catheter related infection (CRI) and bacteremia. UTI, respiratory infection and intestinal infection were not used in the analysis because they had very low frequencies.
- Complex gastroschisis: this variable contains patients that had ICD-9-CM codes for volvulus, intestinal atresia, intestinal necrosis, stenosis and complications of gastrostomy and ileostomy.
- Excluded: patients with severe congenital anomalies, such as brain deformities, skull deformities, and malposition of heart were excluded. Omphalocele, patients awaiting transplants and "do not resuscitate" status were excluded as well.
- Delivery: Mode of delivery was divided into: vaginal delivery or C-section.
- Term: Gestational age was categorized as pre-term or term patients. Pre-term patients were those who had fewer than 37 weeks of gestation; term patients where those with more than 37 weeks of gestation.
- Weight: patients were classified as being below <2,499 gr or ≥2,500 gr. This was done in order to better classify patients into more clinically meaningful subgroups.

- Congenital anomalies: this includes all patients with a congenital anomaly other than gastroschisis, such as "other congenital anomalies," congenital hypothyroidism or tongue-tie, according to the ICD-9-CM codes.
- Cardiac comorbidities: patients with cardiac congenital anomalies and other cardiac-related comorbidity.
- Dysmotylity: patients with esophageal reflux, paralytic ileus, transitory ileus of the newborn, among others were classified as dysmotylity variable.
- Hernias: umbilical, inguinal, esophageal hernias among others were grouped in the hernia variable.
- Hepatic comorbidities: this included diagnoses such as jaundice, ascites, hepatitis, and cirrhosis.
- Respiratory: all non-infection respiratory comorbidities were classified as respiratory variable. This includes: respiratory distress syndrome, respiratory failure of newborn and apnea of newborn among other respiratory diagnoses.
- Other comorbidities: this variable had to be created because there were too many diagnoses to classify each of them as an individual variable.
- Length of stay: this variable was used directly as it is on the KID database in days, with a maximum length of stay of 365 days. Patients were limited to at least 15 days of LOS so they could represent the real gastroschisis population.
- Costs: this was created by multiplying the total charges from the discharge record by the all-payer inpatient cost/charge ratio file CCR_KID.

1.4 Statistical analysis

Data were analyzed using SAS 9.4 computer software (SAS Institute Inc., Cary, North Carolina). A p-value less than 0.05 was considered statistically significant. Variables of interest were summarized using means and standard deviations, medians with 25^{th} and 75^{th} percentiles, or counts and percentages, when appropriate. For the outcomes length of stay and cost, normality was assessed using histograms, density plots and the Shapiro-Wilk test for normality. Commonly accepted normalizing transformations (e.g., log, square-root) were applied and normality of residuals were examined in subsequent models. Failure to meet normality assumptions resulted in nonparametric analyses. Comparisons between categorical variables were made using Chi-square tests in univariate analyses. The Wilcoxon rank sum or the two-sample Kolmogorov-Smirnov test was used to compare continuous outcomes (i.e., length of stay and cost) among groups. Due to the highly right-skewed nature of the data, a normalizing transformation was not identified. As a result, quantile regression models were constructed for each outcome: cost and length of stay. In these models, the median, or 50^{th} percentile, was modeled. Thus, all model estimates are interpreted as the effect of the median cost or median length of stay. The explanatory variables used for the models were chosen by their p-value in univariate analyses, and/or if the authors considered them to be clinically significant based on a review of the literature, such as mode of delivery, sex, weight and gestational age. Results from quantile regression are presented as the effect (increase or decrease) on median cost or length of stay and associated 95% confidence intervals after adjusting for other factors in the multiple variable regression models.

1.5 IRB approval

This study was determined to be exempt from IRB, since all the data was de-identified prior to the study and it is a secondary data analysis.

2. Results

2.1 Demographics

A total of 1,378 discharges from the KID database were analyzed (Figure 1). The demographics for the study population can be seen in Table 1. Fifty-one percent were males, with no statistically difference in rates of infection compared to females.

More than 95% of the patients were underweight, which did not influence the rates of infection. Information about the gestational age was missing in approximately 35% of the patients. Of those with gestational age available (N =920), more than 85% were born before 37 weeks of gestation. White race compromised approximately half of the study population, while the other half was defined as "other race" (Black, Hispanic, Asian or Pacific Islander, Native American and other). The majority of the patients (92%) were seen at urban teaching hospitals. The unadjusted median LOS for patients with infection complications was 39 days (25^{th} – 75^{th}: 27 – 67 days) and was significantly higher than patients with no infection with a median LOS 32 (25^{th} – 75^{th}: 25 – 44 days; p= <0.001). The median costs in USD for patients with infection was $82,232 compared to $73,379 in patients with no infections (p= <0.001). In patients with CG and SG infections were present in 73% and 65%, respectively. A trend that was seen throughout the study was that complex gastroschisis had always significantly higher LOS and costs, both in the unadjusted analysis and on the adjusted model.

Other significant comorbidities and complications were cardiac congenital anomalies and other cardiac comorbidities (p= 0.015), respiratory comorbidities (p= 0.01), hernias (p= 0.023), hepatic complications (p= 0.008), wound complications (p= 0.036), and other comorbidities (p= 0.003).

2.2 Estimated LOS and Costs

Table 2 and Table 3 show the general characteristics of the patients in terms of LOS and costs, respectively. The models were created adjusting for the variables shown in the tables, excluding delivery because of missing data. These models control for all types of infections of interest. Infection increases significantly LOS in both the unadjusted analysis (39 days vs. 32 days p= <0.001) and the adjusted model with an infection significantly increasing median LOS by 4.5 days (95% CI: (2.1 –6.9 days); p= <0.001). Other comorbidities significantly increased median LOS in the adjusted models well. Hepatic comorbidities increased median LOS by 5 days (95% CI: (2.2 -7.8 days); p= 0.001), having dysmotility accounted for 7.5 days increase (95% CI: (5.1 -9.9 days); p= 0.001), cardiac comorbidities increased LOS by 3.5 days (95% CI: (0.8 -6.2 days); p= 0.01), and hernias increased the LOS by 13.5 days (95% CI: (5.3 -21.7 days); p= 0.001). Patients classified as "other race" had a 2.5 days decrease in LOS (95% CI: (0.1 -4.8 days); p= 0.038). Gender, mode of delivery and type of hospital did not have any significant difference in LOS, nor did having other congenital anomalies and respiratory comorbidities.

Having complex gastroschisis increased median costs by $66,171 (95% CI: ($55,814 - $76,528); p= <.001), and having an infection was significant in the unadjusted analysis with $82,232 compared to $73,379 in patients with no infection (p= <.001); however, in the adjusted model, infection did not seem to be significant, with an estimated $4,972 increase (95% CI: ($-1,114 - $11,058); p= 0.11). Hepatic comorbidities increased median costs by $8,363 (95% CI: ($2,144 - $14,581); p= 0.008), dysmotility increased median costs by $18,747 (95% CI: ($12,858 - $24,637); p= <.0001), cardiac comorbidities increased median costs by $7,047 (95% CI: ($542 - $13,551); p= 0.033), and hernias increased median costs by

$21,466 (95% CI: ($5,818 - $37,114); p= 0.009). Gender, race and hospital type did not have any significant increase in costs, nor did congenital and respiratory comorbidities.

2.3 Specific Infections

Tables 4 and 5 are models for specific infections. As mentioned previously, delivery was not modeled due to missing data. Of the four specific infections modeled, three had significant increase in LOS and costs. Sepsis increased median LOS by 11 days (95% CI: (8 -14); p= <.0001), wound infection by seven days (95% CI: (8 -14); p= <.0001), candida infection by 14 days (95% CI: (6.2 – 21.8); p= 0.0004), and catheter-related-infections (CRI) by 15 days (95% CI: (-4.8 – 34.8); p= 0.22). CRI had a significant increase in LOS in the unadjusted analysis with 75 days compared to 36 days in patients without CRI (p= <.0001); however, when we adjusted for all the other characteristics, the increase becomes insignificant.

All specific infections had a significant median increase in costs. When adjusting for specific infections, complex disease increased median costs by $63,639 (95% CI: ($52,923 - $74,356); p= <.0001), sepsis increased median costs by $22,380 (95% CI: ($14,372 - $30,388); p= <.0001), wound infection increased median costs by $32,351 (95% CI: ($17,221 - $47,481); p= <.0001), CRI increased median costs by $57,180 (95% CI: ($12,834 - $101,527); p= 0.011), and candida infection increased median costs by $24,500 (95% CI: ($8,832 - $40,167); p= 0.002).

3. Discussion

Identifying specific infectious complications that drive costs and LOS in patients with gastroschisis is essential to provide better healthcare and improve quality of care. Using a national database can be very helpful since it allows access to a very large dataset with

millions of patient discharges, allowing for the analysis of national healthcare trends, outcomes and charges (Anderson & Chang, 2015). On the other hand, because this database is administrative and not clinically focused, it is difficult to assess the accuracy of coding diagnoses and procedures. GS might only have been classified as an abdominal wall defect, and thus could not be included in the study. We found that the procedure code for gastroschisis closure was missing in many cases, and furthermore, the placement of a silo does not have an ICD-9-CM code. For these reasons, it is very difficult to analyze specific characteristics about this disease.

In addition, there are no codes for time periods, such as first infection diagnosis, timing of closure; therefore there is no way to know, for example, which diagnosis the patient had first. This makes it difficult to study which infectious complication was first, and if one infectious complication led to another or vice versa. Knowing the relationship within infectious complications could have helped to make better conclusions and recommendations. It is also difficult to study individual patients, since the KID's database uses discharges, and one patient can have more than one entry. These issues made our sample size inexact.

ICD-9-CM codes are a very useful tool, but need to be analyzed with care, without over interpreting their meaning. It has been difficult to correctly identify sepsis and other infections using ICD-9-CM codes. Severe sepsis was defined by a 1991 consensus conference as a syndrome that occurs when proven or suspected infection leads to organ dysfunction. As Iwashyna et al. described in their study, "Severe sepsis is a condition associated with high inpatient mortality, and also enduring effects on patient mortality, health care spending, disability, cognitive function, and quality of life." However, sepsis is still not properly analyzed using large databases (Iwashyna et al., 2014). The findings of our study are

similar, showing sepsis to be a major driver of elevated costs for GS patients. One of our limitations was that many patients had other infectious complications, but weren't included in the sepsis category since they didn't have an organ dysfunction ICD-9-CM code. This indicates that sepsis might be under represented in this population.

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i) Tables and Figures

Table 1: Characteristics of the study population with gastroschisis using the Kids' Inpatient Database 2012.

	Infection Group		P value
	No infection N (%)	Infection N (%))	
Total (N = 1378)	449 (32.6)	929 (67.4)	
Gender			
Male	217 (48.3)	486 (52.3)	0.17
Female	232 (51.7)	443 (47.7)	
Weight, (N = 714)			
>2,500 gr	17 (8)	33 (6.6)	0.49
<2,499 gr	195 (92)	469 (93.4)	
Gestational Age (N = 920)			
Term	52 (18.5)	95 (14.9)	0.17
Preterm	229 (81.5)	544 (85.1)	
Delivery (N = 897)			
C section	147 (57.2)	385 (60.1)	0.42
Vaginal delivery	110 (42.8)	255 (39.8)	
Race			
White	234 (52.2)	456 (49.1)	0.29
Other	215 (47.8)	473 (50.9)	
Hospital Type			
Rural/Urban non teaching	25 (5.6)	89 (9.6)	**0.011**
Urban teaching	424 (94.4)	840 (90.4)	
LOS days (median,25th-75th)	32 (25-44)	39 (27-67)	**<0.0001**
Costs USD (median,25th-75th)	$73,379 ($49,628-$103,356)	$83,232 ($51,707-$141,939)	**<0.0001**
Gastroschisis classification, n, (%)			
Simple	349 (77.7)	657 (70.7)	**0.006**
Complex	100 (23.4)	272 (29.2)	
Comorbities/Complications, n, (%)			
Congenital	26 (5.8)	63 (6.8)	0.48
Cardiac	84 (18.7)	228 (24.5)	**0.015**
Dysmotility	220 (49)	485 (52.2)	0.26
Respiratory	273 (60.8)	630 (67.8)	**0.01**
Hernia	16 (3.6)	61 (6.6)	**0.023**
Hepatic	162 (36.1)	404 (43.4)	**0.008**
Wound	10 (2.2)	42 (4.5)	**0.036**
Other	373 (83.1)	824 (88.7)	**0.003**

Table 2: Unadjusted Median for LOS in days and fully adjusted model on median LOS in days.

	Unadjusted Median with IQR in days (d)	Unadjusted P-value	Adjusted Effect on Median Length of Stay with 95% CI in days (d)	P value
Gender				
Male	36 (26-61)	0.31	Ref	0.69
Female	36 (26-55)		0.5d decrease (-2.9 - 1.9)	
Race				
White	37 (27-60)	0.47	Ref	**0.038**
Other	35 (26-55)		2.5d decrease (0.1 - 4.8)	
Hospital				
Rural/Urban Non Teaching	35 (25-59)	0.76	Ref	0.85
Urban Teaching	36 (26-59)		0.5d increase (-4.5 - 5.5)	
Gastroschisis Classification				
Simple	32 (25 - 45)		Ref	
Complex	68 (39.5 - 108.5)	**< 0.001**	30d increase (24.5 - 35.5)	**<.0001**
Complications/Comorbidities				
No Infection	32 (25-44)		Ref	
Infection	39 (27-67)	**<.0001**	4.5d increase (2.1 - 6.9)	**<.0001**
No hepatic comorbidity	33 (25-48)		Ref	
Hepatic comorbity	44 (29-75)	**<.0001**	5d increase (2.2 - 7.8)	**0.001**
No dysmotility	31 (24-43)		Ref	
Dysmotility	45 (30-76)	**<.0001**	7.5d increase (5.1 - 9.9)	**<.0001**
No cardiac comorbidity	34 (25-52)		Ref	
Cardiac comorbidity	41 (28-67)	**<.0001**	3.5d increase (0.8 - 6.2)	**0.01**
No congenital anomalies	36 (26-59)		Ref	
Congenital anomalies	39 (30-75)	0.07	0.5d increase (-6.1 - 7.1)	0.88
No respiratory	34 (25-52)		Ref	
Respiratory	37 (27-62)	**0.004**	2.5d increase (0.7 - 5.1)	0.06
No hernia	35 (26-56)		Ref	
Hernia	61 (40-84)	**<.0001**	13.5d increase (5.3 - 21.7)	**0.001**

IQR=Interquartile rang, CI=confidence interval, Ref=Reference

Table 3: Unadjusted median for costs in USD and fully adjusted model on median costs in USD.

	Unadjusted Median with IQR in USD	Unadjusted P-value	Adjusted Effect on Median Costs 95% CI	P value
Gender				
Male	$81,214 ($52,021 - $132,357)	0.28	Ref	0.29
Female	$79,754 ($49,687 - $122,284)		$3,321 decrease ($-9,491 - $2,849)	
Race				
White	$75,711 ($49,777 - $121,521)	**0.023**	Ref	0.46
Other	$83,571 ($52,789 - $132,584)		$2,220.5 increase ($-3,668 - $8,110)	
Hospital Location				
Rural/ Urban Non Teaching	$74,999 ($38,869 - $125,423)	0.07	Ref	0.09
Urban Teaching	$80,773 ($52,121 - $127,281)		$10,551 increase ($-1,847 - $22,949)	
Gastroschisis Classification				
Simple	$68,150 ($46,913 - $97,187)		Ref	
Complex	$141,370 ($87,074 - $235,582)	**< 0.001**	$66,171 increase ($55,814 - $76,528)	**<.0001**
Complications/Comorbidities				
No Infection	$73,379 ($49,628 - $103,356)		Ref	
Infection	$83,232 ($51,707 - $141,939)	**<.0001**	$4,972 increase ($-1,114 - $11,058)	0.11
No hepatic comorbidity	$75,104 ($50,089 - $110,850)		Ref	
Hepatic comorbity	$87,063 ($54,223 - $155,289)	**<.0001**	$8,363 increase ($2,144 - $14,581)	**0.008**
No dysmotility	$66,469 ($44,880 - $96,536)		Ref	
Dysmotility	$94,811 ($61,856 - $157,367)	**<.0001**	$18,747 increase ($12,858 - $24,637)	**<.0001**
No cardiac comorbidity	$76,357 ($50,089 - $117,840)		Ref	
Cardiac comorbidity	$86,267 ($54,139 - $144,850)	**0.0021**	$7,047 increase ($542 - $13,551)	**0.033**
No congenital anomalies	$79,079 ($50,854 - $126,388)		Ref	
Congenital anomalies	$89,934 ($55,803 - $161,064)	0.23	$7,433 increase ($-8,376 - $23,242)	0.36
No respiratory	$76,910 ($49,625 - $115,693)		($-4,727 - $7,656)	
Respiratory	$82,123 ($52,401 - $133,271)	0.08	$1,464 increase ($-4,727 - $7,656)	0.65
No hernia	$78,523 ($50,252 - $124,503)		($5,818 - $37,114)	
Hernia	$112,707 ($77,533 - $180,241)	**<.0001**	$21,466 increase ($5,818 - $37,114)	**0.009**

IQR=Interquartile rang, CI=confidence interval, Ref=Reference

Table 4: Unadjusted LOS for specific infections and fully adjusted model on median LOS in days.

	Unadjusted Median with IQR in days (d)	Unadjusted P-value	Adjusted Effect on Median Length of Stay with 95% CI in days (d)	P value
Gender				
Male	36 (26-55)	0.3	Ref	0.35
Female	36 (26-61)		1d increase (- 8.8 - 7.0)	
Race				
White (ref)	37 (27-60)	0.47	Ref	**0.006**
Other	35 (26-55)		3d decrease (0.86 - 5.15)	
Hospital				
Rural/Urban Non Teaching (ref)	35 (25-59)	0.76	No difference	1
Urban Teaching	36 (26-59)		(-3.16 - 3.16)	
Gastroschisis Classification				
Simple (ref)	32 (25 - 45)		Ref	
Complex	68 (39.5 - 108.5)	**< 0.001**	32d increase (26.4 - 37.6)	**<.0001**
Specific infections				
No sepsis (ref)	33 (25-49)		Ref	
Sepsis	48 (31-78)	**<.0001**	11d increase (8 - 14)	**<.0001**
No wound infection (ref)	35 (26-56)		Ref	
Wound infection	50 (33-88)	**<.0001**	7 days increase (8 - 14)	**0.0077**
No CRI (ref)	36 (26-57)		Ref	
CRI	75 (37-152)	**<.0001**	15d increase (-4.8 - 34.8)	0.22
No candida (ref)	35 (26-55)		Ref	
Candida	54 (33-91)	**<.0001**	14d increase (6.2 - 21.8)	**0.0004**

IQR=Interquartile rang, CI=confidence interval, Ref=Reference

Table 5: Unadjusted costs for specific infections and fully adjusted model on median costs in USD.

	Unadjusted Median with IQR in USD	Unadjusted P-value	Adjusted Effect on Median Costs 95% CI	P value
Gender				
Male	$81,214 ($52,021 - $132,357)	0.28	Ref	0.91
Female	$79,754 ($49,6874- $122,284)		$369 decrease ($-6,985 - $6,246)	
Race				
White	$75,711 ($49,777- $121,521)	**0.023**	Ref	0.21
Other	$83,571 ($52,789 - $132,584)		$4,130 increase ($-2,358 - $10,618)	
Hospital				
Rural/ Urban Non Teaching	$74,999 ($38,869 - $125,423)	0.069	Ref	0.11
Urban Teaching	$80,773 ($52,121 - $127,281)		$9,364 increase ($-2,167 - $21,245)	
Gastroschisis Classification				
Simple	$68,150 ($46,913 - $97,187)		Ref	
Complex	$141,370 ($87,074 - $235,582)	**< 0.001**	$63,639 increase ($52,923 - $74,356)	**<.0001**
Specific Infections				
No sepsis	$72,557 ($48,043 - $108,160)		Ref	
Sepsis	$98,240 ($61,354 - $184,100)	**<.0001**	$22,380 increase ($14,372 - $30,388)	**<.0001**
No wound infection	$76,886 ($49,743 - $120,293)		Ref	
Wound infection	$110,242 ($73,198 - $201,116)	**<.0001**	$32,351 increase ($17,221 - $47,481)	**<.0001**
No CRI	$78,845 ($50,558 - $123,278)		Ref	
CRI	$181,981 ($78,822 - $276,428)	**<.0001**	$57,180 increase ($12,834 - $101,527)	**0.011**
No candida	$77,804 ($50,249 - $120,606)		Ref	
Candida	$114,955 ($64,636 - $196,171)	**<.0001**	$24,500 increase ($8,832 - $40,167)	**0.002**

IQR=Interquartile rang, CI=confidence interval, Ref=Reference

Figure 1: Selection of patients with gastroschisis from the KID database 2012.

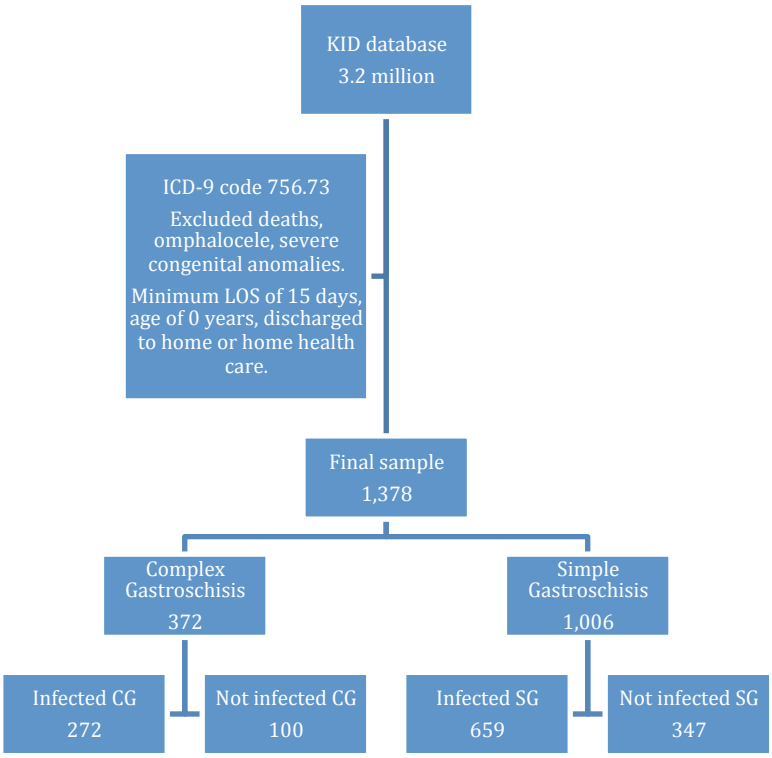
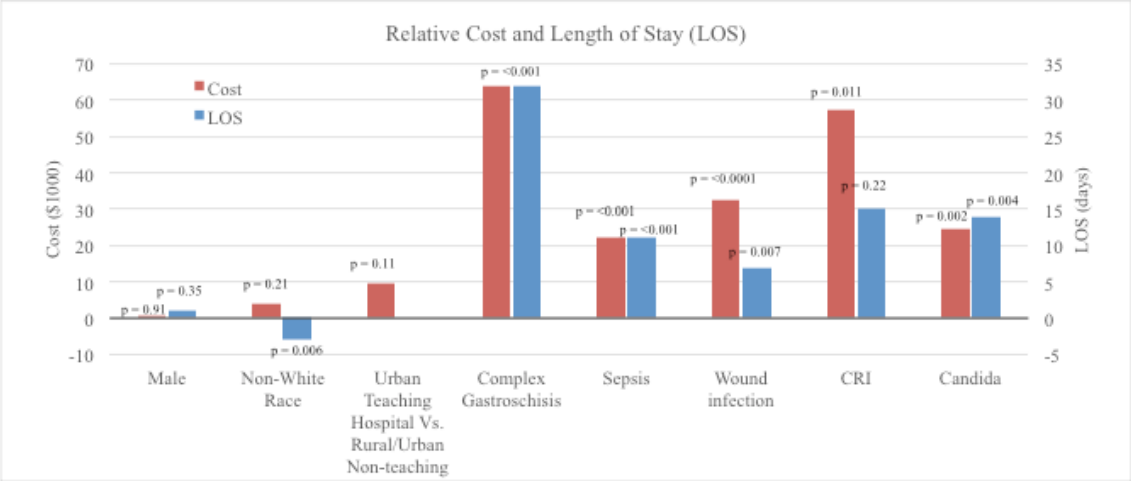


Figure 2: Length of stay (LOS) in days and costs for patients with gastroschisis in the 2012 Kids Inpatient Database comparing patient characteristics.



Chapter 4: Conclusion and Recommendations

Gastroschisis is a costly congenital anomaly that has been increasing in incidence during the past decade. Although many studies have attempted to determine outcomes of gastroschisis, there are still no guidelines as to how to treat this disease, and what needs to be done to decrease the costs and length of stay for these patients. Given the healthcare situation the U.S. is facing, there is a need to develop better treatments and improved management of resources in the hospital setting.

This study is one of the first to investigate a large population of patients with gastroschisis and their outcomes. Analyzing costs of this disease has been particularly difficult due to the variability in healthcare. Costs can vary greatly between similar patients, and with this type of administrative data is challenging to determine the reason for this variability. It may be that ICD-9-CM codes are reported incorrectly, resulting in an incorrect estimate of costs.

Furthermore, because the infection variables created for this study are not mutually exclusive and they had a big correlation between each other, determining which independent comorbidity had the greatest impact was problematic. We can make assumptions by developing groups, but we cannot reach definite conclusion from these results. Likewise, because there are no guidelines to treat this disease, the costs and LOS can vary significantly among hospital locations and even within the same hospital among healthcare practitioners. This has to change. We need to have uniform guidelines and be prepared to provide the best care to patients and their families. Better information needs to be offered early in prenatal counseling so that parents know what to expect for their child, as well as what to expect in terms of how long they will be at the hospital and how much the treatment will cost. The amount of variability in treatment and management seen in this study demonstrates the need to standardize the treatment for these patients.

As public health practitioners, we aim to prevent disease. If this is not possible, we need to be able to give the best information to patients and their families to empower and support them through the health issues they are facing. Unfortunately, with gastroschisis this has not happened at a national level. Because gastroschisis is a disease that affects approximately five in 10,000 births, this congenital anomaly has not received the public health attention it deserves. Single institutions receive very few cases, which hinders the possibility of a significant sample size. Furthermore, gastroschisis prevalence is increasing, and so are the costs of treatment of GS, but nothing has been done to make uniform decisions about GS care.

Therefore, we make the following recommendations:

- Expand and strengthen the collaboration within the International Clearinghouse for Birth Defects Surveillance and Research, the World Health Organization and the United States Centers for Disease Control and Prevention.
- All pregnant women under 20 years of age should be screened for GS. If a woman has a GS fetus, the physician should make an exhaustive history of environmental factors, substance abuse, and familial congenital disorders.
- Once GS is detected prenatally, ultrasounds should be scheduled every two weeks to measure prenatal parameters, such as fetal bowel dilation, olygohydramnios, polyhydramnios, and stomach dilation.
- Physicians should aim to ensure that pregnant women with a GS fetus reaches 37 weeks of gestation.
- Because the mode of delivery remains controversial, larger studies should be conducted to determine the mode of delivery that leads to better outcomes in neonates with GS.

- Whenever feasible, surgeons should aim for primary closure and decrease the days of silo usage as much as possible.
- Rigorous infection control programs should be put into place for this particularly vulnerable patient population.

Although there are still many things to do to improve the outcomes of patients with gastroschisis, the survival rate and prognosis have advanced considerably in the past decade. Advances in surgical technology and materials have made it possible for these patients to have a survival rate of 90%. But this is not enough, survival should be 100% and parents should be aware of the impact of gastroschisis in terms of financial costs and LOS. The well being of the patient is the most important outcome, but it is necessary to know what other impacts gastroschisis can have for a family, a hospital and insurance companies.