Is 24 Hours Enough? A Retrospective Review of Antibiotic Duration After Closure in Gastroschisis

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ABSTRACT

Background: Gastroschisis is a congenital abdominal wall defect exposing intestines to the uterine then external environments, increasing infection risk. Prophylactic antibiotics are often used postnatally but optimal duration remains unclear. The American Pediatric Surgical Association (APSA) recommends discontinuing antibiotics 24 hours after abdominal wall closure in clinically stable patients.

Objective: To evaluate whether extending antibiotics beyond 24 hours post-closure reduces 30-day infection risk in neonates with gastroschisis.

Methods: We performed a retrospective cohort study of neonates with gastroschisis born between 1991 and 2022. Included patients had a silo placed, survived until closure, and had complete antibiotic data. Data collected included demographics, antibiotic use, timing of closure and infection. Patients were classified as receiving a short (≤24 hours post-closure) or prolonged course (>24 hours) of antibiotics. Infections were defined using clinical and microbiological criteria. Statistical analyses included t-tests and logistic regression.

Results: 53 neonates were included (28 short course, 25 prolonged course). The 30-day post-closure infection rate was 57% (16/28) for the short course and 44% (11/25) for the prolonged course, which was not significantly different. Mean pre-closure prophylactic antibiotics was similar between those who did not develop an infection (15.6 days) and those who developed an infection (13.9 days), ($p = 0.667$). Prolonged antibiotics post-closure did not significantly reduce infection risks (OR: 0.82, 95% CI: 0.255–2.65, $p=0.74$). Demographics, such as gestational age, birth weight and delivery type did not affect infections.

Conclusions: Antibiotics beyond 24 hours after abdominal wall closure did reduce infection rates. This supports the APSA guidelines to discontinue antibiotics at 24 hours post-closure.

INTRODUCTION

Gastroschisis is a congenital anomaly in which infants are born with a defect in their abdomen wall leaving their intestines exposed outside of the body. Infants with gastroschisis are more likely to be born to young mothers, mothers with low socioeconomic status, low body weight or a history of smoking. The prevalence of gastroschisis has been increasing over the last few decades, with a frequency of 2.3 per 10,000 births [1][2]. Common complications are the increased reliance of total parental nutrition, sepsis, central line infections, blood infections, intestinal failure, and surgical site infections [3].

There are two primary ways in which a gastroschisis defect is closed: primary repair or delayed closure. The primary repair occurs almost immediately after birth where the herniated viscera are reduced into the abdominal cavity at one sitting. This approach is favoured when the patient is hemodynamically stable, and the size of abdominal cavity is large enough to accommodate the infant’s organs that are outside the body. Evidence shows that primary repair leads to a shorter time to feeds and reduced hospital stays [4]. In delayed closure, a plastic pouch called a silo is placed over the exposed bowels and with serial reductions and gravity, the intestines are reduced into the abdomen gradually over a few days. The abdominal wall defect is then surgically closed. In recent years, surgery has shifted to using delayed umbilical patches using the umbilical cord and occlusive dressing as an alternative to surgical closure after a silo reduction [5]. One of the main complications in gastroschisis, especially in those who undergo delayed closure, is the risk of developing infections due to the internal viscera being exposed for a prolonged period in the neonatal intensive care unit (NICU).

Neonates undergoing surgical procedures, particularly in the NICU, are often given empiric antibiotics. Exposure to antibiotics at a young age can lead to complications such as hepatotoxicity, late-onset sepsis and necrotizing enterocolitis [6]. In addition, it can cause increased multidrug antibiotic resistance, fungal infections and alterations to the gut microbiota [6]. Children with gastroschisis have an inherently vulnerable intestine, therefore a deeper examination to the best course of prophylactic antibiotics is warranted. Clinicians have a responsibility to use antibiotics judiciously to prevent the occurrence of antibiotic resistance. An interdisciplinary approach to antibiotic stewardship involving local institutions, audits, and restrictions for selective antibiotics have been recommended [7].

Antibiotic use in gastroschisis repair has been an ongoing area of research. The American Pediatric Surgical Association conducted a systematic review on the management of gastroschisis, including the timing of delivery, closure methods and antibiotic use, and recommends prophylactic narrow-spectrum antibiotics until the defect is closed [4]. Gastroschisis repair is currently classified as a class I clean surgical procedure, meaning the procedure does not break the sterile field or involve high-risk areas such as the respiratory, genitourinary or gastrointestinal tracts [8]. Clean surgical procedures typically do not require prophylactic antibiotics [8]. However, Ting *et al.* argue that despite gastroschisis repair being considered a class I clean procedure, gastroschisis repair involves a large wound with exposed viscera and should be reclassified to a class II clean-contaminated or class III contaminated procedure. Although this reclassification has been suggested and different antibiotic strategies exist, a standardized protocol for antibiotic administration in gastroschisis repair has yet to be established. Infections in neonates present with non-focal signs and the children can deteriorate quickly. Establishing an evidence-informed and standardized approach for antibiotic administration for children born with gastroschisis repair is critical for improving outcomes [9].

In addition to the abdominal wall defect, neonates born with gastroschisis have an immature immune system which may increase their risk of infection [10]. These patients are often premature, which is often associated with a reduced innate and adaptive immunity. They typically have lower counts of monocytes and neutrophils, impaired ability to clear pathogens and decreased cytokine production which limits the T-cell activation and impairs the ability to fight bacterial and viral infections [11]. During fetal development, there is prolonged exposure of the intestines to amniotic fluid. This can cause the intestines to be thick and matted leading to intrauterine growth restriction and delayed immune maturation [3]After birth, the abdominal viscera are exposed to the external environment, further compromising their host defences [10]. An immature immune system, damage to the intestines in utero and exposure to environmental viruses and bacteria lead to higher risks of infections and sepsis in this population. Standardized antibiotic administration protocols can help reduce this risk.

Clinicians use antibiotics empirically to prevent infections prior to abdominal wall closure. However, some studies suggest that prophylactic antibiotic use may not be necessary in all gastroschisis patients [12,13]. Williams *et al.* report that there is a low risk of early-onset infection and advise against broad-spectrum antibiotic use in all infants with gastroschisis as it can lead to unnecessary exposure to antibiotics or cause side effects [12]. Riddle *et al.* found that empiric antibiotics were associated with an increased incidence of late-onset sepsis and later initiation of enteral feeds [14]. A systematic review by Slidell *et al.* for the American Pediatric Surgical Association highlights the limited available evidence on the use of prophylactic antibiotics prior to their defect closure. They recommend using narrow-spectrum antibiotics that cover skin flora until the defect is closed and for an additional 24 hours afterward [4,15]. They included four key studies on perinatal antibiotic use in gastroschisis. This included Baird *et al.*

who recommend initiating antibiotics at birth and to continue them until the closure is complete [15]. Schlueter *et al.* who suggests that infections are a common occurrence and recommend antibiotics be started at birth and continued at the discretion of the provider [16]. Khalil *et al.* who recommend antibiotics be continued for five days after the closure using cefotaxime and metronidazole [17]. And Ram *et al.* who found that C-reactive protein is not a good indicator of infection [18]. Based on these four articles, APSA concluded that empiric antibiotic therapy from birth until 24 hours after abdominal wall closure is the best practice.

The recommendation from UpToDate is to use broad-spectrum coverage to cover the maternal vaginal flora such as ampicillin and gentamicin [19]. However, there is no suggested duration for the antibiotics. John Hopkins University recommends initiating cefazolin for wound prophylaxis following 48 hours of initial ampicillin and gentamicin for a delayed closure of the abdomen [20]. The choice and duration of antibiotics used for gastroschisis varies by institution.

Recommendations and protocols for medical advancements are based on evidence-based research. The levels of evidence hierarchy help determine the quality of research. Level I evidence provides the highest quality of evidence and are based on well-designed randomized controlled trials, prospective studies and systematic reviews of those studies. This type of evidence is considered the most reliable for guiding clinical decision-making, such as evaluating the effectiveness of interventions or protocols [21]. Despite the varied recommendations, there is no standardized approach supported by level I evidence for prophylactic antibiotics in neonates undergoing a gastroschisis repair [4]. This highlights the importance of research to define the best approach to reduce infection and medication overuse.

Given the gap in high quality evidence, we conducted a retrospective review of neonates. We conducted a retrospective study of neonates with gastroschisis who had a delayed repair closure at the Health Sciences Centre from 1991 to 2022. This study examined their antibiotic regimen perioperatively and the risk of developing an infection within 30 days after their abdominal wall closure. By comparing the infection rates of two antibiotic protocols, we aimed to determine if the APSA recommendations are adequate.

This area of research is particularly relevant for physician assistants, as they often take on the ward management during postoperative care. In a busy clinical setting, determining the appropriate duration of prophylactic antibiotics is essential. By conducting this retrospective review, we aim to determine the optimal duration of prophylactic antibiotics for gastroschisis surgery. This research seeks to provide evidence that the current APSA guideline for antibiotic use in gastroschisis is sufficient. In addition, it serves as an audit to assess how effectively a tertiary care centre has been managing antibiotic use in gastroschisis and support evidence informed decision-making around the optimal duration of antibiotics.

METHODS

Ethics approval:

This study was approved by the University of Manitoba Research Ethics Board under HS19268 (H2016:014). Data was obtained by conducting a retrospective chart review.

Study design and population:

We reviewed the charts of all neonates born at the Health Sciences Centre in Winnipeg from 1991-2022 with a diagnosis of gastroschisis. A total of 111 patients with gastroschisis who had a silo placed were identified. We included only infants who had a silo placed and underwent delayed closure. We then narrowed our study to focus on those who had an abdominal wall closure within 30 days of birth and excluded patients with intestinal ischemia and visceral perforation. We excluded those who did not receive prophylactic antibiotics. We excluded patients who died prior to abdominal wall closure or within 30 days post-closure, and cases with incomplete or missing antibiotic data. We excluded cases for whom data was incomplete or unavailable through online platforms such as scanned charts or electronic personal records.

We separated the population into two categories, those who received a 'short course' of antibiotics and those who received a 'prolonged course' of antibiotics. The short course was defined as the discontinuation of antibiotics within 24 hours of their abdominal wall closure, and the prolonged course was defined as those who received antibiotics for more than 24 hours after their abdominal wall closure. We only counted antibiotic courses prescribed prophylactically. If there was a clear indication that antibiotics were prescribed for an infection, the antibiotics were not considered prophylactic.

Infection criteria:

The primary outcome was infection within 30 days of abdominal wall closure. Infections were defined based on the clinical description and microbiological reports. Sepsis, including suspected sepsis, was defined based on the systemic inflammatory response syndrome (SIRS) criteria of fever, tachycardia, laboratory markers such as elevated white blood cell count or abnormal C-reactive protein. Central line-associated bacterial infection (CLABSI) was defined as any bloodstream infection identified in a neonate with a central line. Bacteremia was defined by the presence of bacteria in the bloodstream, confirmed by bacterial cultures of the blood or by fever without the systemic response. Surgical site infections (SSIs) were defined by erythema, warmth, swelling and purulent discharge near the surgical site. Cellulitis was defined by erythema, warmth and swelling without purulent discharge, regardless of association with the surgical site.

Cases were categorized as having had an ‘infection’ or ‘no infection’ based on the criteria defined. Cases with more than one infection were counted only once.

Data collection:

Data was obtained through a retrospective chart review of the infants’ medical charts and electronic health records. This included surgical notes regarding the silo placement, integrated progress notes, bacterial cultures and blood tests, prescriber orders, and the medication administration records. We collected data on the gestational age, birth weight, maternal age, APGAR scores, sex, delivery type, matting of the intestine, intestinal ischemia, visceral perforation, and intestinal atresia. Data was abstracted into a secure REDCap database.

Data analysis:

Data analysis was performed using R (version 4.4.3, The R project for statistical Computing). Descriptive statistics were used to compare baseline information such as birth weight, gestational age and delivery type for children who did not have an infection versus those who did have an infection. We used various plotting options from the R package *ggplot2* to illustrate our study data.

We compared the mean number of prophylactic antibiotic days of those who had no infection using an independent t-test. We employed logistic regression to determine if days of antibiotics prior to closure was associated with infection when adjusted for the confounding effects on antibiotic usage and infection risk, adjusted analyses were performed, accounting for time to closure, gestational age, birth weight and mode of delivery (vaginal or caesarean section).

To assess whether a prolonged course of antibiotics was associated with a reduced infection risk we performed a Fisher’s Exact test with the short course group as the reference. The Fisher’s Exact Test was chosen over the chi-squared test due to our modest sample size. We also performed a logistic regression while controlling for time to closure, gestational age, birth weight and delivery type.

We tested whether there was an interaction between prolonged antibiotics and time to closure to determine if the effect of prolonged antibiotics depended on how long it took to close the abdomen wall. Again, the model was adjusted for gestational weight, birth weight and delivery type.

P-values less than 0.05 were considered statistically significant, and odds ratio (OR) were assessed with a 95% confidence interval (CI).

RESULTS

Birth Characteristics of Included Cases:

We reviewed 64 children born at Health Sciences Center from 1991 to 2022 with gastroschisis who had a silo placed. We applied the inclusion and exclusion criteria to define our study cohort. We first excluded those who did not have a complete history of antibiotic use available through online platforms such as scanned charts or electronic personal records. We excluded the 5 cases who only received antibiotics after presentation with an infection. There were 6 cases with ischemia or perforation (one with both) who were excluded. This left 53 patients for analysis. Table 1 shows the baseline variables (gestational age, birth weight, maternal age, APGAR score, sex distribution and delivery type) for the group with no infection to those with an infection present. This table includes data on the patients with atresia and perforations.

Overall Infection Rates:

There were 33 patients who had a documented infection within 30 days of abdominal wall closure. Some children had repeated infections; there was an average of 2.55 infections per child within 30 days. Figure 1 shows the infants who had an infection within 30 days of abdominal wall closure and when they began their antibiotic course for the infection. Each purple dot represents one patient infection. Five cases did not receive prophylactic antibiotics, they only received antibiotics after they demonstrated an infection.

Pre-closure Antibiotic Use and Infection Risk:

The average duration of prophylactic antibiotics was similar (p = 0.667) between those who did not develop an infection (15.6 days) and those who developed an infection (13.9 days). This was determined using a t-test without adjusting for confounding variables. Figure 2 shows the prophylactic antibiotic use timeline for each child relative to birth and abdominal wall closure. Figure 3 illustrates the temporal profile of antibiotic use both prophylactically and therapeutically for infected and non-infected cases across time. Figure 4 focuses on the temporal profile of only the mean prophylactic antibiotic usage comparing the infected and non-infected cases before the abdominal wall closure and after. After closure, antibiotic use slowly declined. This figure shows only the prophylactic antibiotics and might suggest that the infection group received fewer antibiotics. However, comparing Figure 3 and Figure 4 highlights the impact of including therapeutic antibiotics, which significantly alter the pattern of antibiotic exposure between the two groups.

After adjusting for confounding variables in a logistic regression, the likelihood of infection was not different for duration of antibiotics and infection (OR: 0.95, 95% CI: 0.828–1.096, p = 0.46). None of the confounding variables were significantly associated with an increased or decreased risk of infection (Table 2).

Comparison of Infection Rates: Short vs. Prolonged Prophylactic Antibiotic Use:

Table 3 shows the breakdown of the infection outcomes by duration of post-closure antibiotics. A total of 27 patients got an infection within 30 days of their definitive repair; 47%

(16/28) of short course patients and 44% (11/25) of the prolonged course acquired an infection. We found no difference in the infection risk at 30 days. The OR of infection was 0.60 (95% CI: 0.17–1.99, p = 0.414) indicating no statistically significant association between antibiotic course and infection risk.

After accounting for time to closure, gestational age, birth weight and delivery type, prolonged antibiotic use was not associated with a reduced risk of infection (OR: 0.82, 95% CI: 0.255–2.65, p = 0.74). These findings suggest that extending prophylactic antibiotics beyond 24 hours after definitive closure offers no additional benefits in preventing infection (Table 4).

Interaction Between Antibiotic Duration and Time to Definitive Repair:

There was no interaction between the duration of antibiotics and the time to abdominal wall closure (OR=0.91, 95% CI: 0.68–1.2, p = 0.51), which indicates that the effect of prolonged antibiotics on infection risks was not affected by the time taken to definitive repair (Table 5).

DISCUSSION

We found that prophylactic antibiotic courses longer than 24 hours after closure of the abdominal wall did not affect the risk of infection. There was no significant interaction between the use of extended antibiotics, the timing of the abdominal wall closure and the demographic variables. The timing of the closure, birth weight, gestational age and type of delivery did not influence the rates of infection.

The optimal antibiotic protocol in neonates with gastroschisis undergoing delayed abdominal wall closure should balance preventing postoperative infections effectively while minimizing unnecessary exposure to antibiotics. The purpose of this study was to assess the current literature on prophylactic antibiotic regimens and how it correlates to clinical practice, by providing insight into the most effective antibiotic dosing regimen for preventing infections post-surgery. We specifically examined if prophylactic antibiotics beyond 24 hours post-closure reduced the infection risk in neonates with gastroschisis. This is particularly important to physician assistants who play an important role in post-operative management and antibiotic stewardship on surgical wards.

In this retrospective analysis of infants with gastroschisis managed using a silo, we found that extending prophylactic antibiotics beyond 24 hours post-definitive repair did not reduce the risk of infection within 30 days. These results are consistent with previous research and suggest that longer antibiotic courses do not provide additional benefits in reducing infection rates. However, it is important to consider that the total antibiotic exposure prior to abdominal wall closure was similar between groups who developed an infection and those who did not.

Our findings are consistent with the studies included in a systematic review by Slidell *et al.* which compiled studies on the prophylactic use of antibiotic use in neonates. Baird *et al.* recommended beginning antibiotic coverage at birth and continuing treatment until the definitive abdominal wall closure is complete [15]. Baird *et al.* also found that extending antibiotics beyond immediately after closure does not add benefit. They recommended coverage with a penicillin and an aminoglycoside. In our study, most patients were treated with ampicillin (a penicillin) and gentamicin (an aminoglycoside). Baird *et al.* found that more postoperative infections occurred when the repair was done in the NICU [15]. We did not document whether the repair was done in the NICU or the operating room so we could not adjust for this potential confounding variable. Similarly, Schlueter *et al.* recommended starting treatment with ampicillin and gentamicin immediately after birth [16] . However, for patients undergoing delayed closure after silo placement, they recommended a 24-hour course of cefazolin following silo closure as prophylaxis against a surgical site infection [16]. Additionally, they found that those who had a silo placed, received antibiotics for 7 days longer than those who had a primary repair [16]. The retrospective review by Khalil *et al.* found that patients were treated with cefotaxime and metronidazole for 5 days postoperatively unless an infection developed requiring different medications [17]. They emphasized the importance of having a strict microbiological protocol informed by the likely pathogens to guide antibiotic therapy. Based on Khalil *et al.*'s recommendation, further research into culturing the bacteria present on the abdominal wall when a silo is placed can help narrow the antibiotics being used.

In a separate study, the findings by Vu *et al.* are similar in their examination of surgical site infections and supports our conclusion of limited benefit of extended antibiotics [22]. Vu *et al.*'s study was not limited to gastroschisis patients. They compared outcomes between neonates who received only 24 hours of postoperative antibiotics after their abdominal wall closure to those who received a longer course. They found that there was no statistical difference in surgical site infections between these two groups. This suggests that short course antibiotics are sufficient in preventing postoperative infections.

Gastroschisis is considered a class I clean procedure. Ting *et al.* recommends that gastroschisis be reclassified as a class II clean-contaminated or class III contaminated procedure due to the higher contamination levels and increased wound infections [9]. The study by Ting *et al.* underscores the importance of considering factors such as the nature of the surgery, and clinical status of the patient before initiating antibiotics. Given that in our study extended antibiotic use did not reduce infection rates, clinicians should consider limiting prophylactic antibiotics to 24 hours postoperatively. This would help reduce unnecessary exposure to antibiotics, which is particularly important in a neonate population. A neonate's immune system is highly plastic, adapting and maturing over time, and the unnecessary use of antibiotics can disrupt its development, potentially leading to harmful antibiotic resistance and microbiome imbalance [9].

Laituri *et al.* looked at the antibiotic use with congenital gastrointestinal surgical anomalies [8]. The aims were to reduce antibiotic use without increasing the rate of infections [8]. Although, these protocols excluded gastroschisis patients due to the presence of an open abdomen, where antibiotics were considered necessary in the perioperative period, they do offer insight to broader antibiotic stewardship. For the other anomalies, they recommend prophylactic antibiotics be given postnatally only if they are a clean-contaminated or a contaminated procedure. If cultures and laboratory findings do not indicate an infectious source, the discontinuation of antibiotics within 48 hours is advised. [13,15]. These findings align with our study, as we did not see any benefit in a longer course of antibiotics after repair. Laituri *et al.* further aimed to assess specific congenital anomalies and the prophylactic antibiotic type and duration for each anomaly. This challenges the common recommendation of prophylactic antibiotic use and promotes a targeted approach to antibiotic administration. This study stressed the importance of evaluating each procedure independently.

Meyers *et al*. led a quality improvement initiative, following the Vermont Oxford's Internet-based Quality Improvement Collaborative for Quality in the NICU and supported the initiative of stopping antibiotics 24 hours after the abdominal wall closure. In addition, they found that the presence of a silo alone without signs of infection in gastroschisis, is not an indication for antibiotics [23]. This supports our study and emphasizes the importance of evidence-based antibiotic stewardship in the NICU.

At the University of Wisconsin, they provided prophylactic antibiotics 1 hour prior to an abdominal surgery and discontinued 72 hours after the procedure. They analyzed 275 neonates, 148 before the protocol and 127 after to examine the compliance of antibiotics. Postnatal antibiotics were only continued when there was a clear clinical indication. This reduced the antibiotic use from two days postnatally to zero. This led to a decrease in inappropriate antibiotic use. For the prophylactic antibiotic coverage, compliance or use of antibiotics prior to surgery did not change since the implementation of the protocol. Despite this decrease in the use of antibiotics, there was no increase in the rate of surgical site infections, hospital acquired infections or multidrug resistant organisms [24]. This highlights the importance of having an antibiotic protocol to decrease the unnecessary use.

In our study comorbid conditions, such as the time to definitive repair, gestational age, birth weight and delivery type did not significantly affect the probability of infections. There was a trend suggesting that longer time to closure may increase the risk of infection; this was not unexpected but not statistically significant. Although, there is debate regarding whether delayed time to closure yields to better post-reduction outcomes. Some suggest that immediate reduction leads to better outcomes due to less infections, while others suggest that delayed closure leads to fewer adhesions but can lead to more infections [14,15].

Gastroschisis can be diagnosed in utero allowing time for creation of a birth plan. Theoretically, delivering neonates with a ventral wall defect should be delivered via caesarean to avoid the maternal vaginal flora [25]. Most of the patients in our study were born via caesarean section. We found that patients were no less likely to develop an infection compared to if they were born vaginally. There was no clear benefit to caesarean section to reduce the rate of infections post-closure. This is in keeping with current literature regarding the mode of delivery for patients with congenital abdominal wall defects [10,26].

Our findings are consistent with the current research. We recommend a standardized antibiotic regimen of discontinuing antibiotics 24 hours postoperatively. These prophylactic antibiotics should be continued for 24 hours post-surgery, then discontinued unless clinically indicated. This duration can help limit unnecessary antibiotic exposure while still providing sufficient coverage to prevent infections.

LIMITATIONS

There are several limitations to this study. The dataset was restricted by the inclusion criteria that focused only on patients who underwent delayed closure within 30 days at a single hospital, resulting in a small sample size. Labeling patients with an infection retrospectively based on chart review can provide documentation is inaccurate. The variability of antibiotic regimens and lack of standardization of the patients may have obscured potential relationships. We did not differentiate between types of infections, which limits our ability to determine which antibiotic regimens are best for specific infections.

We had a variety of antibiotic regimens and the lack of standardizations among patients may have obscured the variability. Many cases received two days of antibiotics after birth, but this was not consistent. Prior to the abdominal wall closure, both groups follow similar antibiotic regimens, with two courses per day. Furthermore, we grouped cases according to the use of antibiotics beyond 24 hours after closure but did not consider the variable antibiotic courses prior to closure. We also did not consider the specific type of antibiotics received by individual cases which limits the details of our conclusion.

CONCLUSION

This retrospective analysis of infants with gastroschisis managed using a silo found no evidence that prolonging prophylactic antibiotics beyond 24 hours after abdominal wall closure reduces the risk of infection within 30 days. The duration of prophylactic antibiotics, whether measured continuously or categorized as short (≤24 hours) and prolonged (>24 hours), was not associated with infection risk, even after adjusting for potential confounding variables. There was no significant interaction between delayed closure and the potential benefits of extended antibiotics. These results align with the APSA recommendations advising against routine prolonged antibiotic use in clinically well infants following their closure. By limiting antibiotic exposure in neonates is important due to the risks of antimicrobial resistance, disruption of gut microbe and adverse drug reactions.

In addition to evaluating the outcomes, this study serves as a retrospective audit of the antibiotic use at a tertiary care center which helps to assess adherence to recommendations to best practice. By identifying variability in practice and lack of benefit from extended antibiotic use, this study supports evidence-informed decision-making around optimal prophylactic antibiotic duration.

Physician assistants play an important role in ensuring adherence to protocols and minimizing the unnecessary antibiotic exposure. This study emphasizes the importance of physician assistants to stay informed on best practices and implement antibiotic stewardship, improving the patient outcomes and reducing risks with overuse of antibiotics.

Further prospective studies are warranted to confirm these findings and explore individualized strategies based on clinical status rather than predefined antibiotic durations.

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APPENDICES
APPENDIX 1: FIGURES

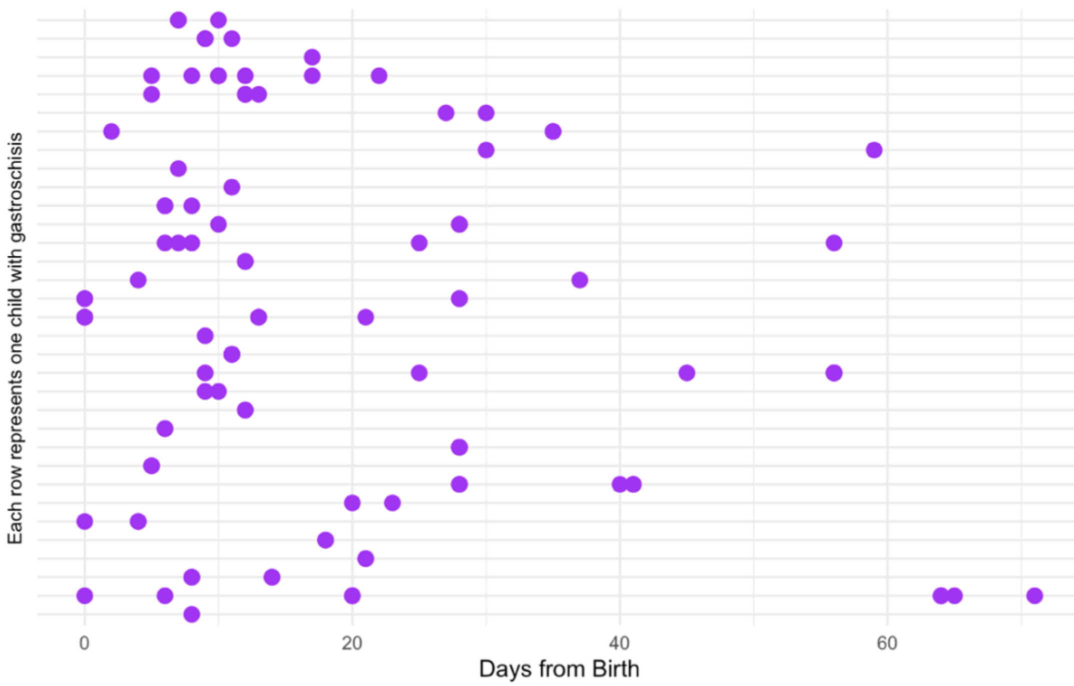

Figure 1: Timing and frequency of infections for each of the 33 children who had at least one infection within 30 days of birth. Each row represents an individual child, and each dot represents the start of an antibiotic course.

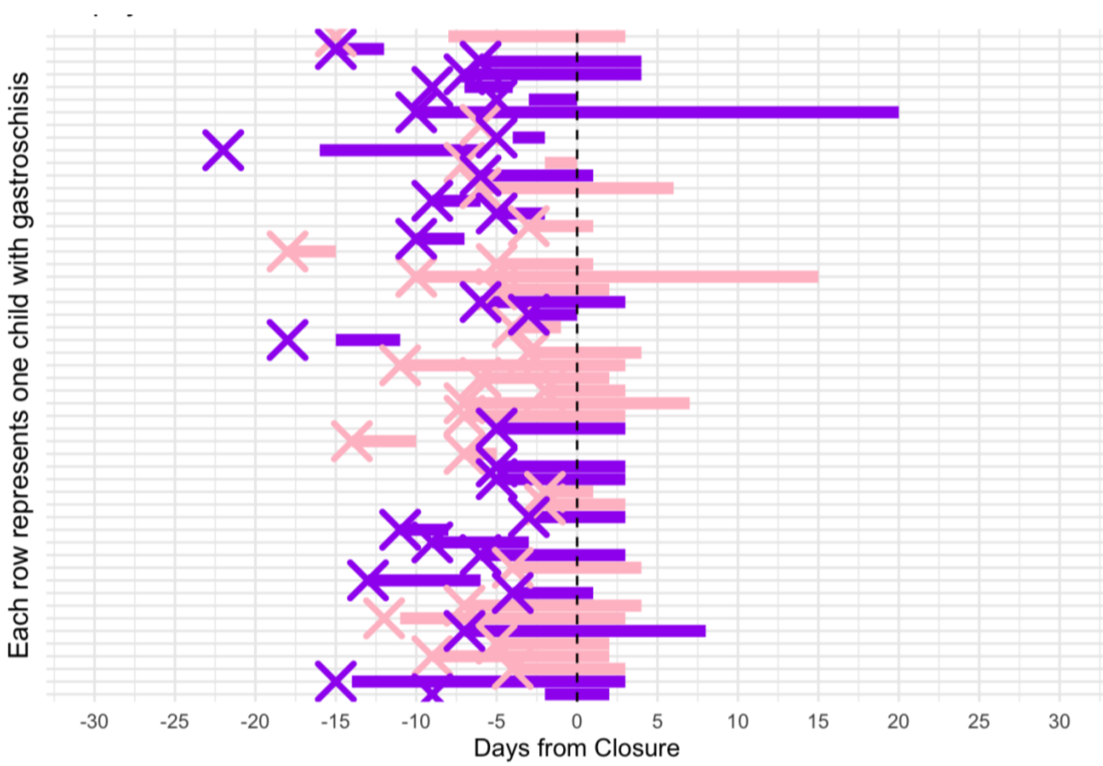

Figure 2: Mean prophylactic antibiotic usage in the peri-closure period for cases plotted for cases who did not have an infection (pink) and those who had developed an infection (purple). The dotted line represents the date of silo removal and abdominal wall closure. The X represents the date of birth.

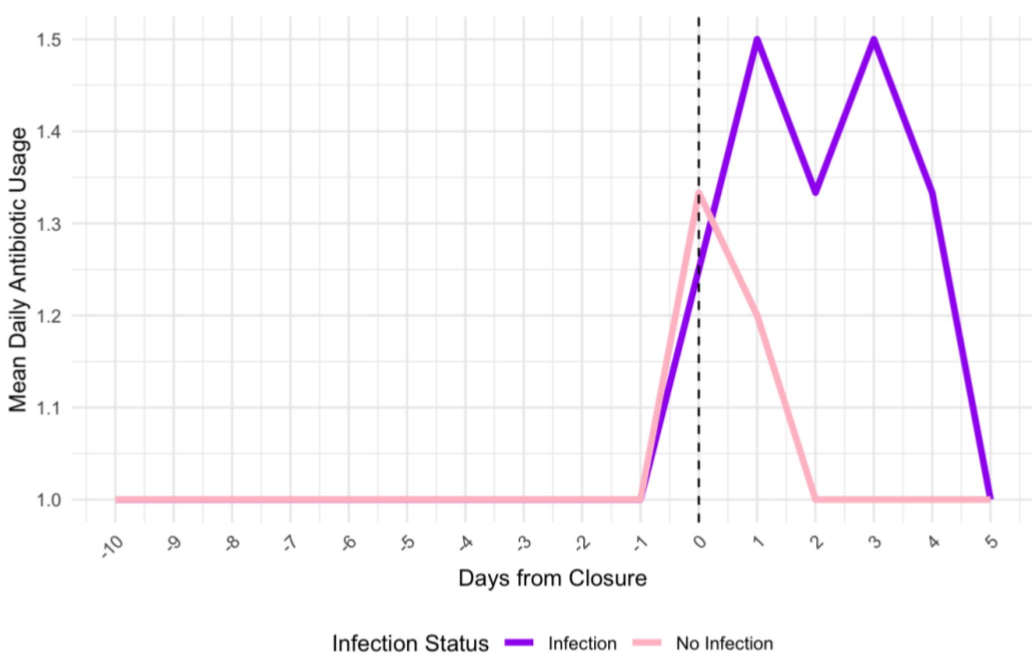

Figure 3: Temporal profile of all antibiotics prescribed for cases comparing those who did not have an infection (pink) to cases who did have an infection after the definitive repair (purple)

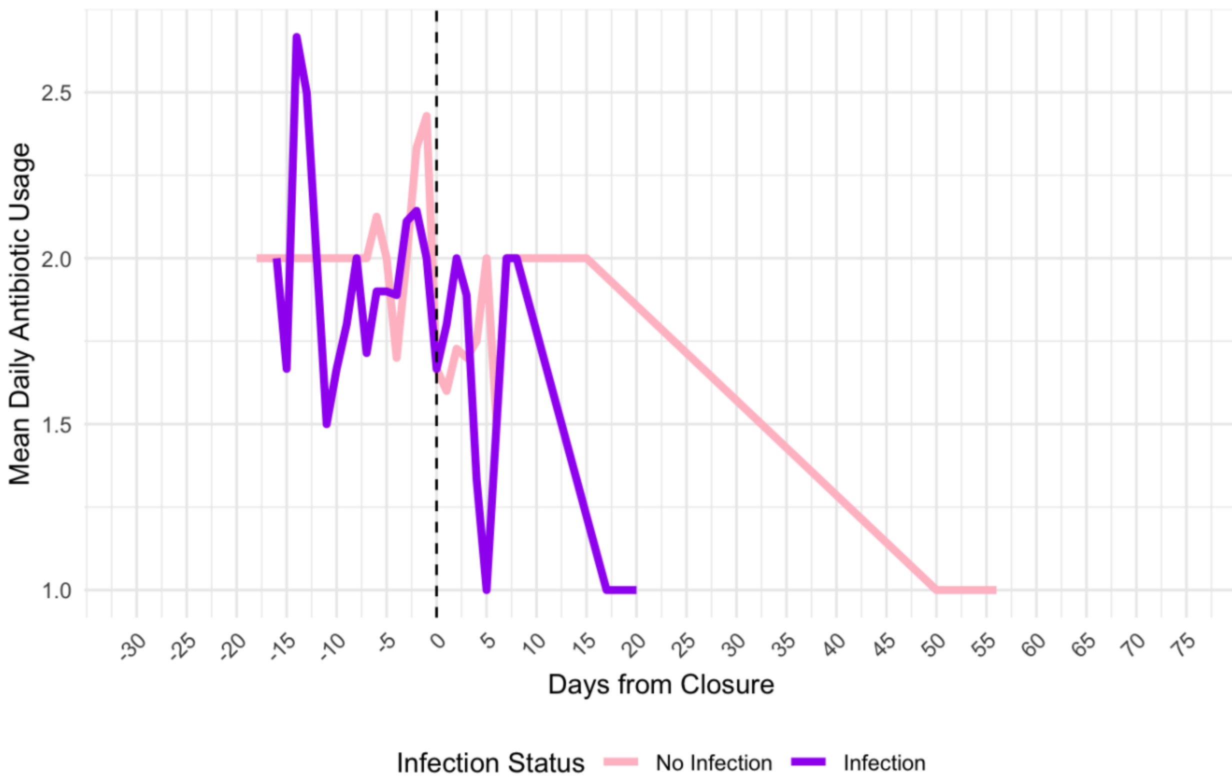

Figure 4: Temporal profile of daily prophylactic antibiotics prescribed for cases who did not have an infection (pink) compared to cases who had at least one infection (purple). The dotted line indicates the relative date of birth.

APPENDIX 2: TABLES

Table 1: Baseline characteristics of the study population for children who had a delayed closure of their gastroschisis including those with ischemia and perforations.

Category	**No infection (n=31)**	**Infection (n=28)**
Continuous Variables		
Gestational Age (weeks)	35.9 ± 1.87	35.8 ± 1.99
Birth weight (g)	2410 ± 490	2574 ± 560
Maternal Age (years)	25.2 ± 14.5	22.3 ± 4.82
APGAR Scores		
1 min	6.32	6.46
5 min	7.87	7.93
Categorical Variables		
Sex distribution		
Male	13 (41.9%)	15 (53.6%)

Female	18 (58.1%)	13 (46.4%)
Delivery Type		
Vaginal	10 (32.3%)	11 (39.3%)
Caesarean Section	21 (67.7%)	17 (60.7%)
Matting Distribution		
None	14 (45.2%)	16 (57.1%)
Mild	5 (16.1%)	6 (21.4%)
Severe	11 (35.5%)	3 (10.7%)
Missing	1 (3.23%)	3 (10.7%)

Table 2: Results showing the effect of the total days of prophylactic antibiotics taken and the odds of developing an infection while accounting for time to definitive repair, gestational age, birth weight and delivery.

Predictor	**Odds Ratio**	**Confidence Interval**	**P-value**
Total prophylactic days	0.95	0.83-1.09	0.46
Time to closure	1.1	0.96-1.25	0.18
Gestational age	0.82	0.54-1.24	0.34
Birth weight	1.0	1.00-1.00	0.21
Delivery type	0.91	0.25-3.27	0.88

Table 3: Infection outcomes by duration of post-closure prophylactic antibiotic use

Antibiotic Duration	**No infection**	**Infection**	**Total**
Short course (<24 h post-closure)	12	16	28
Prolonged course (>24 h post-closure)	14	11	25
Total	26	27	53

Table 4: The effect of prolonged antibiotics in relation to developing an infection while accounting for time to definitive repair, gestational age, birth weight and delivery.

Predictor	**Odds Ratio**	**Confidence Interval**	**P-value**
Prolonged antibiotics	0.82	0.25-2.65	0.74
Time to closure	1.1	0.95-1.23	0.26
Gestational age	0.86	0.59-1.26	0.45
Birth weight	1.0	0.99-1.00	0.27
Delivery type	1.02	0.30-3.51	0.98

Table 5: The interaction between prolonged prophylactic antibiotics and time it takes to close the abdominal wall while accounting for gestational age, birth weight and delivery type.

Predictor	**Odds Ratio**	**Confidence Interval**	**P-value**

Prolonged antibiotics	1.66	0.15-1.77	0.68
Time to closure	1.12	0.94-1.32	0.21
Gestational age	0.87	0.87-0.60	0.47
Birth weight	1.0	0.99-1.00	0.31
Delivery type	0.96	0.27-3.38	0.95
Prolonged antibiotics in relation to time to closure	0.91	0.68-1.2	0.51