Infectious complications in infants with gastroschisis: an 11-year review from a referral hospital in southern Thailand

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Key words:
Gastroschisis; Infectious complication; Nosocomial infection

Abstract

Main Purposes: The study aimed to (1) examine the incidence of infectious complications (ICs) in our referral hospital in southern Thailand in infants with gastroschisis, with analysis of the impact of these complications on outcomes, and (2) identify associated factors to improve the practice at our institution for dealing with this condition.

Methods: A retrospective review of consecutive gastroschisis cases at the major teaching and referral hospital in southern Thailand was conducted for an 11-year period (1996-2006). Cases referred after a primary operation at other hospitals were excluded. The study focused on postoperative nosocomial infections as identified by Centers for Disease Control and Prevention criteria.

Results: Sixty-eight patients with gastroschisis were operated on. Twenty-seven patients (39.71%) underwent primary closure. Mortality was 4 of 68 patients (5.9%). Infectious complication occurred in 43 patients (63.2%). The complications significantly increased mechanical ventilation days (10.8 vs 3.8 days in noncomplicated cases), need for parenteral nutrition (25.3 vs 14.5 days), and postoperative stay (33.7 vs 21.1 days). Common ICs were wound infection (32.35%), isolated septicemia (19.1%), and pneumonia (13.24%). Univariate analysis identified an association between the occurrence of IC and birth order (multigravida), time from birth until arrival at our center (5 hours or more), hypoalbuminemia, hypoglycemia, type of operation (staged closure), use of central venous line, and prolonged use of ventilator. On multiple logistic regression, prolonged referral time, use of a central venous line, multigravida, and staged closure independently predicted the risk of IC.

Conclusion: Infectious complication was significantly related to outcome in gastroschisis cases and should not be overlooked. Our data suggest that prompt referral, limiting central line practice on a selective basis, and an attempt to reduce wound infection in cases that require a temporary silo may improve the overall outcomes.

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Modern neonatal care has had a great impact on the management and outcome of gastroschisis. Developments in surgical techniques, parenteral nutrition, respiratory care, and anesthetic practice have reduced the general mortality rate...
down from 40% to 60% before 1970 [1,2] to less than 5% currently [3,4]. Researchers are now focusing on a reduction of morbidity, of which the leading problem in gastroschisis remains nosocomial infection [3,5]. Being a surgical patient of extreme age, loss of anatomical defense mechanisms and use of a prosthesis are thought to places the gastroschisis infants at risk of infectious complications (ICs). The incidence of nosocomial infections in gastroschisis is not clear. Most studies have reported only incidence rates of sepsis or necrotizing enterocolitis. Wound inflammation with purulent discharge, which met the surgical wound infection criteria, might not be regarded as a complication in gastroschisis by some surgeons. Even though the overall incidence of infection might be underreported, the incidence of sepsis in gastroschisis has been reported at 25% to 38% [4,6-8].

The objective of this study was to review the experience of our institute, Songklanagarind Hospital, the major tertiary referral center in southern Thailand, in the management of neonates with gastroschisis, particularly on postoperative ICs, by means of incidence exploration and identification of associated factors. Using multivariate analysis, we looked for independent risk determinants relating to host factors, choice of operation, and perioperative care factors.

1. Patients and methods

A retrospective review on consecutive cases of gastroschisis operated on in our institute between January 1996 and December 2006 was conducted. Cases of ruptured omphalocele and cases referred after a primary operation at other hospitals were not included in the study. Demographic data, including prenatal diagnosis, birth characteristics, and referral duration (time from birth to arrival at our center), were collected from obstetric records and referral notes. Data regarding initial conditions, associated anomalies, operations, and outcomes were extracted from individual hospital charts or electronic records.

The first operation was performed as soon as the patient had received adequate resuscitation. Prophylactic antibiotics usually began with a combination of ampicillin, gentamicin, and metronidazole. The antibiotics were given for 7 to 14 days, according to the individual patient’s condition. In cases where nosocomial infection was identified, choice of antibiotics was guided by microbiologic study results. Operative management for this condition in our institute was to perform primary fascial closure at the first operation if feasible. In cases with visceroadominal disproportion, a temporary silo was constructed. An in-house prepared silo, using nylon mesh reinforced Steri-Drape membranes (3M, Inc, St. Paul, MN), was sutured directly to the fascia at the defect rim. Protruding viscera under the silo were then gradually reduced on a daily basis over 5 to 9 days. The infant was then scheduled for silo removal and staged closure with abdominal wall fascia or skin flaps. Postoperative care was undertaken in the neonatal intensive care unit (NICU). A central venous line was inserted at the first operation in some cases, according to the operating surgeon’s preference. In certain cases, line insertion was done later at the NICU when peripheral venous access became difficult to establish or the patient required more concentrated nutrient solution. An in-hospital incorporated silicone tube with a cuff was chosen for catheterization via the external jugular vein in most cases. Care of the central line conformed to the practice guideline of the Nosocomial Infection Control Unit of our institute. The line was used only for parenteral nutrition. Dressings were applied in a semiocclusive style using polyurethane film. When catheter infection was suspected, antibiotic therapy was considered first, and the line was removed if there was no response within a few days or the patient had hemodynamic instability.

Infectious complications included infections that began from within 48 hours of admission to 30 days postoperation. Definitions of nosocomial infection in our NICU follow the criteria of the Centers for Disease Control and Prevention (1988) and its modifications [9,10]. According to these criteria, surgical site infection should be diagnosed when there is a purulent discharge from the incisional wound together with signs of inflammation. Necrotizing enterocolitis was considered an IC when its severity grading was at least stage II according to Bell’s clinical staging [11]. Primary catheter sepsis was defined as sepsis syndrome with positive culture for the same organisms in blood drawn from the peripheral vein and the central venous line.

Retrieval of medical records and examination of outcome data were performed under permission of the Research Ethics Committee, Songklanagarind Hospital. Unless stated otherwise, data are presented as mean, percentage, and range. Mean comparisons used unpaired Student’s t test, unequal variances. Univariate exploration for crude association between individual factors and an occurrence of ICs was performed with Pearson $\chi^2$ test or Fisher’s Exact test, as appropriate. Variables having a $P$ value less than .05 were then included in multivariate logistic regression models, which were refined by stepwise exclusion guided by the change in log-likelihood of consecutive models. The $P$ value for significance in the likelihood ratio test was set at .05. Data processing was aided by the Stata program version 6.0 (Stata Corporation, College Station, Tex).

2. Results

2.1. Demographic data

From January 1997 to December 2006, 68 neonates (34 males and 34 females) received the primary operation for gastroschisis at Songklanagarind Hospital. Twelve were born in our institute. Fifteen births (22.06%) were by cesarean
delivery, of whom 7 cases were known to have gastroschisis, and the anomaly was the sole reason for this mode of delivery in 4 cases.

Thirty-six cases (52.94%) were in the first gestation (primigravida). Of the 32 multigravida births, 13 of the mothers (40.6%) had a history of previous abortion. Twenty-nine patients (42.55%) were born prematurely. Regarding intrauterine growth, 48 cases (72.72%) had appropriate birth weight according to their gestational age, whereas 15 and 3 were small and large for their gestational age, respectively. The birth weight in the primigravida cases tended to be lower than in the multigravida, but not at a statistically significant level (2236.14 vs 2492.20 g, \( P = .062 \)). Maternal age was recorded in 42 patients; their average age was 22.8 years (range, 15-39 years), and 20 (47.62%) of 42 were 20 years or younger. Primigravida had a significant correlation with teenaged pregnancy; 80.0% of teenaged pregnancies in this series were in the first gestation compared with 40.91% in the mothers 20 years or older.

Associated congenital anomalies were recorded in 16 cases (23.5%). Among these, 7 were confined to the gastrointestinal tract, with small intestinal atresia/stenosis in 5 cases and a congenital band at the ileum in 2 cases. None of the cases complicated with associated gastrointestinal anomalies had in-hospital mortality.

### 2.2. Management and overall outcome

The average time used for patient transfer to our institute was 6.92 hours (range, 1-36 hours). Metabolic derangement was detected on arrival in 15 (26.79%) of 56 referred patients; mainly severe metabolic acidosis (4 cases), hypoglycemia (4 cases), and hyperglycemia (4 cases). Of all patients, the abdominal fascia was closed primarily in 27 cases (39.71%). One case underwent primary skin flap closure. In 40 patients for whom a silo sac was applied on the first operation, staged closure of the fascia (36 cases) or skin (3 cases) was then performed on postoperatively day 4 to 21 (median, 7.5 days). Sixty-four patients (94.12%) survived and were discharged home, although 3 had intestinal failure and needed long-term nutrition support, and one case was complicated by central diabetes insipidus and needed prolonged hospitalization. Three patients died of uncontrollable septicemia, and one died of abdominal compartment syndrome.

Median ventilator support day was 5.0 days (range, 0-36 days). Median parenteral nutrition support day was 19 days (range, 6-81 days). Median postoperative stay was 27 days (range, 10-592 days). Comparing cases that underwent primary closure with those receiving staged closure operations, there were no significant differences in mean parenteral nutrition support days (21.31 vs 23.58 days, \( P = .446 \)) or mean postoperative hospital stay (43.60 vs 36.84 days, \( P = .065 \)). The mean number of ventilator support days in the primary closure group was smaller than in the staged closure group (4.95 vs 13.20 days, \( P < .001 \)), as was the period until beginning enteral feeding (12.64 vs 19.16 days, \( P = .032 \)). Excluding the 4 complicated patients who were hospitalized more than 90 days, the postoperative stay in cases of primigravida cases (24.78 days) was significantly shorter than that of the multigravida cases (33.03 days, \( P = .015 \)).

### 2.3. Infectious complications

Within 30 days postoperatively, ICs occurred in 43 patients (63.24%). Most of the infections were local infection at the surgical wound sites, septicemia, and pneumonia (Table 1). Patients who had complications were found to require significantly longer ventilatory support, prolonged need of parenteral nutrition, and longer hospital stay (Table 2). Uncontrollable sepsis resulted in multiple organ failure and death in 3 patients. Of these, 2 patients who died early, one case each of primary closure and staged closure, manifested clinical pictures of septicemia without specific organ infection. The other mortality was a premature infant in the staged closure group who developed pneumonia 1 month after birth, complicated with intraventricular hemorrhage and gram-negative catheter sepsis before his death.
Microbiologic studies could identify specific organisms in 31 cases. Methicillin-resistant *Staphylococcus epidermidis* and *Klebsiella pneumoniae* were the most frequent organisms identified.

The mean birth weight in patients with IC was higher than in the group without infection, although the difference was not statistically significant. However, when comparison was done in the subgroup of small for gestational age patients, it was interestingly found that patients with ICs were significantly born with higher birth weight (Table 2).

When patients born outside our institute were analyzed separately, it was found that time from birth to arrival at our center and time from birth to the first operation were significantly longer in the group with ICs.

Data of serum albumin on the first postoperative day, when albumin or plasma had not been administered, were available in 33 patients, and analysis revealed a significantly lower level in the group with ICs.

### 2.4. Factors associated with ICs

Univariate analysis identified various factors associated with an infectious episode (Table 3). The only birth factor that could be identified was related to gestational order; first-gestation infants seemed to be protected from the complication. Perioperative factors increasing the likelihood of infection included an episode of hypoglycemia, hypoalbuminemia, time from birth to arrival, and use of mechanical ventilation more than 4 days. Surgical factors related to an infectious episode were use of a central venous line and staged operation.

On multiple logistic regressions, hypoalbuminemia was excluded from the model because of missing data. Sequential analysis ultimately found that, in our case series, factors independently associated with occurrence of ICs were referral duration longer than 5 hours, use of a central venous line, being a multigravida child, and staged closure of the abdominal wall defect (Table 4).

### 3. Discussion

Gastroschisis is one of the major congenital anomalies in which mortality is currently no longer an expected outcome. Reported survival rates of patients with gastroschisis in this decade have reached 90% to 97% [3,4]. Along with a remarkable increase in the number of cases, the mortality rate in our institute has decreased from 28.6% during 1988 to 1995 [12] to 5.9% in the current study. The challenge is then redirected toward a reduction of morbidity, and the most common morbidity in these patients remains to be nosocomial infections. Nearly two third of our cases had at least one infection site within the first 30 days of hospitalization. This figure is relatively high compared with other series studied in the same period [3,13]. The occurrence of complications resulted in a significantly increased requirement for intensive care and prolonged hospital stay.

Previous studies provide intriguing information regarding the benefit of prenatal transfer and/or early operation [14-16]. An advantage resulting from prenatal diagnosis or inborn delivery was not apparent in our study; however, when the subgroup of referred patients was analyzed, late

| Table 2 | Comparison of selected continuous parameters between cases with and without ICs |
|---------|------------------------|------------------------|------------------------|
|         | ICs                   | Present                | Absent                | P         |
| Birth weight (g) | Overall (n = 66) | 2446.2 (2264.4-2628.0) | 2209.2 (2001.2-2417.2) | 0.084     |
|         | Cases of small for gestational age (n = 15) | 2195.6 (1989.8-2401.3) | 1840.0 (1510.8-2169.2) | 0.047     |
| Serum albumin at POD 1 (n = 33)b (mg/dL) | 2.1 (1.9-2.4) | 2.7 (2.3-3.1) | 0.111     |
| Lowest blood glucose (n = 64) (mg/dL) | 77.6 (69.6-89.5) | 91.1 (80.5-101.7) | 0.040     |
| POD 1 | 65.3 (58.5-72.0) | 78.0 (66.0-90.1) | 0.044     |
| POD 2 | 82.1 (74.9-89.3) | 100.7 (87.3-114.1) | 0.008     |
| Referral time (n = 56)c (h) | Duration from birth to arrival | 8.1 (5.6-10.7) | 4.7 (3.5-6.0) | 0.062     |
|         | Duration from birth to first operation | 13.4 (10.7-16.2) | 9.5 (7.5-11.5) | 0.047     |
| Ventilator days (n = 64)d (d) | 10.8 (8.2-13.4) | 3.8 (2.8-4.9) | <0.001     |
| Enteral feeding begun (n = 60)d (d) | 17.6 (14.7-20.5) | 8.9 (7.7-10.0) | <0.001     |
| Parenteral nutrition days (n = 60) (d) | 25.3 (21.5-29.0) | 14.5 (12.1-17.0) | <0.001     |
| Postoperative stay (n = 60) (d) | 33.7 (28.8-38.5) | 21.1 (18.2-23.9) | <0.001     |

POD indicates postoperative day.

a Birth weights were not known in 2 cases born outside the study health care facility.

b Excluding death cases.

c Cases born in the institute were excluded.

d Excluding death cases and cases with chronic intestinal failure who needed nutritional support for more than 90 days.
arrival and a prolonged birth-to-operation period were found to be associated with an occurrence of ICs. Prolonged exposure of the viscera in nonsterile conditions may help explain this correlation. Based on our evidence, postnatal care including prompt referral to a tertiary care facility must be emphasized for surgical neonates in our region where adequacy of neonatal care and transportation varies.

About half of our patients for whom maternal age data were available were born from teenaged mother, and 80% of these were first pregnancies. The correlation between young maternal age and gastrochisis is well known [13,17], although little is understood of its biologic origins. A recent epidemiologic study reported a correlation between young maternal age and low birth weight [18]; however, the impact of young maternal age or gestational age on surgical outcomes of gastrochisis itself has not been studied. Our study is the first to indicate a protective effect of the primigravida, which was also associated with teenaged pregnancy, on disease-related morbidity in gastrochisis. In line with this finding, a comparison of postoperative stays between uncomplicated gastrochisis cases who were primigravida and those who were multigravida showed significantly shorter stays in the former. Nevertheless, a plausible biologic explanation for this statistically significant association could not be formulated as part of this work, and further studies on this important aspect of the condition are warranted.

Approximately one third of the septicemia cases in this study were primary catheter sepsis, which may explain the identification of central venous catheter insertion as one of the risk factors of ICs. Although a prolonged requirement of parenteral nutrition in patients with gastrochisis made it hardly possible to administer an adequate amount of nutrient solutions solely via peripheral veins, a policy of routine central line establishment at the time of the first operation might have to be reconsidered. Inserting a line later at the NICU only when it becomes necessary may shorten catheter days and lower the infection rate.

A complete reduction of viscera and primary closure of the abdominal wall defect is the treatment of choice for a neonate with gastrochisis when it is feasible. The placing of an artificial silo is reserved for cases with visceroadominal disproportion or in cases with poor compliance to increased abdominal pressure. Although this policy is generally accepted, previous studies have found that the percentage of primary closures varied among institutes and ranged from 14.3% to 92.4% [8,13,19,20]. Our results indicate that primary closure is preferable, because prolonged respirator support and intestinal dysfunction were higher in the staged closure group. This observation was also made in previous studies that analyzed those surrogated outcome parameters against type of operations [13,17]. A greater risk of infection,

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Univariate analysis between an occurrence of septic complication and various prenatal and perioperative parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth order</td>
<td>Birth weight</td>
</tr>
<tr>
<td>First child</td>
<td>18/36 (50.0%)</td>
</tr>
<tr>
<td>Second or more</td>
<td>25/32 (78.12%)</td>
</tr>
<tr>
<td>Mode of delivery</td>
<td>Premature rupture of membranes (PROM)</td>
</tr>
<tr>
<td>Cesarean delivery</td>
<td>9/12 (75.0%)</td>
</tr>
<tr>
<td>Vaginal delivery</td>
<td>34/56 (60.71%)</td>
</tr>
<tr>
<td>Birth status</td>
<td>Birth weight</td>
</tr>
<tr>
<td>Premature</td>
<td>18/29 (62.07%)</td>
</tr>
<tr>
<td>Term</td>
<td>25/39 (64.10%)</td>
</tr>
<tr>
<td>Birth weight</td>
<td>Intrauterine growth</td>
</tr>
<tr>
<td>Less than 2500 g</td>
<td>SGA</td>
</tr>
<tr>
<td>2500 g or more</td>
<td>AGA or LGA</td>
</tr>
<tr>
<td>Intrauterine growth</td>
<td>APGAR score at 1 min</td>
</tr>
<tr>
<td>SGA</td>
<td>≥7 or more</td>
</tr>
<tr>
<td>AGA or LGA</td>
<td>&lt;7</td>
</tr>
<tr>
<td>APGAR score at 1 min</td>
<td>Referral time</td>
</tr>
<tr>
<td>≥7 or more</td>
<td>≤5 h</td>
</tr>
<tr>
<td>&lt;7</td>
<td>&gt;5 h</td>
</tr>
<tr>
<td>Referral time</td>
<td>Serum albumin at POD 1</td>
</tr>
<tr>
<td>≤5 h</td>
<td>&lt;2.5 mg/dL</td>
</tr>
<tr>
<td>&gt;5 h</td>
<td>≥2.5 mg/dL</td>
</tr>
<tr>
<td>Serum albumin at POD 1</td>
<td>Hypoglycemic episode within 72 h</td>
</tr>
<tr>
<td>&lt;2.5 mg/dL</td>
<td>Yes (&lt;60 mg/dL)</td>
</tr>
<tr>
<td>≥2.5 mg/dL</td>
<td>No</td>
</tr>
<tr>
<td>Hypoglycemic episode within 72 h</td>
<td>Hyperglycemic episode within 72 h</td>
</tr>
<tr>
<td>Yes (&gt;180 mg/dL)</td>
<td>Yes (&lt;60 mg/dL)</td>
</tr>
<tr>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Type of first operation</td>
<td>Type of first operation</td>
</tr>
<tr>
<td>Primary closure</td>
<td>21/41 (51.22%)</td>
</tr>
<tr>
<td>Silo sac application</td>
<td>22/27 (81.48%)</td>
</tr>
<tr>
<td>Central venous line</td>
<td>Central venous line</td>
</tr>
<tr>
<td>Not used</td>
<td>8/22 (36.36%)</td>
</tr>
<tr>
<td>Used</td>
<td>34/45 (75.56%)</td>
</tr>
<tr>
<td>Use of mechanical ventilation</td>
<td>≥4 d</td>
</tr>
<tr>
<td>&lt;4 d</td>
<td>9/23 (39.13%)</td>
</tr>
<tr>
<td>≥4 d</td>
<td>31/41 (75.61%)</td>
</tr>
</tbody>
</table>

SGA, small for gestational age; AGA, appropriate for gestational age; LGA, large for gestational age.

<table>
<thead>
<tr>
<th>Table 4</th>
<th>Final logistic regression model showing 4 parameters that were independently associated with an occurrence of IC (log-likelihood = −22.247285, P &lt; .001)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Odds ratio</td>
<td>95% confidence interval</td>
</tr>
<tr>
<td>Central venous catheterization</td>
<td>10.45</td>
</tr>
<tr>
<td>Referral duration* ≥5 h</td>
<td>9.48</td>
</tr>
<tr>
<td>Staged closure</td>
<td>9.12</td>
</tr>
<tr>
<td>Multigravida</td>
<td>8.23</td>
</tr>
</tbody>
</table>

* Time from birth to arrival at our center.
especially wound infection and pneumonia, was found in the
group that underwent staged closures. However, this
observation was not noted in previous series, in which the
overall incidence of septic complications was low [7,16]. In
one report, the authors found a lower incidence of infection
in their patients who had had a preformed silo at the first
operation. However, in that study, there was neither wound
infection nor pneumonia in any group of their patients, and
infection was defined only by positive blood culture. It
should be noted also that in series in which a preformed silo
was used [6,7,16,21,22], silo-associated complication rates
including wound infection were generally lower than when
the old-fashioned silo was used [20,23,24]. Also, it should
be considered that the prolonged use of a ventilator in the staged
closure group was potentially responsible for higher
incidence of pneumonia. Taken together, the data suggest
us that there is still much room for improvement in silo sac-
related infections, and searching for a mean to reduce
infection in gastroschisis cases that require temporary
closure should be a priority.

Recent studies have proposed a novel scheme for
prognosticating an outcome analysis of gastroschisis [3,4].
In these studies, the anomaly was classified into simple and
complex cases that had intestinal atresia, perforation,
 necrotic segment, or volvulus. Complex gastroschisis cases
were more likely to have a prolonged hospital course and
diminished survival. Seven of our patients met the criteria of
complex gastroschisis. Although we had no mortality in this
group, 3 of 7 had intestinal failure and needed long-term
parenteral nutrition. On the other hand, we came across many
cases without associated intestinal problems that were
complicated later by infection that prolonged the hospital
stay and expenditure. From our point of view, simple
categorization of gastroschisis based on gastrointestinal
problems seems to be inadequate to prognosticate treatment
results. To find a crucial factor determining outcome, a study
may have to explore beyond the familiar clinical parameters
into less known epidemiologic factors.

In summary, our study found that two thirds of patients
with gastroschisis had at least one IC in their first month of
life, which had a significant impact on treatment outcome.
Factors independently associated with ICs consisted of a host
factor (multigravida), perioperative care factors (referral
duration and central venous line), and operative procedure
(staged closures).

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