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Original Article

# Gastroschisis survival improvement and early intervention: experience in a developing country

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## *Abstract*

***Background*** Gastroschisis is the most common abdominal congenital defect worldwide. While the mortality rate is 5-10% in developed countries, the rate escalates in developing countries due to less access to surgical care, and studies on the condition are scarce. Gastroschisis mortality and morbidity rates in Indonesia are unknown or unclear, little is also known about influencing factors that reveal epidemiological characteristics.

***Objective*** To identify the rate and factors associated with gastroschisis mortality in Indonesia.

***Methods*** A retrospective cohort study was conducted at Dr. Cipto Mangunkusumo Hospital, Jakarta, which included neonates with gastroschisis who underwent defect closure surgery from January 2015 to September 2020. We explored possible influencing risk factors, including gestational age, birth weight, number of surgeries, age at closure, and presence of gastroschisis complications. Bivariate analysis was done using Chi-square or Fisher's test.

***Results*** Of 49 neonates with gastroschisis, 42 were included in the study. Seven neonates were excluded due to incomplete medical records. The mortality rate of gastroschisis based on our data was 69%. The age at closure (<1 day) was significantly associated with lower mortality rate (P=0.005). In contrast, other factors, including gestational age, birth weight, number of surgeries, and the presence of complicated gastroschisis were not the risk factors of gastroschisis mortality.

***Conclusion*** The mortality rate of gastroschisis is high in Indonesia, specifically at Dr. Cipto Mangunkusumo Hospital, Jakarta. Immediate closure is significantly associated with a decreased likelihood of death. Awareness, diagnosis, and efficient referral of gastroschisis from remote areas to a tertiary facility must be encouraged to reduce the high mortality rate. **[Paediatr Indones. 2024;64:262-9; DOI: 10.14238/pi64.3.2024.262-9 ]**.

***Keywords:*** *gastroschisis; mortality; age at closure; associated factors*

Gastroschisis is the most common abdominal wall congenital defect. The incidence continues to increase globally as reported by high-income countries, yet clinical reports in low-income countries are scarce.[1-3] While the prognosis for patients who receive immediate surgical treatment is generally favourable,[4-6] the mortality rate from gastroschisis in low-income countries is significantly higher than in middle and high-income countries.[3] In developed countries, the mortality rate is 5-10%,[7] whereas in developing countries, namely Brazil, South Africa, and Jamaica, the rates are 52%, 43%, and 79%, respectively.[8-11]

Past studies explored several factors contributing to the gastroschisis mortality rate. Among them are young maternal age, low socioeconomic status, inadequate prenatal care, primigravida, and malnutrition.[1,8-11] Other factors that are widely established are young maternal age, prematurity, low birth weight, complicated gastroschisis, multi-stage closure, closure at neonatal age, as well as external teratogenic factors including maternal smoking,

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prenatal drug use, and alcohol consumption.[1,12]

Factors that influence the gastroschisis mortality rate in Indonesia's primary national referral hospital have not been reported. Therefore, we aimed to determine the gastroschisis mortality rate and explore the potential risk factors, including gestational age (GA), birth weight, number of surgeris, age at closure, and the presence of complicated gastroschisis, in an effort to reduce mortality caused by gastroschisis in the country.

## Methods

A retrospective cohort study was conducted using a medical record data at Dr. Cipto Mangunkusumo Hospital, Jakarta. Neonates who underwent defect closure surgery for gastroschisis from January 2015 to September 2020 in the Division of Paediatric Surgery, Department of Surgery, Universitas Indonesia/ Dr. Cipto Mangunkusumo Hospital, Jakarta, were included in the study. Neonates with incomplete medical records were excluded from the study. We analyzed associations between mortality rate of gastroschisis as the dependent variable and gestational age (GA), birth weight, number of surgeries, age at closure, and gastroschisis complications.

Gestational age was reported in weeks and divided into the following subgroups: preterm (<37 weeks), full-term (37-42) weeks, and post-term (>42 weeks).[13] Birth weights were classified into 1,500-2,499 grams, and 2,500-4,000 grams.[14] History of closure strategy was categorized into two subgroups: primary closure, defined as one attempt at defect closure, and delayed closure, defined as more than one attempt of defect closure. Age at closure was defined as the patient's age during the first gastroschisis-related surgery, classified into ≤1 day (within 24 hours of birth) and >1 days (more than 24 hours after birth). The gastroschisis type was divided into simple and complicated.[1] Complicated case is defined as having at least one other congenital pathology.

Data are presented in a categoric scale. Each potential risk factor was an independent variable and analyzed for an association with gastroschisis mortality rate. Bivariate analysis was conducted using the Chi-square or Fisher's test with *SPSS 20.0* software. The Ethics Committee of Faculty of Medicine, Universitas Indonesia, approved the study protocol, which met the Helsinki Declaration of 1977 criteria.

## Results

All patients presented to the hospital with a homemade silo, either made of plastic/cling wrap, or materials from the saline intravenous bags, applied to temporarily cover the herniated viscera as early management. A total of 49 neonates with gastroschisis underwent defect closure surgery during the study period. Seven subjects with incomplete medical records were excluded. Thus, a total of 42 subjects were included in the study, consisting of 26 females (62%) and 16 males (38%) (**Table 1**). The majority of the surgical procedures took place in 2016, with ten closures (24%) performed. Twenty-nine out of 42 subjects died during post-operative hospitalization period, contributing to a mortality rate of 69%. There were no significant correlations between gastroschisis mortality rate and gender, GA, birth weight, number of previous surgeries, and gastroschisis complications.

**Table 1**. Patient characteristics

| Characteristics | N=42 |
|---|---|
| Sex, n (%) | |
| Male | 16 (38) |
| Female | 26 (62) |
| Gestational age, n (%) | |
| Preterm | 27 (64) |
| Full-term | 15 (36) |
| Post-term | 0 (0) |
| Median (range), weeks | 36 (31-39) |
| Birth weight, n (%) | |
| 1,500-2,500 g | 32 (76) |
| ≥2,500 g | 10 (24) |
| Mean birth weight (SD), g | 2,312.26 (48.1) |
| Closure strategy, n (%) | |
| Primary closure | 29 (69) |
| Delayed closure | 13 (31) |
| Median closure strategy of closure attempt (range) | 1 (1-4) |
| Age at closure, n(%) | |
| 0-1 day | 16 (38) |
| ≥1 days | 26 (62) |
| Median age at closure (range), days | 2 (1-4) |
| Gastroshisis type, n. (%) | |
| Simple | 35 (83) |
| Complicated | 7 (17) |

However, the age at closure had a statistically significant association with lower mortality rate of gastroschisis (**Table 2**). Multivariate analysis was not performed, as only one factor (age at closure) appeared to be significantly correlated.

Twenty two out of 26 patients who underwent surgical closure at the age of > 1 day died in our study, with the mortality rate 85%, while the neonates who underwent closure at ≤1 day had a lower mortality rate (7/16 patients; 44%). The mortality rate among preterm and full-term neonates was 67% (18/27 subjects) and 73% (11/15 subjects) respectively. In our study, neonates with 1,500-2,500 grams birth weight had a mortality rate of 69% (22/32 subjects), and neonates with birth weight >2,500 grams had a mortality rate of 70% (7/10 subjects). A total of 83% of subjects were classified to have simple gastroschisis, with a mortality rate of 66% (23/35 subjects). The prevalence of complicated gastroschisis was 17%, accounting for 7 of 42 patients, include patients with ileum atresia, jejuno-ileal atresia, partial gastric necrosis, minor gastric curavature and ileal perforation, and total esophagogastric junction rupture. The mortality rate was 86% (6/7 subjects) for complicated gastroschisis.

## Discussion

To date, our study is the first to report gastroschisis mortality rate and explore the factors affecting it in Indonesia. Studies that investigate predictors of mortality in developing countries are limited, due to the lack of inclusion of congenital anomalies in national health surveys and limited research.[3] Moreover, factors that contribute to gastroschisis mortality differ between developing and developed countries. Preterm gestational age, low birth weight, lack of prenatal diagnosis, and delayed surgical management are reported to be the main factors affecting mortality in developing countries.[8,9,11] Hence, we explored these risk factors using data from Dr. Cipto Mangunkusumo Hospital, Jakarta, the national referral hospital that receives complex congenital surgical cases from across the nation.[15]

The mortality rate from gastroschisis at Dr. Cipto Mangunkusumo Hospital, Jakarta, during January 2015 - September 2020 was 69%. This number is an essential data piece, as it reflects the national gastroschisis mortality rate. In contrast, the mortality rate of gastroschisis in developed countries is 5-10%.[9,16] The marked discrepancy between these rates emphasizes the importance of this study as an initial effort to reduce the mortality rate in Indonesia and contribute to studies of global surgery.

**Table 2**. Analysis of subjects' characteristics and gastroschisis mortality

| Variables | Outcomes | | P value |
|---|---|---|---|
| | Survived (n=13) | Died (n=29) | |
| Gestational age, n | | | 0.466* |
| Preterm | 9 | 18 | |
| Full term | 4 | 11 | |
| Birth weight, n | | | 0.633* |
| 1,500-2,500 g | 10 | 22 | |
| ≥2,500 g | 3 | 7 | |
| Closure strategy, n | | | 0.360* |
| Primary closure | 8 | 21 | |
| Delayed closure | 5 | 8 | |
| Age at closure, n | | | 0.005** |
| 0-1 day | 9 | 7 | |
| ≥1 days | 4 | 22 | |
| Complicated gastroschisis, n | | | 0.287* |
| Yes | 1 | 6 | |
| No | 12 | 23 | |

*Fisher's one-sided test; **Chi-square test

Among the five factors we explored, age at closure was the only factor that was significantly linked to mortality. A study reported that delayed gastroschisis closure was associated with a prolonged length of stay and total parenteral duration, though they did not include complicated cases in their analysis.[17] A population-based study in Canada revealed that infants with urgent closure had a significantly shorter length of stay in the neonatal intensive care unit (NICU) than those who underwent closure with silo bag.[18] Primary closure was also associated with a lower rate of surgical site infection compared to delayed closure.[19,20]

In our subjects, gestational age and birth weight were not associated with mortality rate of gastroschisis. Both factors may be associated with intrauterine growth restriction (IUGR), directly affecting the neonates. A previous study reported that infants with GA of 33-34 weeks had higher mortality than those with GA of 35-36 weeks and >37 weeks. Premature babies tend to have higher risks of morbidity associated with immature organ development, including the gastrointestinal and abdominal wall.[15] However, babies with older gestational age did not show a better prognosis either, as reported in previous study which hypothesized that prolonged exposure to amniotic fluid had an unfavorable impact on bowel motility at term.[21] Our study did not align with previous study, the mortality rate was higher in full term than preterm neonates (73% *vs.* 67%). Thus, the association between GA and gastroschisis mortality remains inconclusive with considerable heterogeneity between studies.

In our study, subjects with birth weight 1,500-2,500 grams and those with birth weight >2,500 grams had similar mortality rate (69% *vs.* 70%). None of our subjects were documented with birth weight <1,500 or >4,000 grams. Previous findings indicated that birth weight was associated with an increased risk for mortality in gastroschisis.[1] In a large study involving 566 neonates with gastroschisis, neonates with low birth weight (<1,500 grams) had a greater mortality rate compared to those with normal birth weight (>2,500 grams) (31% *vs.* 3%, respectively).[22]

Within 24 hours of life, neonates with gastroschisis lose up to 2.5 times more fluid than healthy ones.[22] An intestine exposed to the open air leads to intestinal edema, and an immediate intervention prevents neonates from developing dehydration, infection, and hypothermia.[23] Thus, primary closure within the first 24 hours of life is indicated to avoid the development of fatal conditions. The median age at closure in our study was 2 days (range 1-4), in conjunction with the high mortality rate of 69%. Prolonged exposure of the intestine to air results in increased edema, creating another challenge for primary closure surgery. Neonates with gastroschisis who undergo closure at the age of > 1 day tend to necessitate multi-stage closure surgery.[22]

The prevalence of complicated gastroschisis was 17% in this study. This number was similar to numerous studies, with reported rates of 11-31%.[24-27] The mortality rate of neonates with complicated gastroschisis in our study was 86%, higher than those in developed countries, such as reported in Germany (17%), Canada (11.5%), and in the United States (10.9%).[24,27,28] A multicenter study in the United States revealed a higher mortality rate in complicated gastroschisis compared to simple cases, at 13% and 4%, respectively.[29] Another study reported that all subjects with complicated gastroschisis died.[8] In developed countries, the mortality rate of simple gastroschisis has been successfully lowered to 5-10%. Thus the presence of complicated gastroschisis was a significant indicator of mortality.[7] We found no statistically significant association between the mortality rate of gastroschisis and complicated type (P=0.287). However, from direct clinical observation of subjects, complicated gastroschisis contributed significantly to morbidity and mortality.

An increased number of surgeries was linked to a higher mortality rate.[30] In contrast, a multicenter randomized controlled trial revealed that silo bag (in multi-stage closure surgery) had a similar outcome to that of primary closure, yet with fewer days on the ventilator.[31] However, a study observed no significant difference between multi-stage and primary closure in 191 neonates with gastroschisis.[16] Another study also found no significant correlation between either type of surgery, primary or silo closure, with gastroschisis mortality.[8] Commercial silo bag is not available in Indonesia, therefore, we use blood bags as an alternative material to silo bag.

Similarly, 29 out of 42 subjects (69%) underwent the primary (single-stage) closure procedure in this study, with a 72% mortality rate. The other

13 (31%) subjects underwent multi-stage surgical procedures, with a mortality rate of 62%. In different circumstances, a study reported that the success rate of a primary closure in one day was 50-83%, depending on the presence or absence of gastroschisis complications.[32]

In Indonesia, hospitals engage a multi-tier health referral system. This system is responsible for delayed patient referrals, particularly with gastroschisis patients, who are often admitted at the age of > 1 day old. Most patients came to our center presented with severe conditions, such as dehydration, hypothermia, severe electrolyte imbalance, and/or septic state. These multi-aspect elements should be considered in the high mortality rate of gastroschisis patients, as reported in this study.

A limitation of our study was that the data did not represent cases from the remote areas. We used the total sampling method from a limited number of gastroschisis cases in our center. Our study did not include patients from other healthcare facilities. Other confounding factors, including sepsis, respiratory failure, respiratory acidosis, as well as congenital heart and pulmonary diseases were not analyzed, but likely contributed to the gastroschisis' mortality rate.

We present a pilot study on the mortality rate of gastroschisis and its associated factors, at Dr. Cipto Mangunkusumo Hospital, during the preceding five years. This report might serve as a preliminary study for further gastroschisis-related research in Indonesia. The mortality rate of gastroschisis at Dr. Cipto Mangkunkusumo Hospital, Jakarta, from January 2015 to September 2020, was 69%. The lower age at closure (< 1 day old) was associated with a lower mortality rate (P=0.005). In contrast, other factors, including gestational age, birth weight, number of surgeries, and the presence of complicated gastroschisis, were not associated with the mortality rate in our study. Immediate closure at age < 1 day showed a significant correlation to lower gastroschisis mortality rate (P=0.005). Therefore, immediate closure is recommended for gastroschisis patient. Further longitudinal studies with more subjects are needed to establish a causal relationship and identify novel factors.

## Conflicts of interest

None declared.

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