



Factors Influencing Mortality in Neonates with Gastroschisis in Bali, Indonesia

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ABSTRACT

Gastroschisis is a congenital abdominal wall defect requiring immediate surgical intervention. The high mortality rate in gastroschisis patients, particularly in developing countries, underscores the importance of a deeper understanding of factors that may influence clinical outcomes. This study aims to analyze factors affecting the risk of mortality in neonates with gastroschisis. A retrospective cohort study was conducted over five years and included 37 neonates with gastroschisis who were treated in the neonatal intensive care unit at Prof. I.G.N.G. Ngoerah Hospital. The majority of subjects were male (54.1%) and preterm (62.2%), with 18 patients (48.6%) surviving and 19 (51.4%) deceased. Surgical management primarily involved primary closure compared to staged closure, with most closures occurring within the first day of life. Sixteen subjects were identified with complex gastroschisis. The risk of mortality decreased by 56% in the simple gastroschisis group compared to the complex gastroschisis group (RR 0.44; 95% CI 0.23–0.87; $p=0.01$). The risk of mortality was found to be lower in neonates with simple gastroschisis compared to those with complex gastroschisis. There were no significant differences in mortality risk based on the method of closure, timing of closure, or incidence of sepsis.

INTRODUCTION

Congenital malformations remain a significant issue and the primary cause of mortality among neonates. Gastroschisis is a congenital condition associated with increased mortality and morbidity rates. It is characterized by a defect in the abdominal wall, resulting in the herniation of visceral organs outside the body, without any of a protective membrane (Bhat et al., 2020). Gastroschisis can be categorized into simple and complex types based on the condition of the intestines. A simple type of gastroschisis occurs when the intestines are in a normal state without complications, but a complex form is characterized by the presence of complications such as atresia, perforation, ischemia, necrosis, or volvulus (Bergholz et al., 2014). Approximately 10% of infants with gastroschisis also suffer from intestinal problems, including stenosis or intestinal atresia (Bhat et al., 2020).

The prevalence of gastroschisis has been rising in recent decades. Previous studies shows that the prevalence of gastroschisis in the US ranges from 4 to 5 per 10,000 live births (Short, 2019). The incidence is reported at a lower rate of 2.74 per 10,000 live births in Europe (Caldeman et al., 2021), whereas in Asia, namely in China, it is observed at 2.63 per 10,000 live births (Gao et al., 2024). Information regarding the prevalence or incidence of gastroschisis in Indonesia remains scarce. A study conducted by Rahayatri et al. in 2024 documented 49 instances of gastroschisis over a two-year period, revealing a death rate of 67% in the preterm neonate and 73% in the aterm neonate (Rahayatri et al., 2024).

Neonatal mortality in cases of gastroschisis is affected by various factors, including antenatal diagnosis, mode of delivery, defect repair procedure, and type of gastroschisis (Brebner et al., 2020). The majority of gastroschisis cases can be detected antenatally with ultrasonography at 12 weeks of gestation, effectively differentiating between simple and complex gastroschisis (Sun et al., 2022). Prior research indicates that the survival rate of infants with gastroschisis can exceed 90% in well-resourced health settings (Bhat et al., 2020; Youssef et al., 2016). The inconsistent distribution and standardization of healthcare facilities in Indonesia pose a difficulty that could impact the death rate of newborns with gastroschisis across different locations.

The management of gastroschisis, encompassing the repair of abdominal wall defects and the repositioning of visceral organs into the abdominal cavity, typically commences within hours post-delivery. The promptness of treatment is crucial to avert fluid depletion, maintain body temperature, diminish the likelihood of infection, and prevent the exacerbation of intestinal circulation abnormalities (Haddock & Skarsgard, 2018). The management of gastroschisis can be categorized into primary closure and progressive closure, the latter involving the use of silos during the initial phase. A meta-analysis by Kunz et al. indicated that progressive closure correlated with improved outcomes and significant reductions in ventilator utilization, the timing of initial oral nourishment, and the incidence of infection. This correlates with a reduction in intra-abdominal pressure and enhancement of splanchnic circulation perfusion, thereby diminishing the risk of infection and necrotizing enterocolitis (NEC) (Kunz et al., 2013). Numerous further investigations have found that there is no substantial difference between primary and progressive closure techniques (Poola et al., 2019; Schmidt et al., 2011).

Understanding the mortality risk factors in neonates with gastroschisis is crucial for establishing the optimum therapeutic approach. The author intends to examine the determinants influencing infant mortality associated with gastroschisis in Bali. This study's findings may serve as a foundation for the formulation of more uniform clinical guidelines for the treatment of gastroschisis in Indonesia.

METHOD

The design of this study is a retrospective cohort and conducted under approval from Medical Ethic Committee of Udayana University with approval number: 283/UN14.2.2.VII.14/LT/2024. Data sampling was carried out using medical records and the registry of patients who received treatment in the neonatal intensive care unit at Prof. I.G.N.G. Ngoerah Hospital, spanning from October 2019 to December 2024. The inclusion criteria consist of neonatal medical record data for individuals aged 0-28 days who have been diagnosed with gastroschisis and received treatment in the neonatal intensive care unit at Prof. I.G.N.G. Ngoerah Hospital. The exclusion criteria include patients who have incomplete medical record

data and those who have undergone treatment for closure of abdominal wall defects at other hospitals. The sample collection method in this study uses total sampling due to the limited number of populations. Data was extracted from medical records, including sex, gestational age, referral status, birth weight, type of gastroschisis, closure method, age at closure, incidence of sepsis, and mortality status. The gestational age is determined using the New Ballard Score (NBS). Gastroschisis is categorized into simple type (without intestinal issues) and complex type (including abnormalities or complications in the intestines, such as stenosis, intestinal atresia, necrosis, or adhesions). The closing procedure is categorized into primary closure and staged closure, with silo installation occurring prior to primary closure. The age at closure is categorized into 0-1 days and greater than 1 day. The occurrence of sepsis is categorized as sepsis and non-sepsis. Mortality status is classified as either survival or death.

The collected data is subsequently entered into SPSS® version 27 software for statistical analysis. The study was conducted in phases, commencing with univariate analysis to examine the frequency, percentage, and distribution of numerical data. A bivariate analysis was subsequently conducted to assess the association among risk factors. Bivariate analysis was conducted with a statistical method for categorical data, specifically the chi-square test or Fisher's exact test. The threshold for statistical significance was established at $p < 0.05$.

RESULT

From October 2019 to December 2024, this study included a total of 37 neonates with gastroschisis. The predominant demographic comprised males, namely 20 out of 37 patients, accounting for 54.1%, and were delivered at a gestational age of less than 37 weeks, indicating premature birth (62.2%). The patients' birth weights varied, predominantly within the range of 1,500–2,500 grams (75.7%). Approximately 59.5% of patients were either referred or born outside the research hospital. Only a small proportion of 6 out of 37 patients (16.2%) were diagnosed with gastroschisis prenatally.

Simple gastroschisis was identified in 56.8% of individuals, while 16 patients exhibited complex gastroschisis, accounting for 43.2%. The technique for closing abdominal wall abnormalities differs, although the majority of patients (59.5%) receive primary closure. Age at closure was also evaluated, with 25 of the 37 patients receiving early closure within 0-1 day. The occurrence of sepsis, encompassing both culture-positive and just clinical cases, was recorded in 91.9% of patients. The majority of patients received treatment for more than 14 days (59.5%), with an average hospitalization length of 20 days. The attributes of the sample from this investigation are presented in Table 1.

Table 2 presents the findings of the bivariate analysis concerning the link between factors influencing mortality status in neonates with gastroschisis. Data interpretation involved evaluating statistical significance using p-value and clinically assessing importance through relative risk (RR) and a 95%

confidence interval (CI). The type of gastroschisis variable exhibited a clinically significant relationship, as evidenced by the p-value and relative risk: $p = 0.01$, RR 0.44, and 95% CI 0.23-0.87. This indicated a 56% reduction in mortality in the neonate group with simple type gastroschisis compared to the complex type. Simultaneously, no substantial correlation was observed between the kind of gastroschisis, closure method, age at closure, prenatal diagnosis, and the prevalence of sepsis affecting mortality in neonates with gastroschisis ($p > 0.05$).

Table 1. Clinical characteristics of neonates with gastroschisis

	Total sample, n = 37 N (%)
Sex, n (%)	
Male	20 (54.1)
Female	17 (45.9)
Gestational age, n (%)	
Preterm	23 (62.2)
Aterm	14 (37.8)
Median (range), weeks	36 (26-40)
Birthweight, n (%)	
<1.500 gram	2 (5.4)
1.500 – 2.500 gram	28 (75.7)
≥2.500 gram	7 (18.9)
Mean (SD), gram	2190.2 (475.3)
Referral, n (%)	
Yes	22 (59.5)
No	15 (40.5)
Prenatal diagnosis, n (%)	
Yes	6 (16.2)
No	31 (83.8)
Type of gastroschisis, n (%)	
Simple	21 (56.8)
Complex	16 (43.2)
Closure methods, n (%)	
Primary closure	22 (59.5)
Staged closure	15 (40.5)
Age at closure, n (%)	
0 – 1 day	25 (67.6)
>1 days	12 (32.4)
Sepsis, n (%)	
Yes	34 (91.9)
No	3 (8.1)
Length of stay, n (%)	
<14 days	15 (40.5)
≥14 days	22 (59.5)
Mean (SD), days	20.2 (16.1)

Table 2. Analysis of risk factors affecting mortality status of neonates with gastroschisis

	Death n = 19	Survive n = 18	RR (95% CI)	p-value
Type of gastroschisis, n (%)				
Simple	7 (33.3)	14 (66.7)	0.44 (0.23-0.87)	0.01*
Complex	12 (75.0)	4 (25.0)		
Closure methods, n (%)				
Primary closure	10 (45.5)	12 (54.5)	0.75 (0.41-1.40)	0.383
Staged closure	9 (60.0)	6 (40.0)		
Age at closure, n (%)				
0 – 1 day	11 (44.0)	14 (56.0)	0.66 (0.36-1.19)	0.19
>1 days	8 (66.7)	4 (33.3)		
Sepsis, n (%)				
Yes	18 (52.9)	16 (47.1)	1.6 (0.31-8.11)	0.60 ^a
No	1 (33.3)	2 (66.7)		

^aFisher exact test; *significance at level <0.05

DISCUSSION

The current study identified 37 cases of gastroschisis, predominantly among male patients. This aligns with a prior study by Salinas-Torres et al., which similarly indicated that the majority of gastrocystic neonates were male (Salinas-Torres et al., 2018). Furthermore, no notable changes were observed concerning referral and referral status. Raymond et al.'s investigation revealed comparable findings, indicating no disparity in fatality rates between neonates born at the primary hospital and those born in other healthcare institutions (or referral cases). Nevertheless, the study revealed that among the neonates delivered outside the primary hospital, there was an escalation in the length of mechanical ventilation utilization (Raymond et al., 2020).

Fourteen out of thirty-seven newborns with gastroschisis were delivered at a gestational age exceeding 36 weeks or at term. This aligns with prior research indicating that the majority of patients with gastroschisis present at a lower gestational age or in a preterm state (Baer et al., 2019; Raymond et al., 2020). Gastroschisis is linked to a placental inflammatory disease and a heightened risk of intrauterine infection. Preterm birth is favored when gastroschisis is identified during the prenatal period to mitigate problems (Mesas Burgos et al., 2015; Overcash et al., 2014). The majority of patients exhibit a low birth weight, defined as less than 2,500 grams. Low birth weight results from growth restriction initiated in utero, mediated by inflammatory mechanisms in the intestines, diminished nutritional absorption, and restricted abdominal capacity, all of which impede foetal growth (Bottu & Manzar, 2024).

Gastroschisis can be classified into simple and complex types, with the majority of individuals in our study exhibiting a simple type (Bergholz et al., 2014). Sixteen patients in this study were born with a complicated type of gastroschisis. This study finds that simple type gastroschisis decreases the mortality risk by 56% in comparison to complex type gastroschisis (p=0.01; RR 0.44; 95% CI 0.23-0.87). This suggests that simple gastroschisis has a protective effect on mortality. A study by Raymond et al. supports

the finding of this study, which states that the survival rates of newborns with simple gastroschisis are 96% and complex gastroschisis are 87% (Raymond et al., 2020).

The primary closing procedure in this study has predominantly been performed on subjects aged 0-1 day. Bivariate study revealed no significant correlation between the closure method and the age of closure concerning the mortality status of infants with gastroschisis. The research conducted by Gurien et al. similarly revealed no significant disparity in mortality between the primary closure group (0-1 day) and the gradual closure group (4-14 days); however, the gradual closure group exhibited an extended treatment duration and a reduced duration of ventilator dependence (Gurien et al., 2017). A study by Rahayatri et al. conducted in Indonesia shown that a rapid closure, occurring within 0-1 day, can reduce the risk of mortality. An extended length prior to closure correlates with the danger of infection, hypothermia, dehydration, and electrolyte imbalances, which may exacerbate the patient's condition and result in mortality (Kamal, 2023).

Individuals with gastroschisis are predisposed to infections, particularly early-onset newborn sepsis. The research revealed that 20 of the 26 neonates with gastroschisis experienced sepsis, and there was no correlation between the occurrence of sepsis and mortality in neonates with gastroschisis. These findings contradict a cohort research study by Fullerton et al., which identified sepsis as the sole statistically significant predictor of mortality (Fullerton et al., 2017). The exposure of visceral organs to the external environment heightens the risk of infection due to microbial contamination, potentially resulting in sepsis (Wallace et al., 2023). Moreover, predisposing variables such as gestational age and delayed intrauterine growth, together with low birth weight, correlate with the patient's underdeveloped immune system, hence elevating the risk of sepsis and mortality (Skertich et al., 2020).

This study has some limitations, the primary one being the limited sample size ($n = 37$), which may impact the ability to identify statistically significant differences or relationships. The second is the retrospective cohort research methodology, wherein data is acquired from medical records that exhibit constraints regarding completeness and correctness. This may result in information bias, particularly if data is absent or inconsistent.

CONCLUSION

The mortality risk was decreased in neonates with simple gastroschisis compared to those with complex types. Nonetheless, there was no substantial disparity across closure procedures, age at closure, prenatal diagnosis, and the occurrence of sepsis regarding mortality risk. Additional research with bigger samples is essential to get more precise, population-representative outcomes, hence facilitating the formulation of more effective and standardized protocols for the management of neonates with gastroschisis.

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