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การศึกษาเปรียบเทียบผลการรักษาภาวะผนังหน้าท้องไม่สมบูรณ์ของทารกแรกเกิด ในจังหวัดบุรีรัมย์ ระหว่างปีพ.ศ. 2554-2563

A Comparative Study of Gastroschisis and Omphalocele Outcomes in Newborns of Buriram Province Between 2011-2020

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บทคัดย่อ

หลักการและเหตุผล : Gastroschisis และ omphalocele คือ ภาวะผนังหน้าท้องไม่สมบูรณ์ทำให้อวัยวะในช่องท้องโผล่ออกมา การเข้าใจความแตกต่างของสองภาวะ จะทำให้สามารถรักษาและให้ข้อมูลแก่ผู้ปกครองได้ถูกต้อง

วัตถุประสงค์ : เพื่อเปรียบเทียบลักษณะของโรค การรักษา และภาวะข้างเคียงของทารกที่มีภาวะ gastroschisis และ omphalocele ในจังหวัดบุรีรัมย์

วิธีการศึกษา : การศึกษาเชิงพรรณนาแบบย้อนหลัง โดยทบทวนเวชระเบียนของผู้ป่วย gastroschisis และ omphalocele ที่รักษาระหว่างปีพ.ศ. 2554-2563 ในโรงพยาบาลบุรีรัมย์ โดยใช้สถิติเชิงพรรณนาร่วมกับวิเคราะห์ด้วย Chi-square และ Mann-Whitney U test

ผลการศึกษา : ผู้ป่วยทั้งหมด 53 ราย แบ่งเป็น gastroschisis 43 ราย และ omphalocele 10 ราย เมื่อเปรียบเทียบกันพบว่า gastroschisis มารดามีอายุน้อยกว่า ($p<0.001$) พบน้ำหนักแรกเกิดต่ำเยอะกว่า ($p=0.014$) สองกลุ่มมีอัตราการวินิจฉัยก่อนคลอดใกล้เคียงกันที่ร้อยละ 30 กลุ่ม omphalocele วินิจฉัยก่อนคลอดได้เร็วกว่า ($p=0.043$) พบ Patent ductus arteriosus มากกว่า ($p<0.01$) นอกจากนี้ยังพบ Beckwith-Wiede mann ร้อยละ 20 และพบตับยื่นออกมาเฉพาะใน omphalocele อีกด้วย ด้านการผ่าตัด gastroschisis ผ่าตัดทุกราย (primary closure ร้อยละ 81.4 stage closure ร้อยละ 18.6) พบลำไส้ตัน ร้อยละ 7 ลำไส้ทะลุ ร้อยละ 7 ขนาดของรูโหว่หน้าท้องเล็กกว่า ($p<0.001$) ในขณะที่ omphalocele ได้รับการผ่าตัดเพียงร้อยละ 80 ด้วยวิธี primary closure ทั้งหมด และปฏิเสธการผ่าตัด ร้อยละ 20 Gastroschisis นอนโรงพยาบาลนานกว่า ($p=<0.001$) ได้รับอาหารทางหลอดเลือดนานกว่า ($p=0.014$) และเริ่มได้กินช้ากว่า ($p<0.001$) อัตราการเสียชีวิตของ Omphalocele สูงกว่าอย่างมีนัยสำคัญ (ร้อยละ 40 เทียบกับ ร้อยละ 2.3 $p=0.003$)

สรุป : Gastroschisis และ omphalocele มีลักษณะที่แตกต่างกัน Gastroschisis ต้องการการดูแลหลังผ่าตัดที่เข้มข้นกว่า ในขณะที่ omphalocele แม้การดูแลหลังผ่าตัดที่ไม่ซับซ้อนเท่า แต่มีอัตราการเสียชีวิตสูงกว่า

คำสำคัญ : ภาวะผนังหน้าท้องไม่สมบูรณ์ ผลการรักษา

ABSTRACT

Background : Gastroschisis and omphalocele are common abdominal wall defects with distinct features. Understanding their differences is essential for appropriate management and counseling.

Objective : To compare clinical characteristics, management, and outcomes of newborns with gastroschisis and omphalocele.

Methodology : A retrospective descriptive study reviewed medical records of newborns diagnosed with gastroschisis or omphalocele from 2011 to 2020 at Buriram Hospital, Thailand. Descriptive statistics, Chi-squared tests, and Mann-Whitney U test were used for analysis.

Results : Total of 53 patients, 43 had gastroschisis and 10 had omphalocele. Mothers of gastroschisis cases were significantly younger ($p<0.001$). and had more low birth weight ($p=0.014$), Prenatal diagnosis rates were similar (~30%), with all cases referred for obstetric follow-up. Omphalocele was diagnosed earlier ($p=0.043$), and showed higher rates of patent ductus arteriosus ($p<0.01$) and Beckwith-Wiedemann syndrome (20%). Gastroschisis was associated with intestinal atresia (7%), perforation (7%), significantly smaller defect size ($p<0.001$), and no liver herniation. All gastroschisis patients underwent surgery: 81.4% had primary closure, 18.6% staged. In the omphalocele group, only 80% underwent surgery (all with primary closure) while 20% denied surgery. Gastroschisis cases required longer hospital stays ($p=<0.001$), prolonged parenteral nutrition ($p=0.014$), and delayed feeding initiation ($p<0.001$). Postoperative complications differed. Mortality was significantly higher in omphalocele (40% vs. 2.3%, $p=0.003$).

Conclusion : Despite similar appearance, gastroschisis and omphalocele differ significantly. Gastroschisis demands more intensive postoperative care but has better survival, while omphalocele has higher mortality despite earlier diagnosis and less complex initial management.

Keywords : Gastroschisis, Omphalocele, Outcomes.

Background

Gastroschisis and omphalocele are the most common abdominal wall defects with key differences. Omphalocele have abdominal organs that protrude into a membranous sac attached to the umbilical cord. It is often associated with chromosomal anomalies, congenital heart defects, and Beckwith-Wiedemann syndrome[1]. Prenatal diagnosis is via ultrasound, though bowel herniation before 12 weeks may be normal.[2] Amniotic tested for karyotyping and fetal echocardiography should be performed. Postnatal care includes: (1) NPO, orogastric tube, fluids, antibiotics and oxygen as needed; (2) covering the sac to prevent fluid and heat loss; (3) screening for associated anomalies; (4) transfer to pediatric surgical center.

Primary closure which involves closing the abdominal wall in a single operation is ideal[3] but large defects may need staged closure with silo reduction followed by surgical closure. Alternatives include tissue expanders, synthetic mesh, or skin flaps.[3] When the sac is too large or anesthesia poses a high risk, application of topical agents such as silver sulfadiazine (Silvadene®) or povidone-iodine (Betadine®) can be used and will take 2-3 months[3], later surgical repair ventral hernia is typically planned at 1 year of age.

Gastroschisis is an abdominal wall defect without a sac, usually right of the umbilicus[4]. Risk factors include young maternal age, maternal infection[5]. Associated anomalies include intestinal atresia and perforation. Postnatal care is similar to omphalocele. Treatment include: (1) primary closure; (2) sutureless closure using the umbilical cord[6]; (3) staged closure.

Literature review shows gastroschisis presents with lower birth weight, more growth restriction, preterm delivery and younger maternal age,[7, 8] while omphalocele has more cardiac and inguinal abnormalities[9] plus larger defects.[10] Postoperatively, gastroschisis requires longer parenteral nutrition and hospitalization with more systemic infections, whereas omphalocele has higher mortality. For long-term follow-up, 62% of omphalocele patients need additional surgeries versus 48% with gastroschisis.[11]

Objective

To compare the clinical characteristics, management and outcomes of newborns with gastroschisis and omphalocele born in Buriram Hospital.

Methods

Study designs

A retrospective descriptive study was conducted by reviewing medical records of newborns diagnosed with gastroschisis or omphalocele. The study protocol was approved by Buriram Hospital Ethic Committee for Human Research (reference number BR 0033.102.1/53, dated 2024 October 31st).

Participants

All newborns diagnosed with gastroschisis or omphalocele between 2011 and 2020 at Buriram Hospital, a tertiary care center in northeastern Thailand, were included in the study. Exclusion criteria were missed diagnoses and cases where definite treatment was provided at other hospitals.

Data collection

Collected data included maternal demographics, prenatal ultrasound findings, gestational age at diagnosis and delivery, route and mode of delivery, birth weight, Apgar scores, associated anomalies, surgical management, intraoperative findings, postoperative care parameters (length of stay, duration of ventilator support, duration of parenteral nutrition, time to feeding initiation and time to fully feeds), Postoperative complications and mortality were also recorded.

Statistical Analysis

Data were analyzed using SPSS. Categorical variables were compared using Chi-squared tests (reported as percentages) and continuous variables using Mann-Whitney U tests (reported as mean ± SD). Statistical significance was set at $p<0.05$.

Table 1 Patients' characteristic (n = 53)

	Gastroschisis	Omphalocele	p-value
Sex			
Female	26 (60.5%)	7 (70%)	0.725
Male	17 (39.5%)	3 (30%)	-
Maternal age, Mean ± SD	19.16 ± 4.04	30.1 ± 8.17	<0.001*
Prenatal ultrasound diagnosis	13 (30.2%)	3 (30%)	1
Mean prenatal ultrasound diagnosis gestational ages (Wks), Mean ± SD	25.84 ± 7.47	15.48 ± 3.92	0.043*
Route of delivery			
Cesarean section	16 (37.2%)	6 (60%)	0.287
Vaginal delivery	27 (62.8%)	4 (40%)	-
Mode of delivery			
Labor pain	38 (97.4%)	7 (70%)	0.023
Elective C-section	1 (2.6%)	3 (30%)	-
Mean GA at elective C-section (wks)	39	38.52 ± 0.21	0.180
Preterm	31 (72.1%)	5 (50%)	0.260
Mean Birth weight (gm), Mean ± SD	2,173 ± 495.26	2,613 ± 894.88	0.109
Mean GA at birth (wks)), Mean ± SD	35.8 ± 2.09	36.4 ± 2.30	0.270
Mean Apgar score), Mean ± SD			
1 min	7.53 ± 2.48	6.3 ± 3.16	0.179
5 min	9.02 ± 1.86	8.6 ± 1.78	0.320
Associated condition			
Perforated bowel	3 (7%)	-	-
Atresia	3 (7%)	-	-
Anorectal malformation	-	1 (10%)	-
Undescended testis	6 (14%)	2 (20%)	0.636
Club foot	-	1 (10%)	-
Low birth weight	35 (81.4%)	4 (40%)	0.014
Hypothermia	2 (4.7%)	-	-

Table 1 Patients' characteristic (n = 53) (continuous)

	Gastroschisis	Omphalocele	p-value
Respiratory distress syndrome	1 (2.3%)	1 (10%)	0.345
Respiratory distress	7 (16.3%)	3 (30%)	0.376
Congenital pneumonia	4 (9.3%)	1 (10%)	1
Patent ductus arteriosus (PDA)	1 (2.3%)	5 (50%)	<0.01
Structural heart disease	3 (7%)	2 (20%)	0.235
Anemia	3 (7%)	-	-
Osteopenia of prematurity	6 (14%)	-	-
Beckwith Widermann syndrome	-	2 (20%)	-

*Statistical significance using Mann-Whitney U test

Result

This retrospective study reviewed 53 newborns with abdominal wall defects at Buriram Hospital; 43 with gastroschisis and 10 with omphalocele. Female predominance was observed in both (gastroschisis 60.5% vs. omphalocele 70%, p=0.725). Maternal age was significantly lower in gastroschisis cases (19.16±4.04 vs. 30.1±8.17 years, p<0.001). Prenatal ultrasound detection rates were similar in both groups (around 30%), all diagnosed cases were referred to the obstetrics follow-up. Two omphalocele cases underwent amniocentesis: one had trisomy 13. No pregnancies were terminated. Ultrasound diagnosis occurred earlier in omphalocele (15.48±3.92 weeks vs. 25.84±7.47 weeks, p=0.043).

Vaginal delivery was more common in gastroschisis (62.8% vs. 40%, p=0.287), usually after labor onset (97.4%). Omphalocele had higher rates of elective Cesarean section (C-section) (30% vs 2.6%, p=0.023). The mean gestational age for elective C-section cases was similar between groups (39 weeks vs 38.52 weeks, p=0.180).

Preterm birth was more frequent in gastroschisis (72.1% vs. 50%, p=0.260). Apgar scores were comparable with gastroschisis showing slightly higher scores at both 1 minute (7.53±2.48 vs. 6.3±3.16, p=0.179) and 5 minutes (9.02±1.86 vs. 8.6±1.78, p=0.320). Gastroschisis infants had significantly lower birth weights (2,173±495.26g vs. 2,613±894.88g, p=0.109) despite similar gestational ages at birth (35.8±2.09 vs. 36.4±2.30 weeks, p=0.270). Notably, gastroschisis had higher rates of low birth weight (81.4% vs. 40%, p=0.014).

Associated anomalies were more frequent in omphalocele. PDA was significantly more common (50% vs. 2.3%, p<0.01), structural heart defects (20% vs. 7%), undescended testes (20% vs. 14%), respiratory distress syndrome (10% vs. 2.3%), respiratory distress (30% vs. 16.3%), congenital pneumonia (10% vs. 9.3%), anorectal malformation (10% vs. 0%), clubfoot (20% vs. 0%), and Beckwith-Wiedemann syndrome (20% vs. 0%). In contrast, gastroschisis was uniquely associated with bowel perforation (7%), intestinal atresia (7%), hypothermia (4.7%), anemia (7%), and osteopenia of prematurity (14%). (Table 1).

Intraoperatively, gastroschisis showed smaller defect size (2.75±0.77cm vs. 4.95±2.16cm, p<0.001) with small bowel (100%), large bowel (89.5%) and uniquely reproductive organ herniation. While omphalocele distinctively showed liver (42.9%) and Meckel diverticulum (28.6%) herniation. The mean time to abdominal wall closure was slightly longer in gastroschisis (41.86±79.79 vs. 33±25.46 hours, p=0.057). All gastroschisis cases underwent surgery (81.4% primary closure, 18.6% staged closure) compared to 80% of omphalocele cases having primary closure, with two cases (20%) denied surgery due to severe conditions and both died.

Postoperatively, gastroschisis required significantly longer hospital stays (27.77±12.77 vs. 17.40±20.54 days, p=<0.001), parenteral nutrition duration (20±10.26 vs. 10.5±5.25 days, p=0.014), ventilator support (5.17±3.74 vs. 3.33±5.79 days, p=0.029) delayed feeding initiation (10.54±4.11 vs. 3.43±0.98 days, p<0.001). Gastroschisis also showed a longer time to full feeding (14.59±9.51 days vs. 9.67±4.97 days, p=0.160), longer antibiotic duration (16.28±8.31 days vs. 10.5±6.44 days, p=0.064) and but not statistically significant.

Postoperative complication, omphalocele had higher jaundice (40% vs. 2.3%, P=0.003), upper gastrointestinal bleeding (20% vs 0%), congestive heart failure (10% vs. 2.3%), acute kidney injury (10% vs. 2.3%) and pulmonary hemorrhage (10% vs. 0%). Gastroschisis cases experienced higher rates of electrolyte imbalance (34.9% vs. 30%), neonatal sepsis (30.2% vs 0%), anemia (20.9% vs. 10%), pneumonia (18.6% vs. 10%) hypoalbuminemia (14% vs. 10%), catheter-related bloodstream infections (4.7% vs 0%), surgical site infections (7% vs 0%) and atelectasis (9.3% vs 0%).

Mortality was significantly higher in omphalocele (40% vs. 2.3%, p=0.003). The single gastroschisis death occurred in a 33-week infant with ileal atresia and perforation who died from septic shock. Four omphalocele deaths included cases with Edward syndrome, multiple cardiac defects requiring palliative care, a preterm infant with persistent pulmonary hypertension and trisomy 13 with multiple congenital anomalies. (Table 3.)

Table 2 Intra-operative finding. (n = 53)

	Gastroschisis	Omphalocele	p-value
Mean defect size (cm)	2.75 ± 0.77	4.95 ± 2.16	<0.001*
Herniated content			
Small bowel	43 (100%)	6 (85.7%)	0.140
Large bowel	34 (89.5%)	4 (57.1%)	0.064
Stomach	19 (48.7%)	1 (14.3%)	0.119
Liver	-	3 (42.9%)	-
Meckel diverticulum	-	2 (28.6%)	-
Ovary	3 (7%)	-	-
Ovarian tube	7 (16.3 %)	-	-
Uterus	2 (4.7%)	-	-
Testis	2 (4.7%)	-	-
Spleen	1 (2.3%)	-	-
Gall bladder	2 (4.7%)	-	-
Bladder	6 (14%)	-	-

*Statistical significance using Mann-Whitney U test

Discussion

This 10-year retrospective analysis compares clinical characteristics and outcomes of 43 gastroschisis and 10 omphalocele patients from Buriram Province. The demographic data consistent with previous literature, the significantly younger maternal age in gastroschisis cases (19.16 vs. 30.1 years, p<0.001)[8] confirms this well-established risk factor and consistent with the findings in Kong et al. study explained by our teenage maternal also had the risk of increased use of recreation drugs, smoking, low socioeconomic status and poor nutritional status[7]. In contrast, omphalocele was associated with older maternal age, consistent with its known link to chromosomal abnormalities.

Prenatal ultrasound diagnosis rates of approximately 30% for both conditions are notably lower than reported in developed countries which report at 80-90%. This may be due to most of our cases being referred from primary and secondary care hospitals which have differences in healthcare infrastructure, routine screening protocols, and access to high-quality ultrasound equipment in our provincial setting. Amniocentesis in two omphalocele cases revealed one trisomy 13. All prenatal diagnosed cases were referred to obstetrics follow-up, demonstrating the value of prenatal ultrasound. A study by Srisan et al. found no survival advantage with prenatal diagnosis, but allow properly planned postnatal management by multidisciplinary teams[9]. Omphalocele was detected much earlier (15.48 vs. 25.84 weeks, p=0.043), likely due to its larger defect size and the frequent presence of associated anomalies. These findings emphasize the importance of comprehensive first-trimester ultrasound screening and maternal blood AFP level.

Almost all gastroschisis cases were delivered after the onset of labor (97.4% vs. 70%, p=0.023) and vaginal delivery was the more common route (62.8% vs. 40%). Literature supports safe vaginal delivery post-labor for gastroschisis, with no proven benefit for preterm induction or delivery after 38 weeks of gestational age[12]. The gastroschisis group had higher preterm (72.1% vs. 50%) and more frequent low birth weight (81.4% vs. 40%) consistent with studies from others.[8,10,13] These outcomes likely result from chemical irritation of the bowel triggering preterm labor. However, our study lacked data on causes of prematurity.

The significantly smaller defect size in gastroschisis (2.75 vs. 4.95 cm, p<0.001) coupled with involving small bowel in all cases explain the higher rates of primary closure feasibility (81.4%) despite the presence of complex intraoperative findings such as bowel perforation (7%) and atresia (7%). The absence of liver herniation in our gastroschisis cases differs from the study by Asta et al.[11] Where liver involvement has been reported as a mortality factor, possibly reflecting the relatively small defect sizes in our population.[10] In contrast, liver herniation (42.9%) and Meckel's diverticulum protrusion (28.6%) were uniquely observed in our omphalocele cases showing clear clinical differences.

Regarding associated anomalies, our study confirms the well-established association between omphalocele and cardiovascular defects, with significantly higher

rates of PDA (50% vs. 2.3%, p<0.01). A study by Ayub et al. also found interrupted IVC and cardiac abnormalities in 20% of omphaloceles. Identifying these conditions is crucial as some cardiovascular condition needs prostaglandin therapy until receive cardiac surgery[14]. Beckwith-Wiedemann syndrome found 20%, exceeds the reported incidence of 10-15% in the literature, possibly due to our small sample size or enhanced recognition. Respiratory problems were present in approximately 30% of the omphalocele group. In gastroschisis, 5-20% of cases had cardiac or pulmonary comorbidities. Other conditions such as hypothermia, anemia, and osteopenia of prematurity were found only in gastroschisis[15]. Anemia in gastroschisis may be caused by persistent malabsorption leading to nutritional deficiency such as vitamins and trace elements[16]. Undescended testis were presented in 14% of gastroschisis and 20% of omphalocele consistent with prevalence from the Raitio et al. study indicating that some patients may require orchidopexy later in life[17].

Although we found similar timing for surgical repair, gastroschisis patients had significantly longer hospital stays (27.77 vs. 17.40 days, p=<0.001), dependency on parenteral nutrition (20 vs. 10.5 days, p=0.014), ventilator support (5.17±3.74 vs. 3.33±5.79 days, p=0.029) and delayed feeding initiation (10.54 vs. 3.43 days, p<0.001). These findings align with multiple studies demonstrating the prolonged recovery period and more intensive care required for gastroschisis patients due to dysmotility and absorption issues from prolonged exposure to amniotic fluid.

The post-operative complication also differed between the two groups. In gastroschisis, the most common complications were electrolyte imbalances (34.9%), followed by neonatal sepsis (30.2%) as also reported by Sugita et al. and possibly linked to anemia[16]. In omphalocele, jaundice was the most common complication (40%).

The mortality was lower in gastroschisis (2.3%), consistent with many reports [11, 15, 18]. Gastroschisis with atresia, necrosis or volvulus was associated with significantly increased morbidity and mortality. Our gastroschisis death case also had bowel perforation[7]. Omphalocele had a significantly higher mortality rate (40% vs. 2.3%, p=0.003) consistent with previous reports from Thailand[9, 19]. Pulmonary hypertension is also known as an independent predictor of mortality and was present in one of our omphalocele death cases[20]. Abdominal compartment syndrome was a modifiable risk factor for mortality but was not observed in this study[11] may be due to our highly experienced surgical and pediatric specialists. This high mortality of omphalocele underscores the critical importance of multidisciplinary management, particularly in providing cardiopulmonary support and genetic counseling[8].

Table 3 Surgical treatment and post-operative outcome.

	Gastroschisis	Omphalocele	p-value
Mean age at abdominal wall closure (Hours)	41.86 ± 79.79	33 ± 25.46	0.057
Mean length of stay (days)	27.77 ± 12.77	17.40 ± 20.54	<0.001*
Mean duration of ventilator used (days)	5.17 ± 3.74	3.33 ± 5.79	0.029*
Mean duration of parenteral nutrition (days)	20 ± 10.26	10.5 ± 5.25	0.014*
Mean time to start feeding after surgery (days)	10.54 ± 4.11	3.43 ± 0.98	<0.001*
Mean time to full feeding (days)	14.59 ± 9.51	9.67 ± 4.97	0.160
Mean antibiotic duration (days)	16.28 ± 8.31	10.5 ± 6.44	0.064
Surgery	43 (100%)	8 (80%)	-
Primary closure	35 (81.4%)	8 (100%)	0.327
Stage closure	8 (18.6%)	-	-
Deny surgery	-	2 (20%)	-
Post-operative complication			
SSI	3 (7%)	-	-
Pneumonia	8 (18.6%)	1 (10%)	1
Anemia	9 (20.9%)	1 (10%)	0.665
Neonatal sepsis	13 (30.2%)	-	-
Jaundice	1 (2.3%)	4 (40%)	0.003
Congestive heart failure	1 (2.3%)	1 (10%)	0.345
Acute kidney injury	1 (2.3%)	1 (10%)	0.345
Electrolyte imbalance	15 (34.9%)	3 (30%)	1
Hypoalbuminemia	6 (14%)	1 (10%)	1
Seizure	1 (2.3%)	1 (10%)	0.345
UGIB	-	2 (20%)	-
Pulmonary hemorrhage	-	1 (10%)	-
Atelectesis	4 (9.3%)	-	-
CRBSI	2 (4.7%)	-	-
Death	1 (2.3%)	4 (40%)	0.003

*Statistical significance using Mann-Whitney U test

Conclusion

Gastroschisis and omphalocele may look alike but there were massive differences. Critical delays from detecting and transferring can be minimized. Prenatally omphalocele can detected since 15 weeks gestational age and should be referred to Maternal-Fetal Medicine specialists for amniocentesis as we found it highly associated with chromosome abnormality and cardiovascular disease. Moreover, Gastroschisis had younger maternal age around 19 years old, a higher rate of preterm, lower birth weight and smaller defect size. Liver herniation was found only in omphalocele which helps in differentiation. Furthermore, a high rate of respiratory complications, sepsis, electrolyte imbalance and hypoalbuminemia can be found in up to 30%. We also provided information for counseling the affected infant's families that though gastroschisis needed more intense postoperative care, needed longer length of stay, parenteral nutrition duration, ventilator support and slower initial feeding. Conversely, omphalocele had a high mortality rate of 40%.

Limitation

The obvious limitation was the retrospective design and the small sample size, particularly in the omphalocele group. Additionally, the study was conducted at a single center, which may not represent the broader population. We are also limited by missing data may cause miscalculations

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