Clinical Outcome of Patients with Gastroschisis: What Are the Differences from the Past?

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Objective: *The aim of the present study was to review the experience in management of neonates with gastroschisis and analyze the differences in the clinical outcome during a 24-year period.*
Material and Method: *A retrospective study of patients with gastroschisis treated at Queen Sirikit National Institute of Child Health (QSNICH) between 1986 and 2009 was conducted. Patients' information was compared between the first period (1986-1997) and the second period (1998-2009) regarding demographic data, modes of operative procedures and results of the treatment. The statistical differences were analyzed by the Chi-square, Fisher exact and student t-test with a p-value less than 0.05 considered significant.*
Results: *During a 24-year period, 919 neonates with gastroschisis were treated at QSNICH; 342 cases (161 males and 181 females) in the first 12-year period and 577 cases (295 males and 282 females) in the second 12-year period. The incidence of gastroschisis at Rajavithi Hospital was 0.26: 1,000 live births in the first period and 1.03: 1,000 live births in the second period. Average birth weight of the patients and average maternal age in both periods were not significantly different ($p > 0.05$). Congenital anomalies were found in approximately 15% of the patients in each period. Regarding modes of the operative treatment, primary closure of the abdominal wall defect was attempted in 23.7% of the patients during the first period and increased to 44% in the second period. The overall survival rate in the second period was better than the first period with statistical significance (92.4% vs. 75.4%, $p < 0.001$). In addition, complications in the second period were less than those in the first period, except for necrotizing enterocolitis, which was more frequent in the second period.*
Conclusion: *The obvious differences in patients with gastroschisis during the 24-year period were the increased incidence, increased successful primary closure of the abdominal wall defect and increased overall survival rate between 1998-2009. Improvement of the clinical outcomes reflected improved neonatal care including surgical techniques, parenteral nutrition, respiratory care and anesthetic practice.*

Keywords*: Gastroschisis, Abdominal wall defect, Primary closure, Staged closure*

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Gastroschisis is a birth defect characterized by incomplete closure of the abdominal wall without a membranous sac coverage. The defect is located to the right side of the umbilicus in almost all of the cases. This disease has increased in prevalence globally over the past two decades with variation by geographic region[1-5]. Since the first successful surgical repair by Watkins[6] in 1943, a dramatic improvement of the survival rate of gastroschisis has been reported in recent years[7-9]. At Queen Sirikit National Institute of Child Health (QSNICH), the incidence of patients with gastroschisis is seemed increasing with improvement of the survival rate. In 1998, the authors' experience during 1986-1997 was reported[10]. More recent (1998-2009) is here in presented for comparison.

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Material and Method

After obtaining approval from the institutional review board, a retrospective review was performed of all patients with gastroschisis treated between January 1986 and December 2009 at Queen Sirikit National

Institute of Child Health. Information evaluation included demographic data, technique of abdominal closure, time interval to the full feeding, duration of total parenteral nutrition (TPN), length of hospital stay (LOS) and results of the treatment. The present study was divided into 2 periods; the first period between 1986 and 1997[10] and the second period between 1998 and 2009. Data of the 2 periods were compared in order to observe the differences. All data were analyzed by using the Microsoft SPSS package version 16 and EpiInfo package version 3.4. Categorical variables were expressed as frequency number and percentage. Comparison between the two periods was carried out using the Chi-square, Fisher exact and student t-test with a p-value less than 0.05 considered statistically significant.

Results

Between 1986 and 2009, 919 neonates with gastroschisis were transferred to Queen Sirikit National Institute of Child Health. During the first period (1986-1997), 342 neonates (161 males and 181 females) were treated at QSNICH, whereas 577 neonates (295 males and 282 females) were treated in the second period (1988-2009). Yearly number of the patients transferred to QSNICH is shown in Fig. 1. Fifty-eight patients in the first period and 103 patients in the second period had been born in Rajavithi Hospital. As the total number of neonates born in Rajavithi Hospital during 1986-1997 and 1998-2009 were 218,816 and 99,658, respectively. Therefore, the incidence of gastroschisis in Rajavithi Hospital was significantly increased from 0.26: 1,000 live births in the first period to 1.03: 1,000 live births in the second period (Table 1). Demographic data including prematurity, birth weight, modes of delivery and birth order of the mother were not significantly different between those in both periods. Percentage of a younger mother group (less than 15 years old) in the second period was higher than that of the first period with statistical significance (5% vs. 1.5%, $p < 0.015$), but the average maternal age was not different between the two periods. Gastroschisis could be antenatally diagnosed in about 25% in the first period and 46% in the second period. Approximately 10% of the patients in both periods had endotracheal intubation before referral to QSNICH.

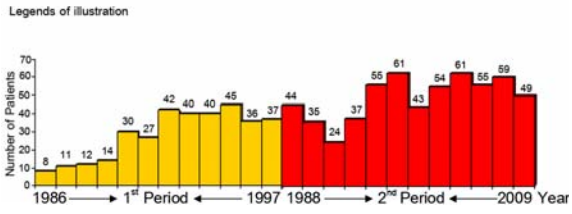

Fig. 1 Yearly number of patients admitted with gastroschisis at Queen Sirikit National Institute of Child Health

Associated congenital anomalies in both periods were not different (Table 2). Some patients had more than one anomaly. Gastrointestinal (GI) anomalies were more common than other congenital defects. Intestinal atresias were indentified in about 10% of the patients in the both periods. Jejunoileal atresia and intestinal malrotation were the most common GI anomalies. Patients with gastroschisis and intestinal atresias had a high mortality rate, 75% and 45% in the first and second periods, respectively. Other congenital anomalies included cardiovascular, genitorurinary, neurological and limb abnormalities.

Definitive management was not different in the operative procedures during the 24-year period. Patients with gastroschisis were treated by primary closure of the abdominal wall defect when possible. When a primary closure seemed not possible due to visceroabdominal disproportion, a two-staged closure was undertaken. A silo pouch or artificial sac used at QSNICH was described by Havanonda[11,12]. It is made of a stockinette pouch which is lined both inside and outside with Steri-Drape® (Fig. 2,3). Primary closure of abdominal wall defect was undertaken more frequently in the second period (Table 3). Comparison of primary closure between the first and second period was statistically different (23.7% vs. 44%, $p < 0.001$). Patients required respiratory support after primary closure were approximately 11% of cases in the first period and 16.5% in the second period ($p < 0.05$). Time interval to full feeding, TPN administration and length of hospital stay (LOS) in both periods were not significantly different. However, the overall survival rate in the second period was higher than that in the first period (92.4% vs. 75.4%, $p < 0.001$). Fig. 4 suggests an improving survival trend of the presented patients during the 24-year period.

Most complications, except for necrotizing enterocolitis (NEC), were decreased in the second period (Table 4). Common pathogens in the first period which obtained from wound, respiratory tract secretion and blood cultures were Pseudomonas aeruginosa, Klebsiella pneumoniae, methicillin resistant Staphylococcus aureus (MRSA) and enterococci, whereas Acenetobactor baumanii, Klebsiella pneumaniae and MRSA were the serious pathogens in the second period. NEC was more often diagnosed in

the second period than that in the first period (9.2% vs. 2.6%, p < 0.001). Common causes of death were similar in both periods including sepsis, severe pneumonia, NEC and intestinal necrosis or perforation (Table 5). Patients with very low birth weight (less than 1,500 g), presence of intestinal atresia and markedly visceroabdominal disproportion proned to mortality. Some cases had more than one related factor which initiated to death.

Discussion

Many reports in the literature demonstrated a significant increase of gastroschisis prevalence in the last 2 decades[1-5]. The present study revealed the prevalence of this anomaly at Rajavithi Hospital increased from 0.26 (between 1986 and 1997) to 1.03: 1,000 live births (between 1998 and 2009). This fivefold increase in prevalence of gastroschisis might be higher than the real overall prevalence in Thailand because an increasing number of mothers with antenatally diagnosed gastroschisis babies were transferred to deliver at Rajavithi Hospital which is a well known tertiary institute for obstetrics. Many investigators proposed the hypotheses of risk factors to induce gastroschisis including young maternal age[13-15], tobacco use[13,16], alcohol consumption[17-19], drug addiction (cocaine, marijuana)[16], medicine administration (aspirin, ibuprofen, pseudo-

Table 1. Demographic data of patients with gastroschisis (n = 919)

Patient information	First period	Second period	p-value
Incidence			
Total numbers	342	577	
Male: Female	161: 181	295: 282	0.263
Prevalence at Rajavithi Hospital (live births)	0.26: 1,000	1.03: 1,000	< 0.001
Antenatal diagnosisby ultrasonography	85 (24.9%)	235 (40.7%)	< 0.001
Birth weight (grams)			
Less than 1,500	5 (1.5%)	13 (2.3%)	
1,500-2,000	76 (22.2%)	158 (27.4%)	
2,000-2,500	150 (43.9%)	246 (42.6%)	
2,500-3,000	84 (24.5%)	128 (22.2%)	
over 3,000	27 (7.9%)	32 (5.5%)	
Average (range)	2,240.8 ± 461.9 (1,000-3,600)	2,236.4 ± 462.3 (900-3,600)	0.888
Gestational age (weeks)	(n = 325)	(n = 550)	
Less than 33	34 (10.5%)	59 (10.7%)	
33-36	143 (44%)	251 (45.6%)	
36-40	148 (45.5%)	240 (43.6%)	
Average (range)	36.6 ± 8.6 (27-40)	36.7 ± 15.2 (24.40)	0.951
Maternal age (years)	(n = 324)	(n = 560)	
Less than 15	5 (1.5%)	28 (5%)	
15-20	155 (47.8%)	281 (50.2%)	
20-25	117 (36.1%)	164 (29.3%)	
25-30	35 (10.8%)	66 (11.8%)	
Over 30	12 (3.7%)	21 (3.7%)	
Average (range)	20.7 ± 5.9 (15-35)	20.6 ± 4.6 (13.5-34)	0.809
Modes of delivery			
Normal labor	267 (78%)	427 (74%)	0.191
Cesarean section	75 (22%)	150 (26%)	0.191
Birth order of mother			
First	224 (65.5%)	398 (68.9%)	0.309
Second and over	118 (34.5%)	179 (31.1%)	0.309
Respiratory support			
Endotracheal intubatation before referral	24 (7%)	57 (9.9%)	0.174

Table 2. Associated congenital anomalies in patients with gastroschisis

Associated anomalies	First period (62 in 342)	Second period (87 in 577)	p-value
Gastrointestinal	38 (11.1%)	55 (9.5%)	0.513
Intestinal atresia	12	20	
Malrotation	15	25	
Other	11	8	
Cardiovascular	8 (2.3%)	17 (2.9%)	0.736
PDA	6	10	
ASD	1	5	
VSD	1	1	
Other	0	1	
Genitourinary	15 (4.4%)	17 (2.9%)	0.334
Undescended testis	15	11	
Other	0	6	
Neurological	3 (0.9%)	4 (0.7%)	0.715
Limb	3 (0.9%)	5 (0.9%)	1.000
Trisomy 21	2 (0.6%)	0	0.138

Fig. 2 Creation of a silo pouch by using Steri-Drape® covering both surfaces of a stockinette tube

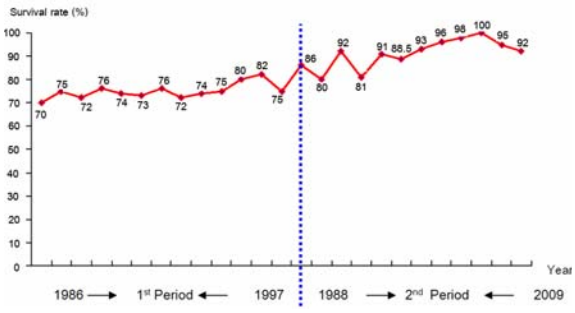

Fig. 4 Yearly survival rate from 1986 to 2009

Fig. 3 Suturing of a silo pouch to the abdominal wall defect with a continuous 2-0 monofilament non-absorbable suture

ephidrine)[16,20-22]. The present study showed that 18 of the total 919 mothers (2%) were under 15 years old at deliveries and overall 50% of the mothers were under 20 years old (Table 1). Some mothers had a history of cigarette smoking, alcohol and drug addictions and insecticide use during pregnancies.

Over 50% of the patients were born prematurely with average birth weight less than 2,500 grams. Gabriel[23] and Brun[24] have suggested that gestational age does not appear to be a predictor of increased morbidity or mortality. However, sepsis appears to be increased in patients with very low birth weight, independent of gestational age. This may be an indicator of poorer immune function in smaller

Table 3. Operative procedures and results of the treatment

Operative procedures / results	First period (n = 342)	Second period (n = 577)	p-value
Primary closure	81 (23.7%)	254 (44%)	< 0.001
Time interval to full feeding (days)	14.2 ± 4.4 (9-38)	15.2 ± 4.6 (10-40)	0.124
Time interval on TPN (days)	14.6 ± 4.9 (5-49)	15.8 ± 8.2 (6-50)	0.269
Length of hospital stay (days)	19.6 ± 5.6 (11-175)	20.5 ± 11.6 (12-162)	0.521
Survival	60 (74.1%)	242 (95.2%)	< 0.001
Staged closure	261 (76.3%)	323 (56%)	
Time interval to full feeding (days)	22.5 ± 8.4 (13-91)	23.3 ± 7.2 (19-94)	0.237
Time interval on TPN (days)	23.5 ± 11.8 (16-105)	24.4 ± 11.2 (16-101)	0.423
Length of hospital stay (days)	30.1 ± 15.1 (17-299)	31.3 ± 22.2 (18-290)	0.497
Survival	198 (76.9%)	291 (90.1%)	< 0.001
Overall			
Survival	258 (75.4%)	533 (92.4%)	< 0.001

Table 4. Comparison of complications between the first and second period

Complications	First period (n = 342)	Second period (n = 577)	p-value
Sepsis	86 (25.1%)	87 (15.1%)	< 0.001
Wound infection	31 (9.1%)	42 (7.3%)	0.400
Wound dehiscence	6 (1.8%)	5 (0.8%)	0.346
Pneumonia	61 (17.8%)	37 (6.4%)	< 0.001
Respiratory failure	49 (14.3%)	44 (7.6%)	< 0.001
Prolonged paralytic ileus	52 (15.1%)	26 (4.5%)	< 0.001
Hyperbilirubinemia	34 (9.9%)	45 (7.8%)	0.318
Necrotizing enterocolitis	9 (2.6%)	53 (9.2%)	< 0.001
Intestinal necrosis/perforation	10 (2.9%)	18 (3.1%)	0.974
Enterocutaneous fistula	9 (2.6%)	5 (0.9%)	0.066

Table 5. Related factors to mortality in gastroschisis

Related factors to mortality	First period Death/Total No. (MR)*	Second period Death/Total No. (MR)*	p-value
Sepsis	49/86 (57%)	34/87 (39%)	0.022
Pneumonia	25/61 (41%)	11/37 (29.7%)	0.263
Necrotizing enterocolitis	4/9 (44.4%)	14/52 (26.4%)	0.429
Intestinal necrosis/perforation	7/10 (70%)	9/18 (50%)	0.434
Very low birth weight (less than 1,500 g)	4/5 (80%)	6/13 (46.2%)	0.314
Intestinal atresia	9/12 (75%)	8/20 (40%)	0.055
Markedly visceroabdominal disporportion	4/6 (66.7%)	7/14 (50%)	0.651

* mortality rate

neonates. These patients require an increased or prolonged need for parenteral nutrition which results in an increased risk of intravenous line infections.

Intestinal atresia in association with gastroschisis, with an incidence of 5.5% to 25%, has been considered a poor prognostic factor[25-27]. This was similar to the present study in both periods. Intestinal atresia with intestinal necrosis and perforation was associated with a need for significantly more surgical procedures, a delayed establishment of oral feeding and a longer length of hosital stay. These increased risks of sepsis and morbidity.

Results of the treatment between the first and second period were significantly different. From 1986 to 1997, only one-fourth of the patients were treated by primary closure of abdominal wall defects. In the second period (1998-2009), most surgeons tried to primarily close the abdomen as much as possible and primary closure was accomplished in 44% of all the cases. Those attempts of primary closure in the second period reflected a higher rate of ventilatory support after operation than that of the first period. However, the survival rate in the second period was significantly increased because of improvement in respiratory and other neonatal care. Additionally, primary closure give more benefit than staged closure in reduction of time interval to full feeding, TPN usage and LOS (Table 3).

NEC has been reported ranging from 4 to 18% of patients after gastroschisis repair[7,28,29]. From the authors experience, NEC occurred in 2.6% after gastroschisis repair in the first period and increased to 9.2% in the second period. It is possible that surgeons increasingly realized to diagnose suspected NEC in many cases with poor feeding and prolonged paralytic ileus. Incidences of NEC after gastroschisis repair from 2 referral hospitals in Thailand revealed 1.8-2%[30,31] which were lower than the incidence 9.2% of the present study. According to the study of Snyder[7], presence of NEC after gastroschisis repair associated with a 5.6-fold increase in mortality and a 5.8-fold increase in sepsis risk. Management of NEC in patients with gastroschisis is precisely the same as that of isolated NEC including bowel rest in 10-14 days, parenteral nutrition, broad-spectrum antibiotic coverage, careful clinical and radiographic monitoring with observation of standard indications for laparotomy. Major serious complications in the second period were decreased when compared to those in the first period, except for NEC. It is difficult to determine what specific factors were responsible for improvement of the clinical outcomes both the overall survival rate and serious complications. However, improved care at the referring hospital, better respiratory and nutritional support, global improvements in neonatal care and improved anesthetic and surgical experience may all have played a role.

Conclusion

During a 24-year period, many changes were found in the present study. The obvious differences included increased incidence of gastroschisis, increased primary closure of abdominal wall defects and improvement of the overall survival rate in 1998 to 2009. Globalized development of neonatal care, especially surgical techniques, parentenal nutritional support, respiratory care and anesthetic practice are the principle factors for improvement of gastroschisis survival. Proper management before transportation and well-co-operated referral system may markedly decease both morbidities and mortalities in some cases.

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Potential conflicts of interest

None.

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ผลลัพธ์ทางคลินิกของผู้ป่วยที่เป็นโรค gastroschisis: มีอะไรบ้างที่แตกต่างจากในอดีต?

รังสรรค์ นิรามิษ, อารดา สุทธิวงศ์สิงห์, วีระ บูรณะกิจเจริญ, ทองขาว รัตนสุวรรณ, อัจฉริยา ทองสิน, วราภรณ์ มหธราดล, ไมตรี อนันต์โกศล, สุขวัฒน์ วัฒนาธิษฐาน

วัตถุประสงค์: *เพื่อศึกษาประสบการณ์การรักษาทารกแรกเกิดโรค gastroschisis และวิเคราะห์ความแตกต่างของผลลัพธ์ทางคลินิก ระหว่างระยะเวลา 24 ปี*

วัสดุและวิธีการ: *เป็นการศึกษาย้อนหลังผู้ป่วยที่เป็นโรค gastroschisis ที่เข้ารับการรักษาในสถาบันสุขภาพเด็กแห่งชาติมหาราชินีระหว่างปี พ.ศ. 2529 และ 2552 ข้อมูลของผู้ป่วยนำไปเปรียบเทียบกันระหว่างระยะแรกที่เคยรายงานแล้ว (2529-2540) กับระยะที่สอง (2541-2552) ในเรื่องเกี่ยวกับข้อมูลพื้นฐานของผู้ป่วย วิธีการรักษา และผลของการรักษา วิเคราะห์ความแตกต่างที่มีนัยสำคัญทางสถิติ โดยใช้ Chi-square, Fisher exact และ student t-test ที่ p-value น้อยกว่า 0.05*

ผลการศึกษา: *ในระยะเวลา 24 ปี มีทารกที่เป็นโรค gastroschisis เข้ามารักษาในสถาบันสุขภาพเด็กแห่งชาติมหาราชินี จำนวน 919 ราย ประกอบด้วย 342 ราย (ชาย 161 ราย หญิง 181 ราย) ในระยะแรก และ 577 ราย (ชาย 295 ราย หญิง 282 ราย) ในระยะที่ 2 อุบัติการณ์ของโรค gastroschisis ที่โรงพยาบาลราชวิถีพบ 0.26: 1,000 ทารกเกิดมีชีพในระยะที่ 1 และ 1.03: 1,000 ทารกเกิดมีชีพในระยะที่ 2 ค่าเฉลี่ยของน้ำหนักแรกเกิด อายุของมารดาไม่มีความแตกต่างกันอย่างมีนัยสำคัญ ทั้งสองช่วงเวลาที่ศึกษา ($p > 0.05$) ความพิการแต่กำเนิดพบได้ประมาณร้อยละ 15 ของผู้ป่วยทั้งหมดในแต่ละช่วงเวลาเกี่ยวกับวิธีการรักษาโดยการผ่าตัด ได้พยายามเย็บปิดผนังหน้าท้องในระยะแรกเพียงครั้งเดียว คิดเป็นร้อยละ 23.7 ของผู้ป่วยในระยะที่หนึ่ง และเพิ่มขึ้นเป็นร้อยละ 44 ในระยะที่สอง อัตราการรอดชีวิตของผู้ป่วยในระยะที่สองดีกว่าในระยะแรก อย่างมีนัยสำคัญทางสถิติ (ร้อยละ 92.4: 75.4, $p < 0.001$) รวมทั้งภาวะแทรกซ้อนในระยะที่สองน้อยกว่าในระยะที่หนึ่ง ยกเว้นลำไส้อักเสบชนิดรุนแรง*

สรุป *: ความแตกต่างที่ปรากฏชัดเจนในผู้ป่วยโรค gastroschisis ระหว่างระยะเวลา 24 ปี คือ อุบัติการณ์ที่เพิ่มขึ้น ความสำเร็จในการเย็บปิดหน้าท้องชนิด primary closure มากขึ้น และอัตราการรอดชีวิตเพิ่มขึ้นในระหว่างปี พ.ศ. 2541 และ 2552 ผลลัพธ์ทางคลินิกที่ดีขึ้นสะท้อนให้เห็นถึงการดูแลรักษาทารกที่ทันสมัยยิ่งขึ้น ประกอบด้วย เทคนิคการผ่าตัด การให้สารอาหารทางหลอดเลือด การดูแลระบบหายใจและทักษะการให้ยาระงับความรู้สึก*