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Review Article

Innovative Approaches to the Surgical Challenges in the Management of Gastroschisis: A Narrative Review of the Literature

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Abstract

Based on our experimental and clinical research, the gastroschisis is formed by raised intraluminal and intraabdominal pressure in combination with potential weak points. The psycho-neuro-endocrine-target organ axis of young mothers, who themselves struggle to meet their macro and micronutrient requirements, places a burden on the placenta. The associated smoking, alcohol, drugs, and other toxins, leads to fetal distress. This activates the same fetal axis, with the final common pathway being activated via the sacral parasympathetic nervous system as a flight or fight response leading to colorectal secreto-motility disorder of the hindgut and small left colon leading to partial functional obstruction of hindgut. This leads to pressure build-up on the proximal colon. An intact ileocecal valve leads to blind loop obstruction, creating the force required to herniate the bowel through the defect at three key points of weakness in the abdominal wall, the most vulnerable being the right paraumbilical region. If the ileocecal valve becomes incompetent, variants of gastroschisis may occur. The fetus, particularly the peritoneum, always has a tendency to heal defects quickly, which forms secondary events in the eviscerated bowel causing the closing and closed gastroschisis with vanishing organs. Recent technological advances in preformed silastic silo innovation, prenatal diagnosis and monitoring for closing gastroschisis, perinatal management, percutaneous central long lines, and innovative minimally invasive bedside procedures, have all made significant contributions. We believe that gastroschisis is the external surgical symptom and peak of the iceberg, secondary to an underlying colorectal motility disorder, providing the force to eviscerate bowel loops through potential weak points and its subsequent sequelae.

Introduction

Gastroschisis is the most common form of congenital paramedian or lateral anterior abdominal wall defect, characterized by the herniation of viscera, mostly the gastrointestinal tract. The evolution and revolution in the management of gastroschisis, from zero to hero performance, is a spectacular success story in neonatal surgery, similar to Wilms' tumor in pediatric oncology with a uniform fatality to nearly 95% survival in just the last six decades. We aimed to promote health, prevent abdominal wall defects in general, and specifically address gastroschisis. Our objectives were to protect against primary damages in utero and secondary damages perinatally, provide effective decompression of the foregut, midgut, and hindgut during the post-reduction period, and drastically improve the health, happiness, and longevity, as well as the quality of life, of affected babies through a holistic understanding of the condition.

Keywords: Abdominal wall defect; Allied disorders of Hirschsprung's disease; Congenital gastrointestinal secreto-motility disorders; Gastroschisis; Hernia; Infant; Newborn; Nutrition; Variants of Hirschsprung's disease; Ventilation.

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Table 1. Classification of gastroschisis

Anatomical side and site	Variants		Embryo pathological			
Classic right sided	Inferior	Superior	Simple	Complex	Variant	Compound-genetic
Variant left sided: (a) Mirror-image; (b) Linea semilunaris; (c) Upper quadrant	Laparoschisis	Scrotoschisis	Uncomplicated/ small	Giant/Open	Closing	Closed

The term "gastroschisis" (gas-troh-skee-sis), first coined by Taruffi in 1894, is derived from ancient Greek literature, meaning gastro = stomach and schisis = split. This term is somewhat misleading, as it is the anterior abdominal wall, not the stomach, that is split. The first reported case of an anterior abdominal wall defect was in 1547 by Conrad Wolffhart, an Alsatian humanist and theologist, who described it as "a large extrusion of intestines from the abdomen and chest, feet by the head, and a tall, pointed skull".[1] In 1953, Moore and Stokes first described the features differentiating gastroschisis from omphalocele.[2] Although gastroschisis has been diagnosed and described since 1547, virtually all of the cases were fatal until the last six decades.[3] The purpose of this publication was to highlight key points in the embryogenesis acquired through a fetal surgery experimental model and transition them into day-to-day clinical practice, thereby further reducing mortality and morbidity in gastroschisis patients. Currently, gastroschisis has received special attention due to the uncertainty surrounding its embryo pathogenesis in light of our understanding of its developmental biology. This includes detailed classification, the recent increase in the incidence of gastroschisis, improved antenatal diagnosis, identification of "high-risk" fetuses and their subsequent monitoring, improvements in delivery timing and mode, perinatal and postnatal management, minimally invasive operative techniques avoiding general anesthesia, and recent advances in ventilatory support, pulmonary surfactant therapy, and parenteral/enteral nutritional support during the postoperative period, along with a holistic review of long-term outcomes. We developed an experimental model of gastroschisis in fetal rabbits and reported our preliminary findings, as there have been no previous investigations or descriptions of a model that would simulate gastroschisis in human beings.[4] We subsequently reported various lessons learned from direct observations in general and their clinical extrapolation to abdominal wall defects and hernia in particular.[5] The significance of this review is the application of experimental fetal surgery findings with their translational application from bench to bedside clinical practice to reduce associated morbidity and mortality. Additionally, we aimed to reduce further damage by using minimally invasive bedside techniques to avoid general anesthesia and major operations. The remarkable results achieved by applying these strategies at multicenter multinational levels have encouraged us to communicate our improved outcomes due to these new strategies.

Definition

The conventional definition of gastroschisis is a paraumbilical, full-thickness abdominal wall defect associated with the protrusion of the bowel through it, with no sac covering the exposed organs. This is an anatomical descriptive definition.[4] In view of our experimental gastroschisis model and extensive prenatal monitoring, clinical observations, gastrograffin contrast enemas, postoperative complications, colorectal biopsies, and long-term follow-up studies, we have modified this definition. Gastroschisis results from an underlying congenital secreto-motility disorder anomaly of the gastrointestinal tract in general, and specifically of the colorectal and hindgut, associated with a full-thickness abdominal wall defect. This defect is typically paraumbilical, most often to the right of the normally inserted umbilicus, allowing herniation of the bowel without any covering sac.[5] The small accidental defect leads to secondary vascular accidents, exacerbating the issue at the time of defect creation, during fetal movement, healing and closing gastroschisis, delivery, soon after birth due to air exposure, positioning, and environmental exposure, and finally during abdominal compartment syndrome following primary reduction and closure. The eviscerated bowel is exposed prenatally to chemically sterile amniotic fluid and meconium, and suffers from heat loss, fluids loss, and infection post-birth due to the absence of any covering sac membrane.

Classification

There are two common subtypes of gastroschisis: *simple and complex*. The simple subtype is characterized by a thick peel covering matted and shortened bowel and mesentery, secondary to exposure to amniotic fluid/meconium. The complex subtype is associated with complications such as intestinal atresia, stenosis, bowel perforation, necrosis, bowel loss, volvulus, or cryptorchidism, primarily due to the constricting effect of the abdominal wall defect. In addition to these common subtypes, we would like to highlight two rarer subtypes of gastroschisis. The first is *variant gastroschisis*, which includes left (mirror image), semilunaris-Spigelian or left upper quadrant, superior, inferior, laparoschisis, and scrotoschisis. The second is *the compound variety*, which includes genetic or chromosomal and rare syndromic associations such as amniotic band syndrome, Nager syndrome, and Tetra-amelia syndrome.[6,7] Developmentally, gastroschisis can be categorized as open, closing, or closed with the loss of midgut (Table 1).[8–10]

Differential features from omphalocele/exomphalos

Although gastroschisis is situated very close to the umbilicus and is an anatomical neighbor to another abdominal wall defect called omphalocele (or exomphalos), there is very little in common between them.[11,12] The differentiating features between these lesions are illustrated in Table 2. The most frequently associated malformations with gastroschisis are digestive malformations such as intestinal malrotation, small intestinal atresia, and microcolon. Extra-digestive malformations include skeletal malformations such as lower limb and spinal congenital anomalies, including arthrogryposis, multiple contractures, and limb-body wall spectrum.[8–10]

Embryo-pathogenesis

There is very little hereditary component involved, and mainly environmental factors are responsible for its development. Several hypotheses have been proposed regarding the embryo pathophysiology

Table 2. Differential features between gastroschisis and omphalocele/exomphalos

Criteria	Gastroschisis	Exomphalos
Abdominal wall	Abnormal orifice defect	Natural orifice hernia
site	Paramedian/fascial clefts	Central midline
opening	abnormal	Natural/normal
sac	Absent/peel present	Amniotic membrane
Incidence	Most common	Less common
prevalence	Increasing	stable
Cause	Environmental	Genetic
Maternal age	Primipara, young (<20 yrs.)	Older Multipara
Assoc Anomalies	GIT	CVS-50%, CNS-40%, Other anomalies-30%, Chromosomal-15%, BWS, Bladder exstrophy
Prenatal diagnosis	USG-Serial monitoring	Associated anomalies
Fetal transport	Tertiary center	Variable
Timing of delivery	Near term, closing early	Term
Mode of delivery	Vaginal	May need C/S in a giant variety
Postnatal management	Bowel condition & abdomen size	Size and abdomen space
Surgical options	Reduction and repair-primary delayed	Primary, delayed, secondary, conservative,
Overall prognosis	Survival & LTO-excellent except for SBS in complex Gastroschisis	Variable @ Associated anomalies
Mortality	SG-2.18%, CG-16.67%	25%
Intrauterine fetal demise	0.5%	Greater
Elective termination	0.1%	Significantly higher
Preterm delivery	25%	Less common
intrauterine growth restriction	5%	Less a problem
Cesarean section	Only for obstetric indication	Much higher rate
Neonatal survival	90 %	50–75%
Neonatal sepsis	12%	Wound sepsis
Necrotizing Enterocolitis	2%	Less common
Short Bowel Syndrome	1.3%	Very rare
Bowel obstruction	8%	Rare
Volvulus	0.2%	Rare
Average to oral feeding	33 days	Bowel normal
Ventilatory support	26 days	In preterm/ primary closure
Hospital duration	SG 38 days (90%)/CG 89 days (10%)	Variable upon type of option
Mortality overall	10%	25%
Mortality Complex Gastroschisis	17%	High in genetic and syndromic
Overall prognosis	Good	Poorer

BWS, Beckwith Wideman syndrome; C/S, Cesarean section; CG, complex gastroschisis; CNS, central nervous system; CVS, cardiovascular system; GIT, gastrointestinal tract; LTO, long term outcome; SBS, short bowel syndrome; SG, simple gastroschisis; USG, ultrasonography.

of gastroschisis, but none has successfully explained and satisfied all features. It is generally postulated and widely believed that abdominal wall weakness or defect leads to herniation. Experimental evidence has suggested that the creation of a partial-thickness or full-thickness abdominal defect alone does not result in herniation or clinical gastroschisis. Instead, the defect, in association with raised intraabdominal pressure in general, and intraluminal pressure in the gastrointestinal tract in particular, may provide the necessary force for the bowel to protrude through the defect.

Therefore, we began investigating the factors or underlying hid-

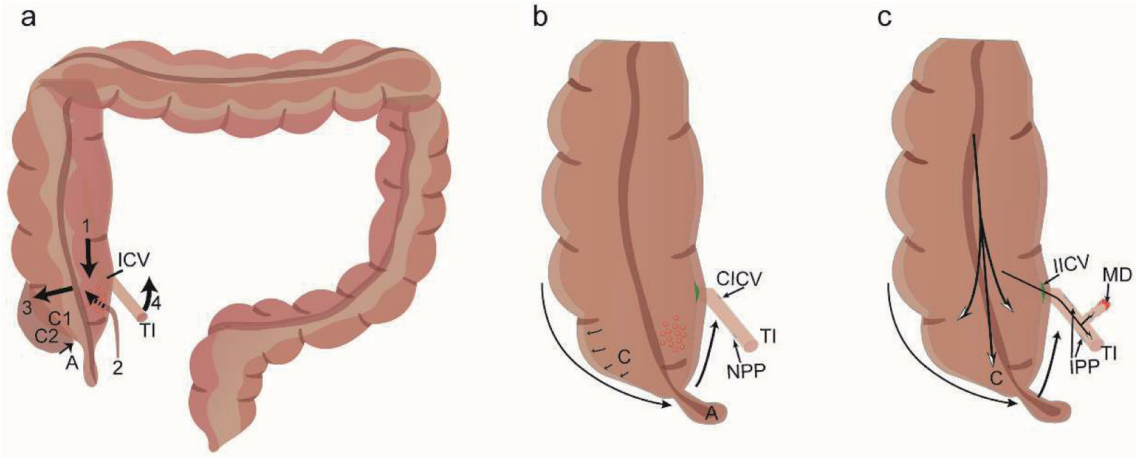

Fig. 1. Colonic anatomy and pathophysiology of left colonic partial functional obstruction. a). The appendix is vertical at birth and ileocecal valve (ICV) enters the cecum with submucous antireflux tunnel. b). With a competent ileocecal valve-the back pressure (arrow 1) distends appendix (arrow 2), distends cecum with lateral wall being able to distend laterally allowing it to move from C1 to C2 position (arrow 3) causes appendix to rotate at 180 degrees medially towards anterior taenia coli (red arrow), the ileocecal valve is pushed up reducing the submucosal tunnel and reducing the ileocecal angle (arrow 4). This explains the lateral overgrowth of cecum and varying positions of appendix in the 180 degrees arc and fetal and early childhood appendicitis. c). Eventually, the ileocecal valve becomes incompetent, payer's patches get inflamed and back pressure on the patent vitellointestinal duct (PVID) remnants like Meckel's Diverticulum to persist as pop off mechanism. This explains the basis of formation of PVID and its remnants, terminal ileal reflux which can lead to the enlargement of Payer's patches causing necrotizing enterocolitis in preterm babies, making lead point of intussusception in infants and backwash ileitis leading to nonspecific mesenteric adenitis, tuberculosis in underdeveloped and developing countries while Chron's disease in developed world in children, adolescents and young adults. A, Appendix; C, cecum; C1, original cecal position; C2, after the force on the lateral wall; CICV, competent ileocecal valve; ICV, ileocecal valve; IICV, incompetent ileocecal valve; IPP, inflamed Payer's patches; MD, Meckel's diverticulum; NPP, normal Payer's patches; TI, terminal ileum.

den lesions or disorders that can lead to raised intraabdominal pressure and intraluminal force. Our deep interest in prenatal diagnosis led us to monitor all cases antenatally, perinatally, and postnatally.[3,13,14] Gastroschisis involves dual elements of abdominal wall weakness and defect associated with herniation of the gastrointestinal tract and is mostly associated with gastrointestinal anomalies, both manifest and latent, in most cases. We reviewed all available literature on gastroschisis, hernia, and gastrointestinal anomalies, visited social media platforms, patient associations, and support groups, correlated experimental, simulator-based, clinical, investigative, and long-term follow-up evidence, and clinically began exploring all opportunities to apply minimal invasive, laparoscopic, or robotic evidence. The earliest prenatal diagnosis of gastroschisis reported was at 12 weeks, by which time the gastrointestinal tract and abdominal wall had already formed and completed.[15,16] Therefore, the causative hidden disorder had been silently working before becoming evident.

Initially, we focused on intraluminal pressure in the bowel in general and associated allied or variant Hirschsprung's disorders in particular, since some cases of gastroschisis and inguinal hernias have resolved spontaneously and the defects closed. This suggests that the disorders are reversible in some cases under favorable conditions and circumstances.[17,18] Prematurity is now associated with gastroschisis, and the small left colon syndrome is an integral part of prematurity. Therefore, we started examining possible areas of increased intraluminal force, and the first structure we noticed was the ileocecal valve, which creates a closed-loop obstruction of the transverse and right colon (Fig. 1a). If the intraluminal pressure is low and the ileocecal valve remains intact and competent, it will distend the cecum and appendix and slide in the anterior abdominal direction from lateral to medial (Fig. 1b). It becomes engaged in the paramedian space between the falciform and round ligaments superiorly and inferiorly and medially between the umbilical fibrous ring with all its structures, including the urachus and lateral umbilical ligaments, and the bladder as an abdominal organ. Once the pressure becomes sufficient and persistent, overcoming only the barriers of peritoneum and skin, gastroschisis finally forms. Conversely, if the intraluminal pressure is high and persistent, the ileocecal valve will initially experience intermittent reflux, followed by continuous reflux, which can alleviate some intraluminal pressure but prevent closure of the remnants of the vitellointestinal duct, leading to Meckel's diverticulum, an associated anomaly with gastroschisis (Fig. 1c). This mechanism resembles the pop-off mechanisms observed in intravesical pressure due to distal obstruction such as posterior urethral valves, resulting in a patent urachus and its remnants.[19–21]

We next looked at the various aspects of the anterior abdominal wall in search of potential spots of weakness where raised intraluminal and intra-abdominal pressure can create defects. We believe that an abdominal wall defect is a cleft deformity and may be preventable if the micronutrient deficiency causing it is identified and corrected.[22] The study of the abdominal wall from the interior view in the midline suggested that the supraumbilical and medial parts are occupied by the liver, round ligament, falciform ligament, and linea alba; the central part by the umbilical fibrous ring; and the infra umbilical part by the linea alba, urachus, and bladder, supported on both sides by the lateral umbilical ligaments (Fig. 2a). In the lateral view, it is apparent that once the vitellointestinal duct has been detached and the urachus closed, the umbilical central opening is filled with vascular structures and firmly closed, with no space available. The supra and infra umbilical portions are covered by strong fibrous structures, buttressed by the liver and urinary bladder respectively (Fig. 2b). In the transverse section of the abdominal wall, three potential points of weakness were identified. The first and most important is the paraumbilical area between the falciform ligament and the right lateral umbilical ligament, having only peritoneal and skin layers as barriers, and medially a fibrous umbilical ring providing a strong background for herniation. The

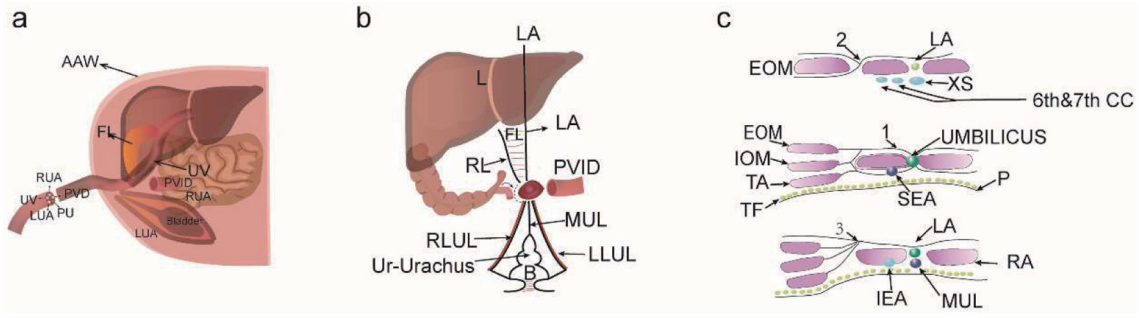

Fig. 2. Fetal, neonatal and child anterior abdominal midline anatomy and pathophysiology. a). Fetal anterior abdominal wall in the midline seen from the left side in sagittal section showing liver, linea alba, umbilical vein and falciform ligament in the supraumbilical part. Umbilical site having PVID with the cord containing two umbilical arteries, one vein, and part of the patent urachus (PU). The infraumbilical part is occupied by patent urachus above, bladder at the bottom centrally and both umbilical arteries surrounding them. This arrangement make right paraumbilical area is the weakest point between strong umbilical ring and the flexible rectus abdominis muscle as demonstrated in B and C below. b). In the term neonate arteries, vein, PVID and PU are replaced with ligaments and mobile ileocecal region with blind loop obstruction and competent ICV, pushes it through the weakest point centrally in right paramedian area as demonstrated. In the preterm neonates with small left colon syndrome of prematurity, it causes umbilical and inguinal hernias right side being in line twice common than the left side. c). Cross sections of anterior abdominal wall at xiphisterna, umbilical and suprapubic areas. Note the right paramedian area is the weakest point between the strong scarred umbilical ring medially and mobile sliding rectus abdominis muscle laterally followed by left hypochondrial area without the support of liver and finally area lateral to the rectus muscles on both sides as Spigelian hernia sites are the potential weak points in that order. The left hypochondrial and Spigelian hernia sites becomes variants of anterior abdominal wall defects seen clinically. AAW, anterior abdominal wall; B, bladder; CC, costal cartilage; EOM, external oblique muscle; FL, falciform ligament; IEA, inferior epigastric artery; IOM, internal oblique muscle; LA, linea alba; L, liver; LLUL, left lateral umbilical ligament; LUA, left umbilical artery; MUL, median umbilical ligament; P, peritoneum; PU, patent urachus; PVD, patent vitellointestinal duct; PVID, patent vitellointestinal duct; RA, rectus abdominis; RL, round ligament; RLUL, right lateral umbilical ligament; RUA, right umbilical artery; SEA, superior epigastric artery; TA, transverse abdominis; TF, transversalis facia; UL, Umbilical ring; UV, umbilical vein; XS, xiphoid process.

second weak point is the spaces between the costochondral junctions and the muscle attachments, as the strong diaphragm supports the liver and spleen, with the distended stomach in between. Finally, the neurovascular gaps in the linea semilunaris have the smallest openings of all but have only skin and peritoneum as barriers, especially vulnerable if the opening is reasonably larger or if there is increased underlying force (Fig. 2c).

Finally, we examined the effects of hindgut problems on the midgut, manifesting as gut rotation abnormalities such as nonrotation, malrotation leading to midgut volvulus, and affecting the foregut with partial gastric outlet obstruction and secondary gastroesophageal reflux. The normal rotation occurs when there is no hindgut anomaly (Fig. 3a). Partial functional obstruction of the hindgut leads to incomplete rotation by lifting up the right colon (Fig. 3b). Severe hindgut problems lead to complete malrotation, moving the duodenojejunal flexure downward and creating a "C" shape in the duodenum, while the cecum and appendix attempt to take serosal attachments with the gall bladder and lesser omentum; formation of Ladd's bands leads to partial gastric outlet obstruction and predisposes the midgut to volvulus formation (Fig. 3c). Hindgut problems in preterm babies are commonly referred to as meconium plug syndrome or short left colon syndrome. There is

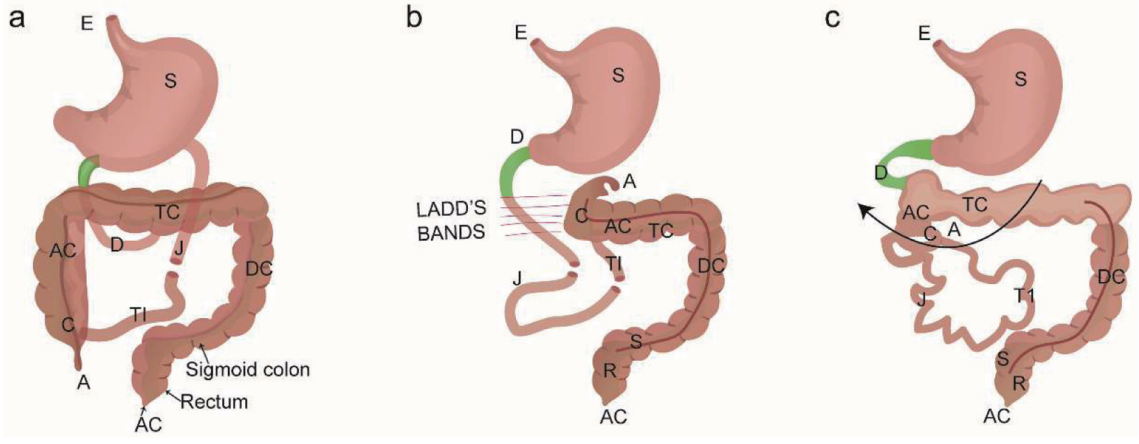

Fig. 3. Midgut normal rotation, malrotation and with volvulus. a). Midgut normal rotation. Note the foregut is coloured green, midgut as yellow and hind gut is having red color. b). Midgut malrotation with all of the small bowel on the right side, ileocecal region in the epigastrium with Ladd's bands across the duodenum to gall bladder and most of the large bowel on the left side of the abdomen reducing the small bowel mesentery very narrow based. c). Midgut malrotation with volvulus leading to strangulation and catastrophic loss of midgut if not being managed urgently. A, appendix; AC, ascending colon; C, cecum; DC, descending colon; D, duodenum; E, esophagus; J, jejunum; LADD'S BANDS, adhesion bands between cecum and gall bladder across the duodenum; R, rectum; S, sigmoid colon; TC, transverse colon; TI, terminal ileum.

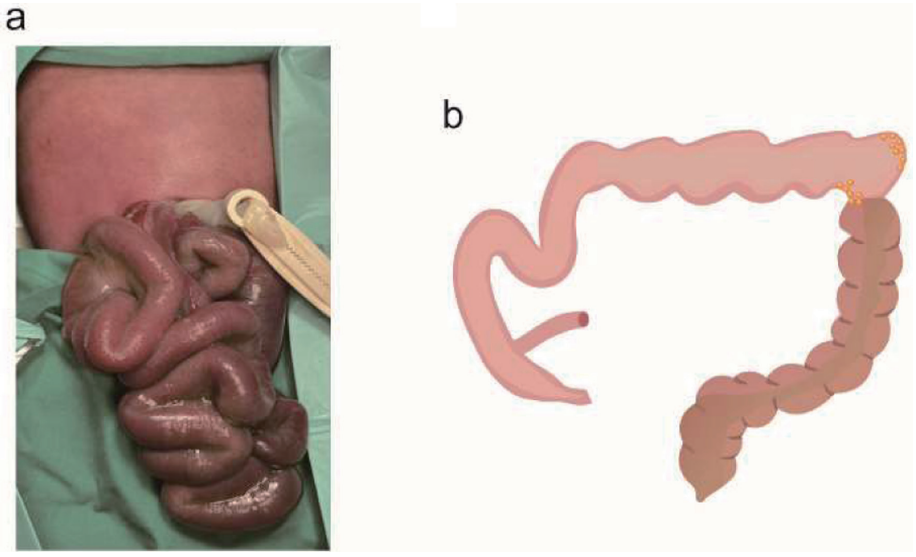

Fig. 4. Appearance of gastroschisis at birth and water-soluble contrast enema in small left colon syndrome or fetal distress with functional partial hind gut obstruction. a). Note the peel over the prenatal bowel protrusion while the fresh bowel near the defect has been pushed during birth canal by compression and just after birth due to fetal stress, coughing, crying and straining. b). Water soluble contrast enema showing ill formed flexures, a prominent transition zone at splenic flexure area at the junction of mid and hind gut, redundant transverse and right colon with free reflux into the appendix and ileocecal valve.

typically a small transition between the midgut and hindgut even in full-term babies, but in preterm babies, premature ganglion cells or other congenital motility disorders cause the maximum problems with the right colon, cecum-appendix, and right paramedian defects in most cases. Few cases have a predominant obstruction at the left hypochondrial transition between the midgut and hindgut, leading to left hypochondrial defects. Some cases have their transition lower in the rectosigmoid region, in which case they present with neurovascular bundle defects in the linea semilunaris as Spigelian-type herniation on the left side lateral to the rectus abdominis muscle, typically occurring only on the left side.

The clinical correlation was done with prenatal diagnosis using transvaginal ultrasound as early as possible, sequentially monitoring the lesion (Fig. 4a). At birth, observation showed the ileocecal pole at its peak with full distention resembling an apex of a mountain (Fig. 4b), and postnatal Gastrograffin enema displayed the aftermath of Hirschsprung's disorder causing partial left colon obstruction and its resultant backpressure effects (Fig. 4c).

Epidemiology

The epidemiological risk factors include young mothers <20 years (four times more common), maternal smoking, alcohol, drugs, and substance abuse, maternal stress and undernourishment, medications including both drug abuse and over-the-counter medications, high-risk pregnancies such as prematurity and small for gestational age, and increasing incidence.[23,24] Additionally, genitourinary infections in early pregnancy, environmental exposure to solvents and colorants, and genetic factors play their role in the risk factors for gastroschisis.[25,26] The most important element is that most associated anomalies and malformations are related to the gastrointestinal tract itself, so we need to examine this system in detail to find some answers. Many young mothers belong to lower socioeconomic backgrounds with gross macronutrient and micronutrient deficiencies in the developing world, while macronutrient excess and micronutrient deficiency in the Western world contribute to malnutrition and obesity as additional risk factors. Disparities in surgical health service delivery and outcomes are also observed in the Western world, ultimately contributing to many congenital defects related to the environment, including gastroschisis.[27]

Young teenage mothers from lower socioeconomic backgrounds often struggle with disturbances in the psycho-neuro-endocrine-gastrointestinal system axis during major adolescent growth spurts. This can lead them to take medications like antidepressants and easily fall into alcohol, smoking, and substance abuse.[28] These factors and circumstances ultimately lead to placental insufficiency, affecting fetal homeostasis and causing fetal distress, which then affects the final common path of the fight-or-flight response along the psycho-neuro-endocrine-gastrointestinal tract axis of the fetus. Unfortunately, the "flight" response is limited, as the fetus must retain meconium at all costs to avoid affecting the amniotic fluid and leading to pulmonary aspiration with meconium. As a life-saving measure, the fetus has no choice but to retain the meconium and responds by escalating the sacral parasympathetic response, leading to left colon spasms, while nicotine increases the drive forward, creating additional pressure buildup that provides extra force, resulting in abdominal wall clefts at the weakest points. Iron and calcium stores in the fetus are only deposited during the last months of pregnancy, and severely growth-restricted babies struggle with postnatal anemia, particularly as total prenatal nutrition does not provide adequate iron supplementation.[29] Similar, but more intense, problems have been observed in developing countries.[30]

We first reported the possible primary cause of intussusception as congenital colorectal motility disorders associated with ileocecal reflux and micronutrient deficiencies, along with backwash ileitis and hypertrophy of Peyer's patches and small intestinal bacterial overgrowth in 1997.[31] Since then, we have launched a special campaign for parent and public education, mobilizing professionals, government support, and involvement of spiritual and religious institutions to improve nutrition, end child marriages, increase the legal marriage age to 21, and extend health benefits to pregnant mothers. These initiatives were initially implemented

locally and subsequently applied regionally and nationally. Now, with both the Prime Minister and the President of India being spiritual scholars at the God Fatherly Spiritual University in Mount Abu, Rajasthan, India, this campaign has been taken to the global stage at the United Nations Organization. Lower dietary intake of vitamin D may also be associated with an increased risk of certain congenital anomalies, including gastroschisis.[32]

Antenatal diagnosis, monitoring and management

We have a dedicated team for prenatal diagnosis, with regular multidisciplinary clinical meetings and treatment planning sessions tailored to each individual patient's diagnosis. Their progress is reviewed periodically. The most important element is monitoring the closure of gastroschisis to avoid the morbidity and mortality associated with bowel loss, especially midgut loss. There has been an increased reported incidence in the past 10 years, mainly due to the widespread use of prenatal ultrasound. Early detection of these malformations and associated anomalies allows for multidisciplinary counseling and planning for delivery in a center equipped with high-risk pregnancy assistance, pediatric surgery, and neonatology.[33]

Place, timing, and mode of delivery

Although improved antenatal screening and diagnosis have significantly improved the prenatal detection of gastroschisis, these improvements have not translated into improved neonatal prognosis for babies born with the condition. Babies with gastroschisis may benefit from delivery in a tertiary care center equipped with resources such as high-risk obstetrics, neonatology, neonatal intensive care units, and neonatal surgeons—opting for a trial of labor rather than scheduled cesarean birth for most patients. Congenital anomalies account for about 20% of all neonatal deaths globally. There is no indication of preterm delivery or cesarean section as the primary mode of delivery in the majority of cases. Spontaneous labor or induction of labor around 37–38 weeks of gestation with vaginal delivery is the preferred timing and mode of delivery in most cases to avoid prematurity and related respiratory distress from the section.[34] Early delivery (cesarean or vaginal) may be recommended if parameters suggest an intestinal compromise. However, in Oman and Saudi Arabia, we receive babies with giant midgut closing gastroschisis from Yemen that were not diagnosed prenatally, requiring better healthcare even without positioning precautions, resuscitation with fluids, antibiotics, or oxygen administration with a gangrenous appearance upon arrival (Fig. 5a). After initial resuscitation, correcting the position, and straightening the mesentery in a warm environment with fluids and antibiotics leads to improvement (Fig. 5b). Further change in color is noted after administering 100% oxygen (Fig. 5c). We prefer reducing gastroschisis as much as possible without tension and forming a preformed silastic silo with continuous monitoring and a possible second look in 24–48 h if necessary to save as much bowel in such critical scenarios. This case suggests that targeted quality improvement initiatives could be implemented to reduce adverse surgical outcomes in infants. Near-term elective delivery (at 36–37/40 weeks) appears to be the optimal timing for pregnancies complicated by gastroschisis, associated with less bowel morbidity and shorter total parenteral nutrition days.[35]

Perinatal management

A well-prepared delivery room equipped with all necessary tools and staff including obstetricians, anesthetists, neonatal specialists, and surgical teams should be available during actual delivery. The prognosis of a fetus with gastroschisis can be significantly improved through optimal planning of delivery location and timing. A multidisciplinary team should be present to optimize conditions for the fetus immediately upon birth.[36] In the development and course of gastroschisis, the eviscerated bowel and abdominal wall between the umbilical ring and the medial aspect of the rectus muscle suffer a temporary ischemic injury initially, followed by narrow defect pinching on the mesentery, causing secondary ischemic events, especially when the fetus is in awkward positions. Due to pain and discomfort, the fetus moves, and the intestines float freely in an aseptic chemical environment. When the fetus moves into a prone position, blood flow is maximized, reducing or eliminating ischemic insult. During birth, pressure in the birth canal of a teenage primiparous mother compresses cord structures and the eviscerated bowel, further causing ischemic injury. Once the fetus is delivered, air swallowing and subsequent distention of the stomach push lots of air into the gastrointestinal tract, pushing out more bowel, stomach, and other organs, increasing intraabdominal pressure, and reducing ventilatory capacity. The exposed bowel loses heat and fluid and becomes susceptible to sepsis as there is no protective sac. The prone position during resuscitation creates a right angle at the abdominal-gastroschisis angle, and transporting the baby from the delivery room to other areas may induce further stress. Therefore, we prefer our young, enthusiastic junior doctors to assist the obstetric and anesthesia teams in the delivery room and take charge of the baby immediately upon birth. Our experience with gastrointestinal secreto-motility disorders through various experiments has concluded that air in the gastrointestinal tract is detrimental to the antimesenteric blood supply of the bowel, affecting movements, secretions, or absorption, as the blood supply is circumferential from the mesenteric side to the antimesenteric side. For this reason, we treat patients promptly to prevent gas from filling the stomach and bowel, which is difficult to decompress effectively even with nasogastric tubes, especially for gas that has moved beyond the stomach. Rectal saline washouts10 ml/kg twice a day at the end of the bowel are only partially effective, as most disorders occur at higher levels in the rectosigmoid and left transverse colon regions.

Surgical management

The goal of surgical management for gastroschisis is to achieve complete reduction and closure, whether primary or staged, without causing further ischemic injury due to excessive intra-abdominal pressure or abdominal wall tension. There is a spectrum of management options in gastroschisis, ranging from bedside primary reduction and sutureless closure in small gastroschisis[37] to gentle staged bedside reduction and closure using a preformed silastic silo.[38] Recently, however, there has been a significant trend towards gentle staged closure, which has gained widespread acceptance. It is recognized that much of the mortality and morbidity in gastroschisis is related to complications associated with increased intra-abdominal pressure and decreased visceral perfusion.[39] Careful selection of closure strategy for individual patients ensures optimal outcomes.[40] Our preference is for immediate personal attention at the time of delivery, with preliminary assessment and preservation of blood supply to the gastroschisis bowel, ensuring no kinking or banding of the mesenteric vessels to maintain vascularity of the eviscerated bowel during resuscitation and stabi-

Fig. 5. Giant closing midgut gastroschisis. a). Upon arrival without resuscitation and stabilization and vascular compromise as the protruded bowel at right angle to the defect kinking blood vessels and reducing the vascular supply. b). During initial resuscitation and stabilization—note the preservation of vascular supply by holding the protruded contents perpendicular to the abdominal wall defect thus, allowing full blood supply. c). Administration of 100% oxygen improves the color and viability of the gut by higher oxygen delivery to tissues.

lization. Procedures include nasogastric decompression at the upper end, a warm saline enema of 10 mL per kilogram body weight for rectal washout, rectal paracetamol suppository for analgesia, central venous access, followed by gentle reduction and primary closure using the umbilical cord to cover the defect as a one-stage procedure in small gastroschisis with minimal evisceration and no peel. Moderate to large-sized gastroschisis can be managed in the NICU procedure room using a preformed silastic silo with a spring-loaded base. This involves daily or alternate-day gradual reduction of the contents and sutureless closure of the defect at the final session without anesthesia. In cases of small defects, local anesthesia infiltration to extend the defect laterally or vertically aids in reducing the rare dumbbell variety of gastroschisis, which narrows in the middle and expands at both ends to achieve closure. The basis of all atresia, stenosis, and segmental dilatation spectrum involves vascular accidents, some of which can be prevented.[41] We avoid general anesthesia in the majority of cases, as we believe it adversely affects the rapidly developing central and autonomous nervous systems, potentially contributing to colorectal and allied Hirschsprung's disorders.

Post-operative management

The greatest relief provided by delayed silastic preformed silo is freedom from physiological abdominal pressure monitoring via invasive methods such as bladder catheter, intragastric and arterial pressure measurements, and central venous pressure. Apart from very premature babies on ventilation, blood gas monitoring is rarely required. Similar to how surfactant aids pulmonary function, we believe that warm saline, glycerin suppositories, or Gastrograffin enemas act as local surfactants for the hindgut, resolving secretory and excretory abnormalities. As the abdomen stretches over the first several days after closure, compliance usually improves, leading to reduced inspiratory pressures and decreased oxygen requirements. We prefer to initiate oral feeds as early as possible, starting with an oral rehydration solution or balanced solution in the initial phase, which is well tolerated, followed by diluted feeds and then full feeds to promote gastrocolic reflux. Simultaneously, rectal stimulation with warm normal saline three times a day aids by hydrodistending the ano-recto-colic junction, facilitating relaxation and reflux to decompress gas if not meconium. Early-onset infection in gastroschisis is rare. Excessive antibiotic exposure in neonates increases the risk of necrotizing enterocolitis and mortality.[42,43] A multi-institutional review demonstrated that sutureless abdominal wall closure in neonates with gastroschisis was associated with reduced use of general anesthesia, antibiotics, surgical site/deep space infections, and decreased ventilator time.[44] Prematurity and birth weight are significant predictors of length of stay in patients with uncomplicated gastroschisis.[45]

Post-operative complications

Causes of perioperative mortality related to the closure of the abdominal wall defect itself include the development of necrotizing enterocolitis, sepsis from silo-related abdominal wall infections, and the acute effects of increased intra-abdominal pressure on visceral perfusion, venous return, and pulmonary function. Abdominal compartment syndrome used to be a significant complication but has become almost nonexistent since we switched to using bedside preformed silos and avoiding general anesthesia, except for preterm babies requiring ventilation who may experience problems such as oxygen toxicity and barotrauma-related complications. Total parenteral nutrition-related liver disease and cholestasis complications may be reduced by cyclical administration of TPN, addition of taurine, avoidance of sepsis, and reduction of copper and manganese. Early initiation of partial enteral feedings is perhaps the most critical factor in avoiding this serious complication.[46] The combination of gastroschisis and Hirschsprung's disease has been reported and may be mistaken for routine dysmotility.[47]

Immediate outcome and prognosis

Current mortality rates reported for gastroschisis are 5–10%. For prognosis, gastroschisis can be divided into low and high-risk groups. Among gastroschisis cases, 20–30% of patients with intestinal atresia, stenosis, or perforation constitute a higher-risk group with a mortality rate of approximately 30%. Patients without these complicating features have nearly 100% survival. Recently, a study comparing and evaluating the utility of three different risk stratification scores for gastroschisis neonates—simple/complex gastroschisis, gastroschisis prognostic score, and risk stratification index—has been conducted. These are three easily obtainable risk stratification scores for predicting outcomes in gastroschisis patients; however, their predictive ability did not show a statistical difference in this study. The Gastroschisis risk stratification index appeared to perform moderately well in predicting mortality.[48] Another study has examined predictive risk factors for protracted intestinal failure.[49]

Medium- and long-term management

Gastrointestinal mucosal and muscular dysfunction, prolonged TPN dependence, and the concomitant development of cholestatic liver disease characterize a subset of patients with a much poorer prognosis. The coexistence of multiple intestinal atresia and short bowel syndrome with gastroschisis is not uncommon, occurring in 5–25% of cases. Recurrent operations for adhesive obstruction, anastomotic dysfunction, and persistent bowel dysmotility and dilatation are common in these patients. The development of necrotizing enterocolitis (NEC) and subsequent stricture formation, as well as catheter-related sepsis, can occur. Delayed onset of enteral feeds and development of TPN-related liver disease can precipitate NEC. The incidence of NEC may be lower in patients with gastroschisis fed with maternal breast milk than in those fed with commercial formulas. Gastroesophageal reflux, adhesive bowel obstruction, volvulus, and abdominal wall hernias are observed but decrease with age. Pulmonary complications in preterm babies and concerns regarding growth and development in preterm and intrauterine growth-restricted babies are also notable but typically improve over time. Mothers who had complex gastroschisis requiring massive intestine resection experienced severe vitamin B12 deficiency and macrocytic anemia.[46] Ultra-short bowel syndrome secondary to gastroschisis may necessitate interventions such as intestinal plication, bowel lengthening procedures, intestinal transplant, bridging liver transplant, or combined liver and intestinal transplant in the long term, especially for babies with complex gastroschisis who underwent extensive bowel loss or resection due to ischemia-related complications.[50] Long-term evaluation in pediatrics must necessarily address growth and development, both of which pose real challenges in operated gastroschisis patients.[51]

Conclusions

Our research represents a radical departure from traditional "wisdom" that has hindered progress in understanding the true nature of these conditions. Our innovative research offer breakthrough for all concerned. Gastroschisis patients, once considered "hopeless cases" beyond surgical help, have been a specialty of ours for years, and we have taken on these patients' challenges when others would not. These challenges have provided us with opportunities to uncover hidden mysteries. Many of the issues related to gastroschisis and its complications may be alleviated if the underlying embryo-pathology is clearly understood and if the causative factors responsible for these disorders are addressed simultaneously. Our studies may pave the way for understanding the embryopathogenesis clearly and ultimately allowing promotion of health of the mothers and preventing it. Those who escape promotion of health and prevention can have early prenatal diagnosis and monitoring for closing lesions. The key element of management for the rest is timing and place of delivery, perinatal presence and supervision by neonatal surgical team and prompt bedside preformed silo reduction, percutaneous longline insertion and effective decompression of gut. Our ongoing prospective cohort multicenter study applying the same protocol and new studies elsewhere will bring new knowledge to alleviate these challenges

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Conflict of interest

The authors declare that they have no conflict of interests.

Author contributions

Writing the first draft of the manuscript (RP). All authors contributed to the study's conception and design, prepared materials, collected data, performed analysis, and commented on or edited previous versions of the manuscript. All authors read and approved the final manuscript.

Ethical statement

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was performed in accordance with the ethical standards of Postgraduate Institute of Child Health & Research and KT Children Govt University Teaching Hospital. Informed consent was obtained from all individual participants included in the study.

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