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Abdominal Wall Defects and Hernias-Lessons Learnt from Observations from the Experimental Fetal Surgery Gastroschisis Model in Rabbits and their Clinical Extrapolation

Review Article

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Abstract

Purpose: We developed an experimental model of gastroschisis in fetal rabbits and reported our preliminary report of the techniques and results as there has been no reports of investigation or a description of a model that would simulate the gastroschisis in human beings [1]. In this article we wish to report various lessons learnt from direct observations in general and their clinical extrapolation in abdominal wall defects and hernia in particular.

Introduction: The aims and objectives were to see feasibility of a gastroschisis model in fetal rabbits, to see whether our local practice is in line with international standard in creating a successful model in the fetal rabbits, to evaluate hypothesis whether abdominal wall weakness or defect leads to herniation of bowel and gastroschisis, to assess the outcomes of various groups of fetuses, and extrapolate the observations in translational research to various clinical settings.

Methods: The experiment was carried out on a total of 25 New Zealand white does during their 15th through 29th day of gestation. The rabbits have bicornuate uterus and each contains on an average three fetal rabbits making a total of six which were randomly colour coded except group 1 controls so that at birth they can be attributed to appropriate groups.

Group 0: Control with no operative procedure.

Group 1: Maternal hysterotomy, aspiration of amniotic fluid, amniotomy and marking of the fetus only.

Group 2: Maternal hysterotomy and injection of 2 ml of amniotic fluid intraperitoneally to non-operated fetus.

Group 3: Maternal hysterotomy and 4 mm partial thickness abdominal wall defect.

Group 4: Maternal hysterotomy and 4 mm full thickness abdominal wall defect.

Group 5: Maternal hysterotomy and 4 mm full thickness abdominal wall defect with evisceration of small intestine.

All the operative procedures were video recorded and photographs of key steps were taken. Observations were made at birth and following results were noted.

Results: In all fetuses of control group 1 and group 2, no change was noted. To our surprise, group 3 and group 4 fetuses have healed their abdominal wounds partial and full thickness defects without any scar and our hypothesis that abdominal wall weakness due to partial abdominal wall defect and a full thickness defect were responsible for herniation of bowel and gastroschisis proved incorrect while group 5 showed typical features of clinical and histological changes of gastroschisis and in one case classic changes of closing gastroschisis were observed with attempts at closing the defect and stenosis of the bowel loop signifying that the mechanical effects of the defect and chemical effects of amniotic fluid exposure can bring about the typical changes of gastroschisis and experimental model is feasible in fetal rabbits. This led us to extrapolate the observations to clinical setting later on.

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Conclusions: It is feasible to create an experimental gastroschisis in fetal rabbits and typical changes of clinical gastroschisis is seen in the group in which full thickness abdominal wall defect with evisceration of bowel loops only and the hypothesis that an abdominal wall weakness or defect leads to herniation proved incorrect. Important observations of this fetal gastroschisis model observations to clinical settings are very impressive and interesting and may be able to unfold the mystery of associated other gastrointestinal anomalies and associated manifest and latent intestinal dysmotility and dysfunction leading to long term morbidity and mortality.

Keywords: Abdominal wall defect/hernia, experimental gastroschisis, fetal surgery, intrauterine surgical research.

Introduction

Although gastroschisis has been diagnosed and described since ancient times, virtually all of the cases were fatal until the last century. Gastroschisis is a congenital secreto-motility disorder anomaly of gastrointestinal tract associated with full thickness abdominal wall defect which is paraumbilical most often on the right of normally-inserted umbilicus, allowing herniation of bowel without any sac. There are two common subtypes simple and complex gastroschisis. The simple subtype is covered by thick peel, matted and shortened bowel and mesentery secondary to exposure to amniotic fluid and the complex variety is associated with intestinal atresia, stenosis, bowel perforation, necrosis, bowel loss or volvulus mainly due to constricting effect of the abdominal wall defect. There are two rare subtypes of gastroschisis namely variant gastroschisis such as left mirror image, superior, inferior, laparoschisis, scrotoschisis and the compound variety which is closed gastroschisis with short gut and rare syndromic /chromosomal anomalies. It is generally postulated and widely held belief that abdominal wall weakness or defect leads to herniation Intrauterine manipulations and experimental models may be used to simulate some of the congenital abnormalities resulting from embryonic maldevelopment and some of these abnormalities of abdominal wall herniation such as gastroschisis. In fetuses with gastroschisis, toxic products in the amniotic fluid and constriction at the defect of the abdominal wall are considered causative of damage to the eviscerated bowel [2]. Gastroschisis has been selected an experimental model as it has dual elements of abdominal wall weakness and defect associated with herniation of gastrointestinal tract and mostly associate with gastrointestinal anomalies, manifest and latent, in most cases. There is no hereditary component involved and mainly it is the environmental factors responsible for its creation. The epidemiological risk factors include young mothers<20 yrs.: 4 times more common, maternal Smoking and substance abuse, maternal state with stress and undernourishment, medications including drug abuse and over the counter medications, high risk pregnancies: prematurity and small for gestational age (SFGA) and increasing incidence. Most important element is that most of the associated anomalies and malformations are related to gastrointestinal tract itself so we need to look at this system in detail to find some of the answers. Experimental evidence has suggested that creation of partial thickness or full thickness abdominal defect alone does not result in clinical gastroschisis but the defect in association of raised intraabdominal pressure in general and that of intraluminal pressure in the gastrointestinal tract in particular.

Subjects and Methods

For the period 1983–1985, Gastroschisis experimental fetal surgery model program was undertaken as part of fetal surgical research program at the Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh with a grant from Indian Council of Medical Research, New Delhi. The program was started by Prof Mrs. Krishna Yadav MS, FRACS, chief investigator in 1983 and the corresponding author has been co-investigator and main fetal surgeon to take the project forward in 1984-1985 during the postdoctoral pediatric surgery fellowship at the PGIMER, Chandigarh.

The experiment was carried out on a total of 25 New Zealand white does during their 15th through 29th day of gestation. The rabbits have bicornuate uterus and each contains on an average three fetal rabbits making a total of six which were randomly colour coded except group 1 controls so that at birth they can be attributed to appropriate groups.

Group 1: Control with no operative procedure (Fig.1A).

Group 1: Maternal hysterotomy, aspiration of amniotic fluid, amniotomy and marking of the fetus only (Fig. 1B).

Group 2: Maternal hysterotomy and injection of 2 ml of amniotic fluid intraperitoneally to non-operated fetus (Fig.2A).

Group 3: Maternal hysterotomy and 4 mm partial thickness abdominal wall defect (Fig. 2B).

Group 4: Maternal hysterotomy and 4 mm full thickness abdominal wall defect (Fig. 2B).

Group 5: Maternal hysterotomy and 4 mm full thickness abdominal wall defect with evisceration of small intestine (Fig.1C).

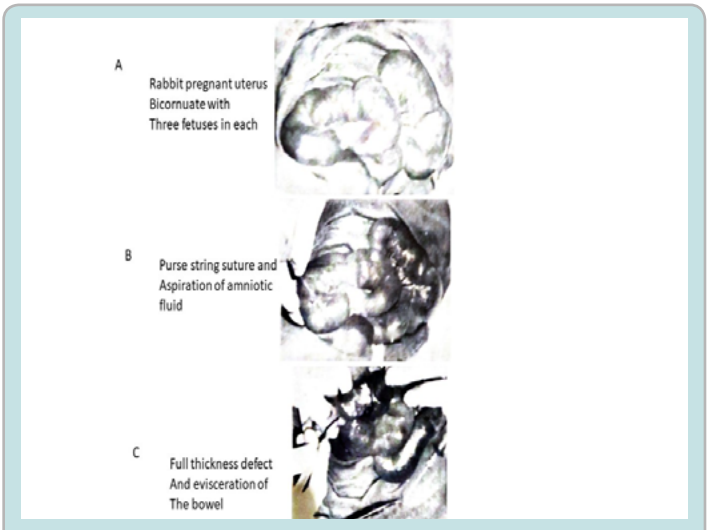

Figure 1: Bicornuate uterus of the pregnant rabbit containing three fetuses in each horn, 1B: Needle aspiration of the amniotic fluid after applying purse string sutures on the uterus, 1C: Creation of fetal gastroschisis by partial exteriorization of the right side of the fetus and full thickness right paraumbilical defect with herniation of the bowel.

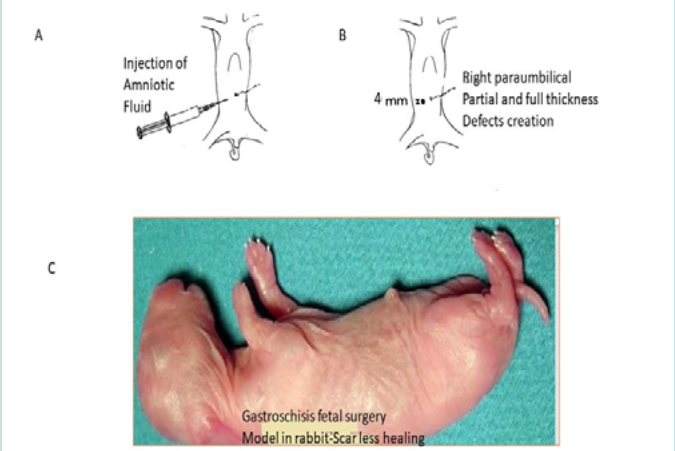

Figure 2: 2A: Group 2: Maternal hysterotomy and injection of 2 ml of amniotic fluid intraperitoneally to non-operated fetus. **2B:** Group 3 & 4 with 4mm right paraumbilical partial and full thickness abdominal wall defects without bowel evisceration, **2C:** Newborn rabbit fetus at birth from groups 1 to 4 showing no scar and perfect healing.

Detailed technique and preliminary results were published earlier [1]. Rabbits are considered as the most suitable and best laboratory animals as they meet all the requirements of moderate size, free and easy availability, relatively low cost, precision of dating pregnancy, relatively short pregnancy, easy handling and modest food and housing requirements In this report we wish to review our observations in detail and its extrapolation to clinical situations by translational research.

Gastroschisis clinical review from prenatal to long term follow up has been done and the findings extrapolated from the fetal and prenatal diagnosis to postnatal management and complications in the light of our observations from the experimental fetal surgery model. The obvious limitation of this experimental study was that we could not administer various risk factors like smoking, alcohol, substance abuse together with psycho-neuro-endocrine-target organ axis of the young mothers and an environment similar to the clinical one with regards to toxic environmental, maternal, placental and fetal effects in creation of the experimental gastroschisis.

Results

Experimental fetal surgery gastroschisis model is feasible in rabbits. The hypothesis that abdominal wall weakness with partial thickness defect and with that of full thickness defect alone does not create herniation of gastroschisis contents and typical clinical changes associated with it and something else is responsible for pushing the bowel loops through the defect.

The fetal abdominal wounds heal perfectly well without leaving any significant scar. Only in the final group where the full thickness defect was created and the bowel loops were exteriorised, typical gastroschisis changes were observed including prematurity, intrauterine growth restriction and low birth weight in this group. We used this finding of perfect healing in clinical situations by providing perfect balanced diet and restriction of all toxic ingredients clinically and building up patients for elective surgery with filters similar to placenta and pregnancy like dietary and drug restrictions clinically and supplementing with micronutrient therapy and in emergency settings adding cocktails of parenteral micronutrient therapy intravenously.

The one off injection of amniotic fluid in the peritoneal cavity created some microscopic changes in the bowel serosa but clinically have no long term impact and the duration of exposure to amniotic fluid and bowel remaining away from the peritoneal cavity protection seems to be important and the lesions diagnosed early in the pregnancy will have worst prognosis and the simple gastroschisis have better prognosis as compared to complex variety as dual forces of effects of amniotic fluid exposure and constriction effects of defect are at work in the complex group. Variant gastroschisis have similar prognosis except the superior variety and the worst prognosis is in the compound group with prenatal closing gastroschisis and rare genetic or syndromic cases with complex associated anomalies.

Discussion

Gastroschisis is the most common form of abdominal wall defect with herniation of bowel, there has been a steady increase in its prevalence over the past several decades. In our experimental model most cases were simple type except one case of closing gastroschisis with intestinal stenosis. Most cases have paraumbilical defect on the right side but few left sided lesions and anecdotal cases of inferior gastroschisis have been reported [3,4,5]. Few cases of rare abdominal and abdominal wall hernias have been reported in infants and children [6,7,8]. The early regression of the right umbilical vein in most right sided lesions and left umbilical vein in left-sided gastroschisis may explain the pathogenesis of producing potential weakness in the abdominal wall [9]. An alternative hypothesis is one that reconciles a disorder of right-left axis orientation as the primary abnormality in morphogenesis [10]. The premature functionally abnormal left colon in combination of the fetal distress due to toxic environmental risk factors associated with formation of gastroschisis can lead to raised intraluminal pressure, in transverse and right colon initially and via ileocecal reflux to the small bowel later, and lead to raised intraabdominal pressures finally pushing bowel out to herniate through the defect.

Gastroschisis is a congenital condition which was successfully created in experimental model by creating the full thickness abdominal wall defect but the typical changes were only seen when the bowel was exteriorised. These findings were in confirmatory with clinical investigative, laparoscopic and operative findings of contralateral patent procesus vaginalis in unilateral inguinal hernia but clinical hernia is seen in only a minority of patients despite the defect exists on the contralateral side in these neonates and infants. The gastroschisis have in over 90% of cases associated anomalies restricted to gastrointestinal tract so we started looking for any associated anomalies which may contribute for the bowel to come out of the abdominal cavity and responsible for bowel dysmotility and dysfunction in long term.

Before we go to the clinical extrapolation of this experimental model to clinical situations, it is important to understand the phenomenon of spontaneous resolution of inguinal hernia in infants and children similar to the closing gastroschisis and role of congenital secreto-motility disorders of hind gut or left colon which has been observed recently and highlighted the association [11]. We read with interest the article entitled, “Spontaneous regression of clinical inguinal hernias in preterm female infants”

by Fleming MA et al [12], which was published in the August 2021 issue of Pediatric Surgery International. The authors proposed that the preterm infant girl with an inguinal hernia should have ultrasonography performed at presentation. If the hernia contains only intestinal loops, an expectant policy may be advisable and surgery may be required for the ovary. A few previous reports have supported their findings in fetus and preterm neonates [13,14]. A traditional approach has been to repair them surgically sooner than later. Recent concerns over general anesthesia in neonates and infants has further led to reconsider such natural cure options recently.

A large sized study by a senior pediatric surgeon [15], was carried out with the sole aim to corroborate or refute the teachings and myths of the pediatric inguinal hernia. In this study, three of the results have not corresponded with previous teachings and myths: (1) a hernia of a premature baby should be fixed sooner than later; (2) routine contralateral groin exploration is not indicated in any situation; and (3) teenage recurrence rate is 4 times greater than the overall series. One percent spontaneous regression of the inguinal hernia was documented including the full term and male babies in this large study. Anecdotal cases of spontaneous regression of pseudohernia in association with bilateral spontaneous descent of testes have been reported [16]. Spontaneous regression of most of the congenital hydrocele and the umbilical hernia is an acceptable and evidence-based fact.

The corresponding author comes from a family of several generations of teacher-trainer of Shusuruta surgery of Indian system of medicine called Ayurveda and had observed spontaneous and personally assisted regression of inguinal hernias, undescended testes and hydroceles in neonates and infants by mechanical, physical, chemical and thermal stimulation of dermatomes in the distribution of L1-L2 and S2-4 for one week leading to spontaneous regression in many cases over two and half decade before entering the allopathic modern medical education. These inguinal lesions spectrum, in Ayurveda, is considered secondary to underlying hindgut dysfunction due to the imbalance between the sympathetic and parasympathetic nervous systems supplying hindgut and primarily addressing to correct it. Hernia is a secondary surgical symptom and cautiously treat on wait and watch basis and surgery reserved only if complications supervene despite correction of underlying hind gut dysfunction first.

During the undergraduate studies, corresponding author has been clerk to three Professors of Surgery at Pediatric Surgery division at MPSMC and IGH, Jamnagar during which this phenomenon of spontaneous regression of inguinal hernia in infants while awaiting surgery was brought to their attention based on manual records held in each unit during that period but this observation received no attention. During general surgical residency training, an audit on the management of acute anal fissure in adolescents and adults by conservative medical treatment, Lord's anal dilatation, lateral internal sphincterotomy and posterior fissurectomy along with internal anal sphincterotomy leaving the wound wide open to heal by secondary intention revealed few cases of unilateral and bilateral inguinal hernias spontaneously regressed or became symptom free in the last group of patients undergoing radical surgical management of this problem but was attributed to the correction of constipation and not received significant attention.

While at PGIMER, Chandigarh on a postdoctoral pediatric surgery fellowship training; fetal surgery gastroschisis model in rabbits clearly showed that partial thickness abdominal wall defects and even the full thickness abdominal wall defects healed completely. Gastroschisis was observed only in the third group where bowel loops were pulled out of the abdomen and no gastroschisis herniation was noted in the first two groups refuting our hypothesis that weakness in the abdominal wall or a defect leads to herniation and we started looking for other reasons [1]. One of the Australian trained Professors at PGIMER routinely performed internal anal sphincterotomy and extended transanal anorectal circular muscle anorectal myomectomy during full thickness rectal biopsy for chronic constipation in infancy similar to Heller's cardiomyotomy for esophageal achalasia. The benefit of increased rate of spontaneous regression of associated inguinal hernia in even full-term infants and even in males was evident as a by-product of this procedure in anecdotal cases [17]. She used to routinely treat chronic idiopathic constipation in toddlers by regular daily enemas for couple of months followed by gradual reduction of enema regime and some of the cases of associated inguinal hernias spontaneously regressed in this group of patients but that was certainly less than the surgical group in infants.

At the University of Maiduguri Teaching Hospital (UMTH), Borno state, Nigeria where the corresponding author operated on a final year medical student with acute anal fissure with posterior fissurectomy, internal anal sphincterotomy in association with extended anorectal circular myectomy for his associated chronic constipation. However, as a by-product of this emergency procedure, his recurrent rectal prolapse, bilateral inguinal bubonocele and symptoms of recurrent appendicitis which he was scheduled for an appendectomy after his final year examinations but was not disclosed at the time of his surgery were all relieved and the long term follow up clearly showed a permanent cure and no further surgery was required for him. Inspired by this index interesting case, an extensive clinical, imaging and radiological, manometric, electro-physiological, pathological and multidisciplinary prospective cohort studies of these cases of their association and /or cause and effect relationship started at UMTH and continued thereafter.

After an extensive research and large prospective cohort series of cases; for the first time in 1997 we reported our observations in a review article on intussusception in which the editorial was given by the late Prof R K Gandhi as Chief Editor [18]. In this article, we clearly indicated that the congenital colorectal motility disorder as the predisposing factor in infants and children for hernia, intussusception, rectal prolapse, recurrent abdominal pain among others and promotive, preventive, curative, supportive, palliative and rehabilitative strategies to address underlying congenital colorectal motility disorder allowed spontaneous regression of inguinal hernia even in full term and male infants more than expected.

This policy of giving information and options to parents with infants with inguinal hernia as a form of their informed decision making process whether to address the underlying problem of hernia first or both the hernia and colorectal motility disorder or apply delayed cautious wait and watch policy for the hernia and correct the congenital colorectal motility disorder has been put into practice at our units at MP Shah Medical College, and Irwin group of university teaching hospitals, Jamnagar, PGICHR

and KT Children Govt University Teaching Hospital, and H J Doshi Trust Hospital, Rajkot, Gujarat state, India; Medical College and God Fatherly Spiritual University teaching Hospital at J. Watumull Global Hospital and Research Centre, Mt Abu, Rajasthan and MGM Institute of Health Sciences and associated university Teaching Hospitals, Mumbai - Pune Hwy, MGM Campus, Kamothe, Panvel, Navi Mumbai, Maharashtra 410209, India.

We found spontaneous regression of inguinal hernia in infants and children more than we anticipated. We, therefore, support these important observations made in this study by Fleming et al and believe that more prospective randomized control studies would enable us to establish and research more on this intriguing topic that would be great interest to patients, parents, the public and medical professionals.

In order to extrapolate these experimental model observations and observed phenomenon of spontaneous regression of inguinal hernias similar to the closed gastroschisis indicating that the defect can get closed if the underlying condition changes and their association with hindgut secreto-motility disorders to clinical situations, the corresponding author decided to undergo vigorous international pediatric surgical international fellowship with foreign training number at Wales Deanery as the incidence of gastroschisis is highest in the Wales and later on taken extended training with national training number in England and spent several years of training in primary, secondary and tertiary care settings [19].

Extensive epidemiological, clinical, investigative, definitive treatment and dealing with various complications and long term follow up of these cases allowed further extrapolation of findings. The epidemiological observations indicated that gastroschisis probably does not have a genetic cause because it occurs sporadically, with a relatively low recurrence rate. The observed increasing incidence of gastroschisis over time seems to be associated consistently with lower maternal age [20]. The psycho-neuro-endocrine-target organ axis was soon apparent with teenage young age mothers associated with periconceptional tobacco smoking and use of recreational drugs such as alcohol, marijuana, and cocaine ultimately leading to final common pathway and target organ injury in the form of early interruption of the fetal omphalo-mesenteric arterial blood supply and primarily affecting the hindgut during distress as diving reflux completing the loop.

Secondary ischemic injuries at birth by compression at the abdominal wall and gastroschiasis axis needs expert assistance at birth by pediatric surgical team to avoid injury due to acute kinks at herniation site in supine position, dehydration, loss of heat and predisposing to infection at the same time. These deliveries takes place at night-time and quite often immediate expert help may not be available at some of the centres. General anesthesia and particularly muscle relaxants were recognised as additional risk factors for worsening associated hind gut left colon dysfunction related delayed recovery. Therefore, a new approach of minimal intervention management with delayed midgut reduction without general anesthesia to help avoid general anesthesia, muscle relaxants, and ventilation with obvious resource benefits was developed [21]. However, this one size fit all approach fell short of its universal application and later on the same authors developed "selection and conversion criteria" to ensure safe application of the technique for few exceptional situations [22]. The effectiveness of routine staged reduction and closure at the bedside, using preformed silos with no general anesthesia aims to avoid general anesthesia, a period of ventilation, and out-of-hours operating, thereby reducing costs and post-operative morbidity and mortality [23].

Gastrograffin lavage peroperatively in gastroschisis offers no potential advantage in reducing ventilatory requirements, parenteral nutrition, and hospital stay. It also does not achieve greater primary closure rates, but may allow diagnosis of abnormal left colon or hindgut and with hydrodistension of the left colon as temporary supportive treatment may reduce the incidence of intestinal obstruction secondary to hydrostatic distention of spastic small hind gut/ left colon functional obstruction, ileocecal reflux and small intestinal bacterial overgrowth, necrotising enterocolitis followed by stricture formation or bowel distention with functional obstruction due to bowel dysmotility and dysfunction with post-operative adhesive obstruction [24].

Post-operative contrast enemas in gastroschisis patients showed abnormal left colon motility with reflux through the ileocecal valve with small intestinal bacterial overgrowth predisposing to enterocolitis and associated Meckel's diverticulum and /or other remnants of patent vitello-intestinal duct as pop off mechanisms similar to distal obstruction in posterior urethral valve and patent urachus in the urinary tract [25,26].

Similarly in patients with associated constipation post-operatively showed mucosal associated lymphoid tissue abnormalities and neuromuscular variants of motility disorders in most cases which can predispose them for associated necrotising enterocolitis, abdominal wall and internal hernia formation and associated non rotation or malrotation by affecting the midgut loop and rotation of the midgut loop. Bowel matting, complex gastroschisis, and secondary intestinal obstruction were associated with short bowel syndrome-related intestinal failure in gastroschisis [27].

Post-natal management of gastroschisis depends on the size of the baby and size of the herniated contents such as bigger babies tolerate better and smaller the herniation is better as most babies are premature as a cause and effect of gastroschisis, condition of herniated viscera due to amniotic fluid insult is better in simple type, while small size of the defect causing complex variety leads to vascular compromise and short gut with atresias and finally the size of the abdominal cavity leading to the abdomino-visceral disproportion requiring techniques of delayed primary closure. As the gastroschisis defect is asymmetrical and predominantly unilateral on the right side, relatively small defect with absent sac meaning that sudden development with no time for the peritoneum to stretch and predominant midgut herniation centred around ileocecal area and associated anomalies being gastrointestinal, it prompted us to look for the reason in the left colon/ hind gut.

We found that prematurity related small left colon was very common with immature ganglion cells and other motility disorders like hypoganglionosis or hyperganglionosis or dysganlionosis of the hind gut and classic Hirschsprung's disease is rare but has been described with gastroschisis [28]. The left colon or hind gut neuromuscular functional abnormalities leads to high pressure on the right colon leading to ileocecal reflux and we have seen patent vitellointestinal ducts and Meckel's diverticulum as pop off mechanism and secondary associated anomalies as a result

[29,30]. The high pressure in the hind gut leads to pressure on the duodenojejunal flexure leading to midgut malrotation and volvulus as secondary effects and pushing the stomach up making gastro-esophageal reflux as tertiary effect. The development of hernias and undescended gonads or herniated gonads looks more of prematurity related events and small left colon of prematurity can build pressure on the right colon and lead to ileocecal reflux leading to raised intra luminal and intraabdominal pressure predisposing them for hernias and therefore right sided lesions are twice as common as the left side ones. A causal relationship between amniotic fluid exposure and peel formation is supported by the finding that peel formation is prevented by amniotic fluid exchange in experimental gastroschisis [31].

The spectrum of intestinal wall morphology extends from complete normalcy to complete atresia and resorption of the midgut. Alterations in gastrointestinal function by mucosal abnormality, motility disorder of neuromuscular tissue and intestinal length is recognized even in infants with minimal or no apparent peel. The intestine itself is characterized by a variable degree of injury even in the cases of no or minimal peel and takes same time to full feeds post-operatively]32]. The amniotic fluid of the gastroschisis babies have shown presence of urine, meconium and most importantly digestive enzymes which suggests the baby has passed these in utero due to fetal distress and due to toxic intrauterine environment and effects of various substance abuse associated in these cases leading to flight or fight response of the hind gut and some of the flight response may allow these to pass in the amniotic fluid and fight response may allow the hindgut to increase parasympathetic response by developing abnormalities observed clinically. Prenatal sonographic findings such as bowel dilation, wall thickness, and “matting “or peel formation, dilated stomach, polyhydramnios, increased amniotic fluid beta-endorphin levels, possibly are the signs of fetal stress, these events have also been found to correlate with increase postnatal morbidity [33]. As the progressive nature of intestinal injury and fetal compromise in gastroschisis becomes better understood, the use of frequent sonography, cardiotocography, and fetal home monitoring has been recommended by some to detect fetal distress sooner and direct the use of preterm delivery [34,35]. As bowel injury in gastroschisis is convincingly linked to prolonged exposure to amniotic fluid components (digestive enzymes, meconium, fetal urine), another potentially useful intervention may be amniotic fluid exchange. Several reports of this technique in gastroschisis combined with severe oligohydramnios confirm its feasibility [31,36].

Conclusion

Gastroschisis experimental model in rabbits is feasible and possible. The observations obtained through this model are very useful in the clinical management of the lesion and its extrapolation to clinical management by way of translational research. The association of left colon dysmotility and secondary intestinal dysfunction seems to be responsible as hidden possible cause of the gastroschisis in the first place and consequent long-term morbidity and mortality. The fetal surgery and prenatal diagnosis and monitoring in gastroschisis has helped managing the lesion with timing, mode and place of delivery, immediate attention of expert neonatal surgical team at birth avoiding secondary injury, bedside spring loaded silastic silo reduction avoiding general anesthesia and allowing gradual reduction of the eviscerated structures and delayed fascial closure with long line placement for total parental nutrition allow time for the injured intestinal tract to become functional. The evidence for clinical extrapolation of these associations is, however, only tentative and needs confirmation by carefully controlled cohort, case-control or double blind randomised prospective studies may lead the way to understanding the pathogenesis of this distressing condition and thus preventing it.

Compliance with ethical standards:

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Contributions:

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by all authors. The first draft of the manuscript was written by RP, and all authors commented on or edited previous versions of the manuscript. All authors read and approved the final manuscript.

Ethics declarations:

Conflict of interest:

Authors declare that they have no conflict of interest.

Ethical approval:

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.

Informed consent:

Informed consent was obtained from all individual participants included in the study.

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