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Outcomes of antenatally detected omphalocele and gastroschisis: a single-centre study over 11 years

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INTRODUCTION

Anterior abdominal wall defects (AAWDs) represent a wide spectrum of congenital anomalies where the infants' stomach, intestines, or other organs protrude through an unusual opening in the abdomen. AAWDs, which are attributed to aberrations in foetal development, have different manifestations. They include gastroschisis, omphalocele, limb-body wall complex, torque deformation sequence, ectopia cordis, bladder, and/or cloacal exstrophy. The prevalence of AAWDs is about 2 to 7 per 10000 live births (LB), while antenatal detection rates vary from 44% to 86%.[1-4]

Chromosomal, cardiac and, other abnormalities are more common in association with omphalocele than gastroschisis.[5,6] Routine ultrasound screening of these foetuses has helped establish a diagnosis in the second trimester so that parents have option to continue or terminate pregnancy.[7] Prenatal diagnosis and counseling have resulted in Mid-trimester Pregnancy Termination (MTPT) rates ranging from about 30% to 63%.[1,2,8] In a large survey, Calzolari et al have reported termination rates of 33.2% in omphalocele and 26.5% in gastroschisis following antenatal diagnosis.[2] In recent years, improved antenatal diagnosis has facilitated the transfer of care to tertiary care centres early. Besides, outcomes have improved with the advances in maternal in-utero and neonatal transport services, operative techniques, and pre/postoperative care with long-term follow-up programmes.

We aim to describe the antenatal characteristics and foetal, neonatal, surgical, and developmental outcomes of foetuses with AAWD in our hospital. The insights will potentially provide useful information to facilitate antenatal counselling and for parents to make informed decisions regarding their pregnancies.

METHODS

Definitions: Omphalocele is a herniation of the bowel, liver, and other organs into the intact umbilical cord and covered by peritoneum, Wharton jelly, and amnion. If the umbilical defect is > 5 cm, it is major, and < 5 cm is minor.[9] Gastroschisis is characterised by an intact umbilical cord and evisceration of the bowel through a defect in the anterior abdominal wall to the umbilicus' right, with no membranous covering.[8] Small for gestational age (SGA) is defined as birth weight less than 10th centile for gender and gestation.[10] Failure to thrive (FTT) was defined as weight for age less than 5th centile in the standard growth chart on multiple occasions during follow-up examination.[11] The classification of necrotising enterocolitis (NEC) is based on published clinical and radiographic definitions by Bell et al.[12] Complications of surgery include liver tear, perforation of the bowel, silo base disruption, shock leading to death, and blood culture positive sepsis. Hernia includes ventral hernia or incisional hernia and inguinal hernia. Rehospitalisation rates were calculated as the mean number of hospital admissions for 3 years after initial admission. Multiple admissions were defined as 2 or more admissions per annum.

For pregnant women on routine follow-up in our institution, a dating scan is performed within the first 14 weeks, a screening scan at 20 weeks, and a growth scan in the third trimester. Mothers carrying a foetus with AAWD will be managed by a fetal medicine (FM) specialist. Detailed scans are performed and offered an amniocentesis for foetal karyotyping and chromosomal microarray analysis. Each case is discussed in detail at the weekly multidisciplinary birth defect clinic with the FM specialist, sonographers, neonatologists, and specialists from related departments. Management plans are formulated in these meetings, which include follow-up ultrasound scans or discussions with the parents regarding the options to either conserve or terminate the pregnancy.

Our hospital is the nation's largest tertiary referral centre for obstetric, neonatal, and paediatric medical and surgical services. We retrieved data of all mothers diagnosed with foetal AAWD's between the years 2006 and 2016 from the Birth Defect Registry.

We harvested data for foetuses diagnosed with AAWDs from electronic medical records (EMR). Data collected included associated malformations in the foetus, chromosomal analysis, and MTPT. For live-born infants information was obtained from case records and EMR in a standardised data collection form. Maternal demographics, data on perinatal and neonatal characteristics, surgical methods, and their outcomes, along with late complications for the two most common anomalies, omphalocele and gastroschisis, were collected and compared for any differences.

We analysed the data using SPSS version 19 statistical software. The student's T-test was used for continuous variables, and Fisher's exact test and chi-square test were used for categorical variables. Statistical significance was declared at $p < 0.05$, with a 95% confidence interval. We obtained Centralised Institutional Review Board approval (CIRB 2017/3085) for this study.

RESULTS

The incidence of AAWDs in our hospital is 2.56/10000LB, omphalocele and gastroschisis being 1.75 and 0.84/10000 LB. Details were unavailable for 38 cases as these were lost to follow up after screening scan as this is a tertiary referral centre for fetal diagnosis and therapy. The outcomes of the remaining 105 cases are as shown in the flow chart (Fig. 1). Of the 34 live-born infants, 23 (67%) had omphalocele; (minor (OMmi) 9, major (OMma) 14) and 11 (33%) had gastroschisis. We compared the outcomes between the two major groups; omphalocele and gastroschisis.

Maternal and neonatal demographic characteristics and perinatal outcomes are shown in Table 1. Maternal age was lower in those who had foetuses with gastroschisis (p = 0.001). Perinatal outcomes like mode of delivery, Apgar score at 5 min, and need for resuscitation at birth were not different between the groups. Among the live births, the number of infants with associated anomalies in omphalocele and gastroschisis were 14/23(60.8%) and 3/11(27%), (p = 0.141) respectively. However, when antenatal cases [MTPT (60), IUFD (10)) and live births (23)] were included, we found associated anomalies in 58/93 (62%) foetuses with omphalocele, and in 3/12 (25%), (p = 0.026) with gastroschisis. There were no significant racial differences in the incidence of AAWDs. Female infants (9/11, 82%) outnumbered males in the gastroschisis group (p = 0.003).

In the live-born infants, karyotyping was done for 82% of cases with omphalocele and gastroschisis. Among the infants with omphalocele, there was 1 case each of Trisomy 18, USP9X gene mutation ChrX;c.1986-IG>T;p (mutation associated with multiple congenital anomalies/intellectual deficit phenotype), whereas in infants with the defect gastroschisis there were no karyotype abnormalities. Both groups had one infant with a normal variant mutation. We analysed the treatment received and surgical outcomes, and the result is shown in Table 2. We had 23 live-born infants with omphalocele, of which two infants did not undergo surgical treatment (1 extreme preterm and 1 trisomy 18). Operative complications, postoperative hernia development, and resource utilization like duration of hospital stay, rehospitalisation rates for three years were similar between the two groups (Table 2). Amongst infants with gastroschisis, necrotizing enterocolitis with Bell stage 2 and above was noted in two infants with gastroschisis but none with omphalocele. One infant who had gastroschisis with malrotation and arthrogryposis multiplex congenita was excluded from the statistical analysis for morbidity. This baby was hospitalised for over two years, never attained full feeds, and eventually succumbed at the hospital.

The survival rate in live-born infants with omphalocele and gastroschisis were 82.6% and 90.9%, respectively (p = 0.649), while overall survival was 85%. Failure to thrive (weight < 5th centile) was noted in 9 (52%) infants in the omphalocele group and one infant from the gastroschisis group. Although at birth 73% of infants with gastroschisis were SGA, on long-term follow up only 1(11%) had FTT, whereas, in the omphalocele group, about half were SGA, and their weight remained < 5th centile in later years (Table 2). A total of six infants were lost to long-term follow-up. Developmental assessment for children was done by Denver Developmental Screening tests. Among the survivors, the mean rehospitalisation rates for infants in the omphalocele group were 3 (± SD 4.4) days, whereas for those in gastroschisis group was 0.7 (± 1.06) days p = 0.167. Four infants in the omphalocele group required multiple hospital admissions (> 2 per annum). Three infants had associated anomalies; 2 with cloacal exstrophy and 1 with Dandy-Walker malformation, and the fourth due to medical reasons. All others required admission to the hospital for procedures like hernia repair or thumb/polydactyly excision. In the omphalocele group, all except three children went to mainstream schools. Special education was required due to autistic spectrum disorder (ASD) in 2 of the cases and to USP9X gene mutation in one. No infant required multiple hospital admissions in the gastroschisis group, and all the survivors attend regular mainstream schools.

DISCUSSION

The incidence of omphalocele over 11 years (2006-2016) in our hospital was 1.75/10,000 LB and 0.84/10000 LB for gastroschisis. Our previous reported incidences of omphalocele and gastroschisis were 2.17/10000 LB and 0.46/10000 LB for 1993-2002.[13] The decrease in the incidence of omphalocele could reflect a higher rate of detection and directed counselling towards the foetus's termination, especially in the presence of associated major malformations and aneuploidy. Epidemiologic studies in the UK by Rankin et al. report prevalence rates at

1.22 and 2.63 per 10000 LB for omphalocele and gastroschisis, respectively.[1] Juin et al reported a rising trend in Australia over 18 years with an increase of omphalocele from 2.6 to 3.6 and gastroschisis from 1.1 to 1.7 per 10,000 LB.[14] Although our gastroschisis rates suggest a rise, it is relatively low compared to other developed nations. The low incidence could be attributed to differences in the prevalence of smoking and drug abuse. Theories related to the origin of gastroschisis include teratogenic insult to vascular disruption theory. Vascular disruption theory was supported by the observations of increased incidence of gastroschisis in young smokers, alcohol and drug abusers, raising the risk by 3.6-fold.[15] Recent reports from Singapore quoted an incidence of drug abuse at a low of 0.7% versus 27% in the USA among pregnant women.[16,17] While genetic and environmental factors have been attributed to the pathogenesis of gastroschisis, omphalocele's origin results from the body cavity's developmental arrest between the 8th and 12th week of gestation and failure of midgut loops of the bowel to return to the abdominal cavity.[18]

Since 1967, fetuses' survival with major AAWDs has improved due to early antenatal diagnosis, the availability of suitable prosthetic material for the closure of the defects, and improved perioperative care standards.[19] Antenatal ultrasound detection of AAWDs can vary from 44 to 86 %.[3,4] A recent report from Tunisie showed detection of 71.4% and 77.8% in the second and third trimesters, respectively.[20] Antenatal confirmation of omphalocele and gastroschisis improved from 46% and 38% in 1993-2002to 87% and 90%, respectively, in this present study. The confirmed diagnosis was made at a mean gestational age of 22 weeks in our cohort, similar to Brantberg et al.[13,21,22]

The MTPT rate of antenatally detected cases in our centre was 37% for isolated omphalocele, compared to 58% across all cases of AAWD. (61/105) Similarly, Fratelli et al reported a 31% termination rate in cases of isolated omphalocele, and Arnaoutoglou et al. found a 63% termination rate in a study of 41 cases of AAWD.[5,8] Omphalocele is often associated

with complex anomalies and aneuploidies, which can contribute to a high percentage of termination of pregnancies when compared to gastroschisis, as was also noted in our series.[15,22] Stoll et al reported major associated malformations in 74.4% of foetuses with omphalocele and 16.6% of foetuses with gastroschisis.[6]

Overall, 32% of mothers diagnosed with AAWD fetuses continued the pregnancy in our centre. In live-born infants with gastroschisis, the mean maternal age was 22.2 years, significantly lower than the mothers in the omphalocele group with a mean age of 31.8. Rankin et al. reported a similar age-specific prevalence of gastroschisis with an increased rate in the 11-24 year-old mothers.[1]

Mode of delivery was by caesarean section in 87% and 73% for omphalocele and gastroschisis cases, respectively, in our centre. This was the preferred method of delivery in known cases of AAWD. A study of 90 cases of AAWD by Brantberg et al. revealed caesarean section rates of 69% for omphalocele and 64% for gastroschisis.[21,22] Earlier studies have shown that there were no differences with regards to the mortality and outcomes for these babies with AAWD based on the mode of delivery.[23,24]

In our study, male sex preponderance was observed in the omphalocele group, whereas females dominated amongst infants with gastroschisis. Most other reported studies showed equal sex distribution.[15,22] Associated anomalies were much higher with omphalocele than gastroschisis when antenatal cases were included, similar to that reported from several centres.[1,4,5]

Mortality in the omphalocele group (17%, 4/23) was primarily due to extreme prematurity (1), cardiac anomaly (1), Trisomy 18 with Tetralogy of Fallot (1), and extensive ischemic bowel possibly due to vascular disruptive sequence with ruptured sac (1). All infants with OMmi in our cohort survived, and mortality occurred only in the OMma subgroup 28.5%

(4/14). Vachharajani et al similarly reported a mortality rate of 33% in OMma and 8% in OMmi.[25]

Primary closure was possible in 62% (20/32) of all cases that underwent surgical repair. Similar results were reported by Rahn et al (67%) in a cohort of 33 cases over 10 years.[26] Fullerton et al., in a large series of 4420 neonates with gastroschisis, reported NEC in 4.5% of infants, but in our cohort, the incidence rate was 18%, and this difference could be attributed to the small size of our cohort.[27] Rehospitalisation rates were higher in the omphalocele group when compared to gastroschisis, but the difference was not significant, probably due to the small numbers in our cohort.

The neurodevelopmental outcome is an important aspect of counselling for the conservation of pregnancies with AAWD. In a meta-analysis, the neurodevelopmental delay was reported in up to 24% of a cohort of 128 patients after surgical treatment for AAWD.[28] In our cohort, among the survivors, the majority (16/29, 89%) achieved normal developmental milestones, while the remaining patients (3/29, 11%) required special education.

In conclusion, the prevalence of AAWDs in our centre is lower when compared to other developed countries. Maternal age was significantly lower in neonates with gastroschisis compared to omphalocele. MTPT rates in isolated omphalocele were high but at par with reports from developed nations. Associated anomalies, notably aneuploidy, was were more than twice higher in omphalocele than gastroschisis. More than 60% of the infants in both groups underwent primary repair. Overall, survival in AAWDs was 85%. Nearly 90% of these infants had normal neurodevelopment outcomes. Multiple readmissions were noted mainly in those with associated major malformations. This study shows a more favourable prognosis for isolated omphalocele and gastroschisis without aneuploidy and other associated anomalies.

Early antenatal ultrasound diagnosis with close follow-up and management in a tertiary centre with neonatal surgical and intensive care facilities can give a favourable prognosis in

isolated omphalocele and gastroschisis. Perinatal physicians can counsel towards conserving pregnancies where foetuses have isolated omphalocele without associated malformations or aneuploidy. It is recommended for survivors to have structured neurodevelopmental follow-up assessments facilitating early enrolment in intervention programmes, if necessary.

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FIGURES

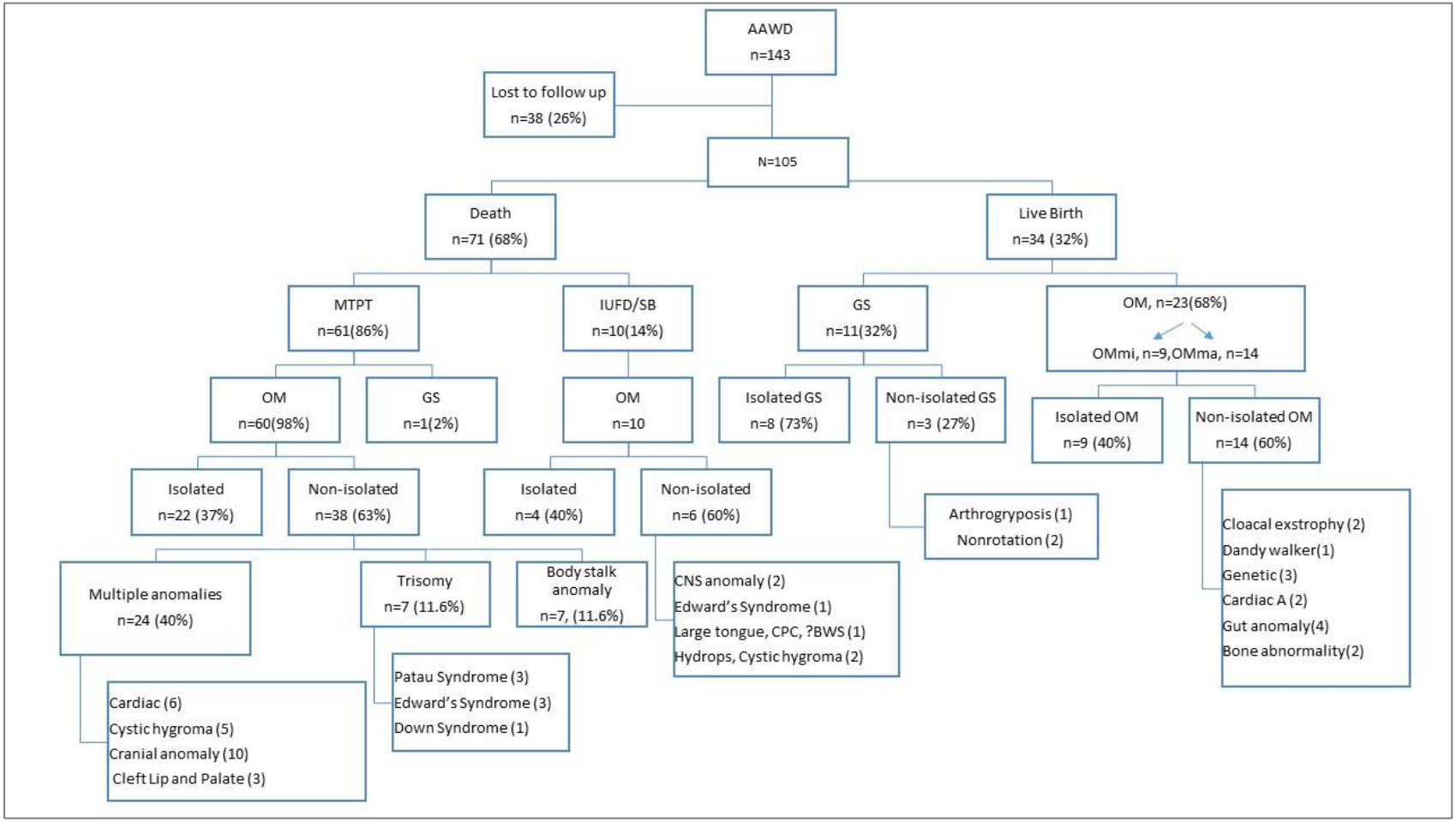

Fig. 1 Flow diagram illustrating the outcome of antenatally diagnosed omphalocele and gastroschisis.
AAWD, anterior abdominal wall defect; IUFD, intrauterine foetal death; MTPT, midtrimester pregnancy termination; OM, omphalocele; OMma, omphalocele major; OMmi, omphalocele minor; SB, stillbirth.

Table 1. Maternal and Neonatal demographic characteristics and perinatal outcomes.

	Omphalocele (n=23)	Gastroschisis(n=11)	p-value*
Maternal Risk Factors			
Age in years, mean (±SD)	31.8 (5.3)	22.2 (3.9)	0.001
Medical issues, n (%)	6 (26)	1 (9.1)	0.369
GA at booking, weeks (±SD)	15.2 (6.3)	14.9 (8.6)	0.922
GA on diagnosis, weeks (±SD)	22.4 (8.3)	22.3 (8.0)	0.966
Perinatal Outcomes			
LSCS delivery, n (%)	20 (87)	8 (73)	0.363
Apgar <5 at 5, n (%)	2 (8.7)	0 (0)	1.000
Resuscitation at birth, n (%)	13 (56.5)	5 (45.4)	0.464
Neonatal Risk Factors			
Male sex, n (%)	17 (74)	2 (18)	0.003
Birth weight, mean gm (±SD)	2447 (758)	2030 (409)	0.099
GA at birth, mean weeks (±SD)	35.7 (3.1)	35.7 (1.9)	0.942
IUGR <10th centile at birth, n (%)	12 (52)	8 (73)	0.295
Race Chinese, n Malay, n Indian, n Others, n	 10 11 1 1	 4 6 0 1	0.414
Associated anomalies, n (%)	14 (60.8)	3 (27.2)	0.141

*Statistical analysis: For categorical variables Fisher's exact test, Chi-square (χ^2) test and for continuous variables Student's T-test.
GA, gestational age; IUGR, intrauterine growth restriction; LSCS, lower segment caesarean section

Table 2. Neonatal and Surgical Outcomes for liveborns with omphalocele and gastroschisis.

	Omphalocele (n=23)	Gastroschisis (n=11)	p-value*
No surgery (ELBW and Trisomy 18), n (%)	2 (9)	0 (0)	0.549
Primary closure, n (%)	12 (52)	8 (73)	0.464
Staged closure, n (%)	9 (39)	3 (27)	0.464
Early surgical complications, n (%)	10 (43)	5 (45)	1.000
Other surgeries, n (%)	5 (22)	1 (9)	0.637
Survival, n (%)	19 (82.6)	10 (90.9)	0.649
Day of 1st feed, mean (±SD)	9.2 (6.1)	11.7 (4.2)	0.261
Age on full feeds in days, mean (±SD)	17.65 (9.2)	23.8 (14.2)	0.161
Duration of hospital stay, days, mean (±SD)	35.4 (29)	38.7 (29.1)	0.766
Gestation at Discharge, weeks (±SD)	40.9 (5.5)	41.3 (3.9)	0.826
NEC - Bell stage 2 or more, n (%)	0(0)	2 (18)	0.09
Lost to follow up, n (%)	4 (17)	2(18)	1.000
FTT (weight < 5th centile), n (%)	9 (39)	1 (11)	0.227
Rehospitalisation rates (3 years) Mean (±SD) Median (Range)	2.5 (4.1) 1 (1,14)	0.7 (1.08) 0 (0,3)	0.164
SPED School, n (%) among survivors (n = 19)	3 (15.7)	0 (0)	0.532
Hernia Repair, n (%)	10 (43)	5 (50)	1.000

*Statistical analysis: For categorical variables Fisher's exact test, Chi-square (χ^2) test and for continuous variables Student's T-test.
NEC, necrotizing enterocolitis: FTT, Failure to thrive: SPED, Special education school: SD=Standard Deviation.