Prenatal Diagnosis of Fetal Ventral Wall Defects: Associated Anomalies and Chromosomal Aberrations

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Original Article

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ABSTRACT

Objective: To describe the prenatal findings, associated anomalies, chromosomal abnormalities of fetuses with ventral wall defects (VWDs).

Methods: Detailed fetal anomaly scan, postnatal assessment, and chromosomal analysis were performed in 200 fetuses with VWDs.

Results: The omphalocele subtype was the most frequently encountered with 121 cases (60%), among them Pentalogy of Cantrell (POC) and OEIS complex (omphalocele, exstrophy of bladder, imperforate anus, spinal defects) were presented in 6 cases and 5 cases, respectively. The second most common variety was gastroschisis in 63 cases (31.5%). Additionally, 12 fetuses were found to have body stalk anomaly, while ectopia cordis and bladder exstrophy each were detected in 2 fetuses. Abnormal karyotype was found in 93 cases (49.4 %); the most frequently was trisomy 18(64.5%) followed by trisomy 13 (22.5%), trisomy 21(5.37%) and 45,X (4.3%). One case of POC had ring chromosome 13 karyotyping, one case with ectopia cordis had 45,X and a case of body stalk anomaly with sacrocooygeal teratoma was associated with monosmy 21. Major structural anomalies were detected in 104 cases (86%) with omphalocele and 22 cases (34.9%) with gastroschisis.

Conclusion: Our study highlights the clinical and genetic heterogeneity of VWD especially the severe forms.

Key Words: Associated anomalies, chromosomal aberrations, prenatal diagnosis, ventral wall defects.

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INTRODUCTION

Fetal ventral wall defects (VWDs) are among the main categories of congenital anomalies constituting a broad and diverse group of defects with distinct phenotypic appearance sharing a common feature, that is, herniation of viscera through an anterior body wall defect[1]. They still represent a source of perinatal mortality and morbidity in spite of the great advances in neonatal surgical care[1,2].

VWDs occur in 2 per 10 000 live births, with omphalocoele and gastroschisis are the most commonly encountered[2]. Less common malformations include ectopia cordis and Pentalogy of Cantrell (POC), OEIS complex (omphalocele, exstrophy of the bladder, imperforate anus and spinal defects) , bladder and cloacal exstrophy, and the body stalk anomalies[2,3].

Omphalocele refers to a midline membrane-covered herniation of intra-abdominal viscera including gut and/or liver into the umbilical cord base, with an incidence ranging from 0.8 to 3.9 cases per 10,000 births[4]. Omphaloceles containing only bowel loops are believed to result from failure of normal regression of the physiologic

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gut herniation. Additionally, it can also be a component of larger defects of more commonly occurring component malformations including POC and OEIS complex[5]. POC is a rare thoraco-abdominal wall closure defect with the estimated prevalence of 1/65.000 to 1/200.000 births characterized by the presence of five major malformations. These include defect in midline supraumbilical abdominal wall, defect in lower sternum, diaphragmatic pericardial defect, anterior diaphragmatic defect accompanied by various intracardiac malformations. Additionally, Ectopia cordis (EC) is usually encountered in fetuses with POC[6].

On the other hand, gastroschisis is characterized by an intact umbilical cord and evisceration of the bowel and or viscera through a usually right paraumbilical defect, with no membranous covering. Gastroschisis incidence has been found to be rising worldwide and varies between 2 and 4 of 10,000 live born[7]. Gastroschisis can be part of body stalk anomaly constituting a rare heterogeneous group of lethal congenital malformations occurring in one in 10,000– 40,000 births[8]. They present with a thoracic and/or abdominal wall defect covered by amnion, an absent or very short umbilical cord with the anterior fetal wall almost attached to the placenta, lower extremity anomalies in association with scoliosis facial anomalies[9].

The etiology of gastroschisis and omphalocele is controversial and their pathogenesis is still unclear. The reported overlapping patterns suggested that congenital defects involving VWDs are not independent conditions, however, they belong to a broader and common spectrum of malformations[3]. Moreover, although VWDs are accompanied by multiple malformations with well-defined embryological origins yet they are thought to share a common embryological mechanism representing a defect in the lateral body wall folding responsible for closing the abdominal, thoracic, and pelvic parts of the anterior body wall during the fourth week of embryonic development[1,10].

In most cases VWDs are associated with concurrent malformations, syndromes or chromosomal aberrations and the severity of associated anomalies predicts the prognosis. Most frequent associated anomalies are cardiac, craniofacial, central nervous system (CNS), gastrointestinal, genitourinary, and musculoskeletal defects[11]. Non-isolated VWDs are associated with high fetal morbidity and mortality; the mortality rate is 80% in the presence of associated malformations and it increases to almost 100% when cardiovascular anomalies or chromosomal aberrations are present[12,13]. Prenatal features of VWDs may be diverse and challenging requiring a high level of suspicion and knowledge with the imaging findings of this group of anomalies as outcomes are vastly different[2,12].

The aim of this study was to describe the prenatal ultrasound findings, associated anomalies and chromosomal abnormalities of fetuses diagnosed with VWD.

PATIENTS AND METHODS

A cohort of 200 fetuses was diagnosed with (VWDs) based on ultrasound findings during the period from January 2018 to February 2020. The cases were collected from a cohort of pregnant females referred to the Cairo Fetal Medicine Unit (Cairo University) for detailed fetal anatomy scan after initial diagnosis of an abdominal wall defect. This prospective study was approved by the Medical Ethical Committee of the Obstetrics & Gynecology Department at Cairo University and written informed consents were obtained. All patients were subjected to detailed fetal anomaly scan by fetal medicine specialists with a minimum of 5 years' experience using Voluson E8 or Voluson E6 (GE Medical Systems, Zipf, Austria) ultrasound machines with 4- to 8-MHz curvilinear abdominal probes and 5- to 9-MHz curvilinear vaginal probe. Gestational age was calculated from the reported reliable last menstrual period or adjusted to fetal biometry based on ultrasound measurements of the biparietal diameter (BPD) where appropriate.

Genetic counseling and testing (amniocentesis for karyotyping or FISH) were offered to all cases. The patients with associated malformations were classified as having either a chromosomal abnormality, sequence, complex, or non-syndromic multiple congenital anomalies (MCA) by the experienced geneticist. Special emphasis was made on the cases of VWD and cases with the severe forms of the defect even if isolated. Parents were informed of the findings including the prognosis, and for each patient with associated malformations, a complete description was obtained, including photographs, karyotype. Additionally, a three-generation pedigree was constructed for each family to detect any consanguinity or similarly affected family members. Postnatal examination was done to all cases who continued pregnancy.

RESULTS

Further details about the findings of the fetuses are described in (Tables 1,2 and Figures 1 to 7).

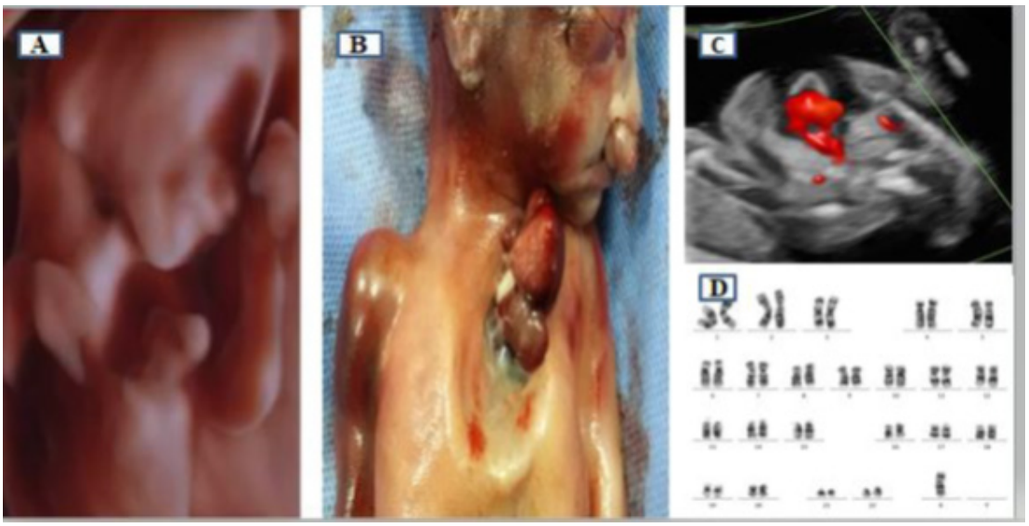

Fig. 1: Fetus with Ectopia cordis, bilateral cleft lip/palate and 45, X karyotyping A)Three-dimensional surface rendering showing extra-thoracic ectopia cordis and bilateral cleft lip and palate in a 13-week fetus. B) Postmortem image confirming the presence of the above findings. C) The fourchamber view showing extra-thoracic ectopia cordis with protrusion of the heart outside the fetal chest. D) G banding karyotype with 45,X (Turner syndrome)

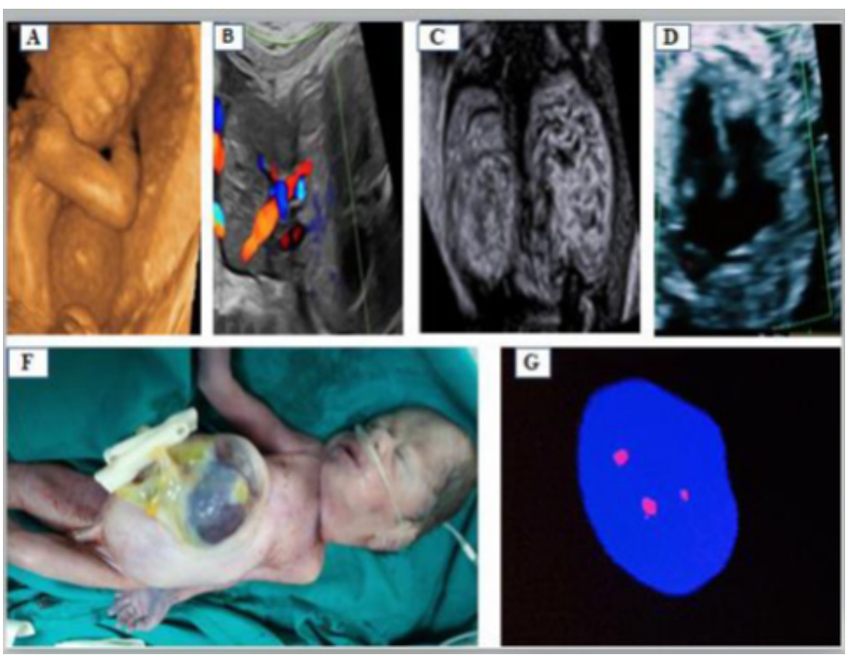

Fig. 2: Feus with large omphalocele and Trisomy 21 A) Three-dimensional ultrasound rendering image of a fetus with omphalocele, B) Axial view the axial view of the abdomen demonstrates a large omphalocele containing the liver; color Doppler shows the umbilical vein. C) Coronal US image of multicystic dysplastic kidney (MCDK). D) Four chamber view of the fetal heart showing atrio-ventricular septal defect. F) Postmortem image confirms the presence of the above findings, G) FISH using LSI 21 spectrum orange probe (Vysis) shows 3 signals (trisomy 21)

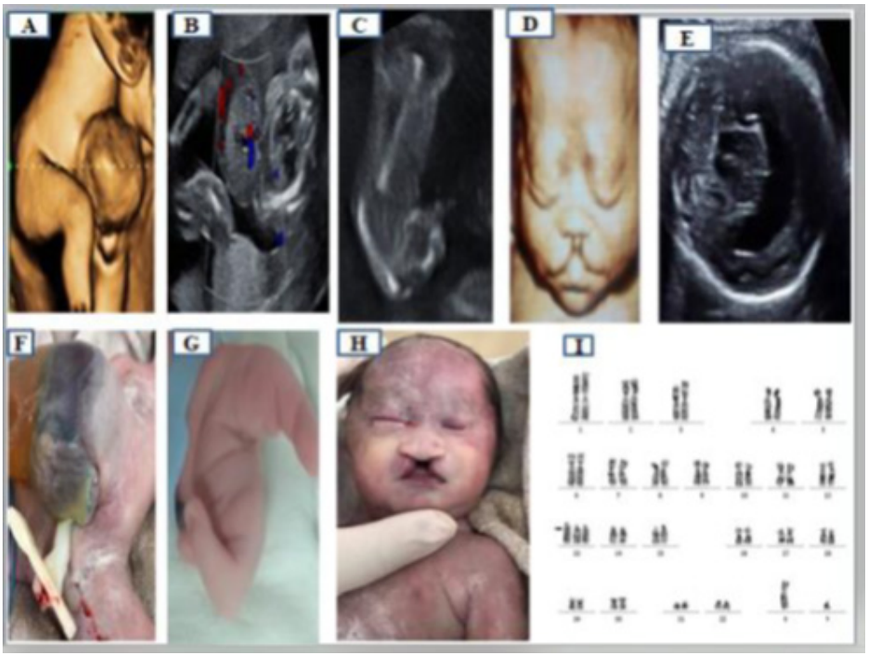

Fig. 3: Fetus with omphalocele, semi-lobar holoprosencephaly (HPE), radial ray defect, and Trisomy 13. A)Three dimentsional surface-mode rendering showing the omphalocele B) Axial view the axial view of the abdomen demonstrates a large omphalocele containing the liver; color Doppler shows the umbilical vein. C) Two dimentional ultrasound demonstrating absent radius with radial ray defect, D) Three-dimensional surface rendering of face showing hypotelorism, hypoplastic nose with flat nasal bridge, and a midline cleft associated with absence of the philtrum (premaxillary agenesis). E) Axial ultrasound (US) image of semilobar holoprosencephaly showing lack of cleavage of the anterior half of the hemispheres, with fused ventricles and absent falx and interhemispheric fissure anteriorly .F, G, H) Postmortem image confirms the presence of the above findings, I) Chromosomal examination using G-banding technique showing trisomy 13.

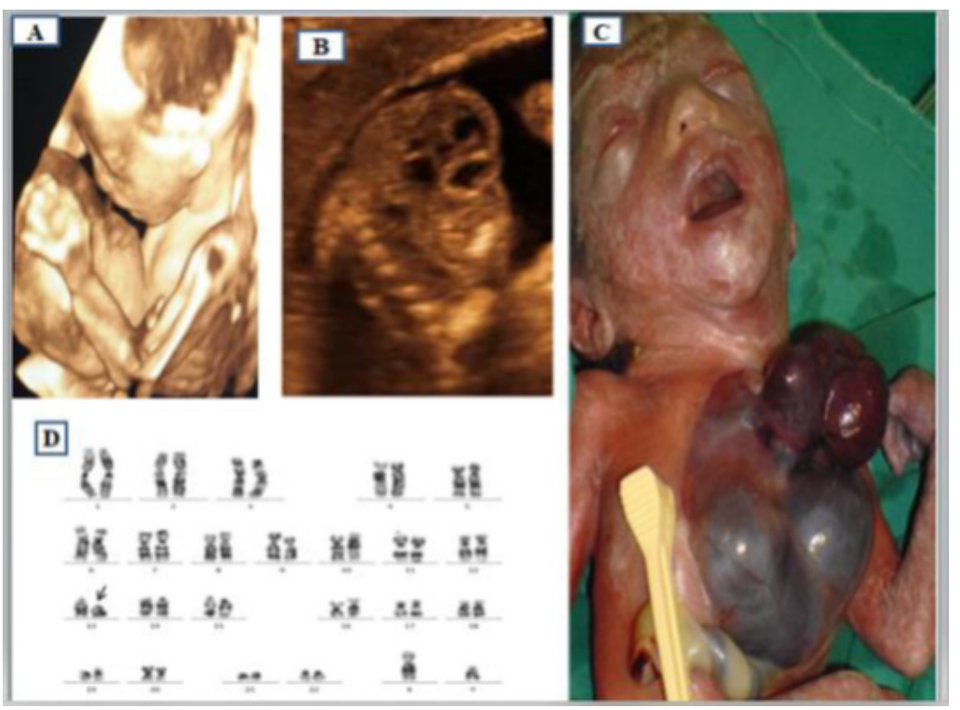

Fig. 4: fetus with Pentalogy of Cantrell and ring chromosome 13 karyotyping A)Three-dimensional surface rendering showing supra-umbilical omphalocele with protrusion of part of the fetal heart B) Transverse US image through the upper abdomen in a fetus with pentalogy of Cantrell shows an omphalocele that contains a portion of the heart with complex abberant structural defect C) Postmortem image confirms the presence of the above findings,D) G banding karyotype with 46,XY,r(13)

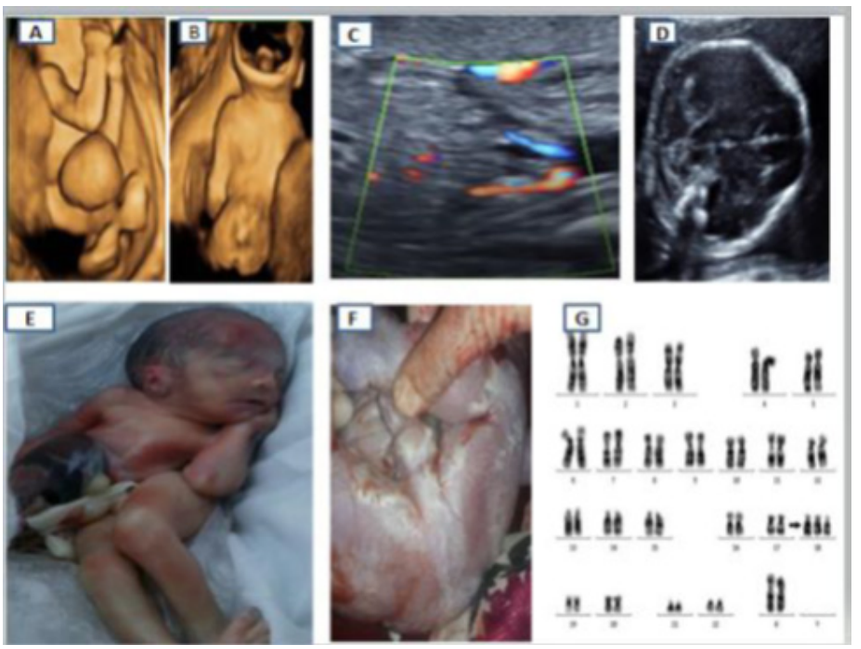

Fig. 5: Fetus with OEIS complex and Trisomy 18 Karyotyping A)Three dimensional surface rendering showing large infra-umbilical omphalocele. B) Bladder exstrophy: axial color Doppler US image shows the umbilical arteries; the bladder should be seen as a fluid-filled struc¬ture between them. C)Three dimentional surface rendering of fetal back showing scoliosis and small sacral neural tube defect, D) Axial transventricular brain of fetal brain showing Chiari II malformation with moderate ventriculomegaly, frontal scalloping (lemon sign); banana-shaped cerebellum and obliterated cisterna magna. E) Postmortem image confirms the presence of the above findings, F) postmortem image showing imperforate anus, G) hromosomal examination using G-banding technique showing 47, XX, +18 karyotyping.

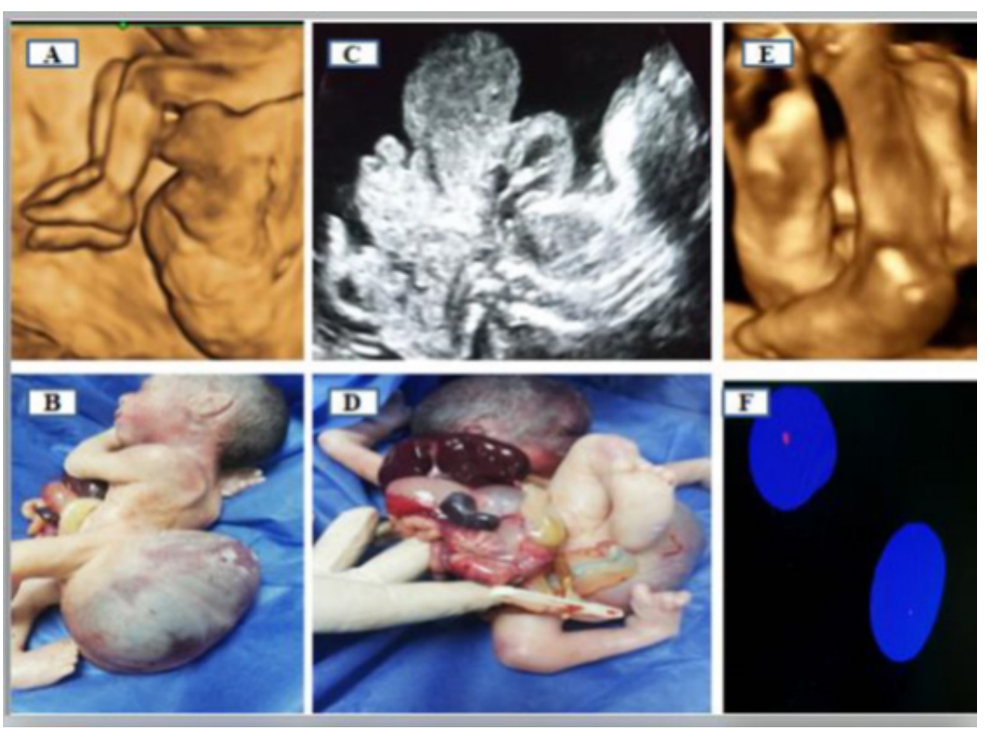

Fig. 6: Fetus with amniotic band syndrome, sacrococcygeal teratoma and Monsony 21 karyotyping. A) Three dimensional surface rendering showing Sacrococcygeal teratoma as large solid mass in a fetus with abdominal wall defect, B) Postmortem image confirms the presence of the above findings. C) Two dimensional US image showing a large VWD with hernia¬tion of the heart, liver and multiple loops of bowel. E) Three-dimensional surface rendering mode of lower extremities showing hyperextended knees and bilateral arthrogryposis with deformed lower limbs. D) Postmortem image confirms the presence of the above findings. F) FISH using LSI 21 spectrum orange probe (Vysis) shows single signal (monosomy 21)

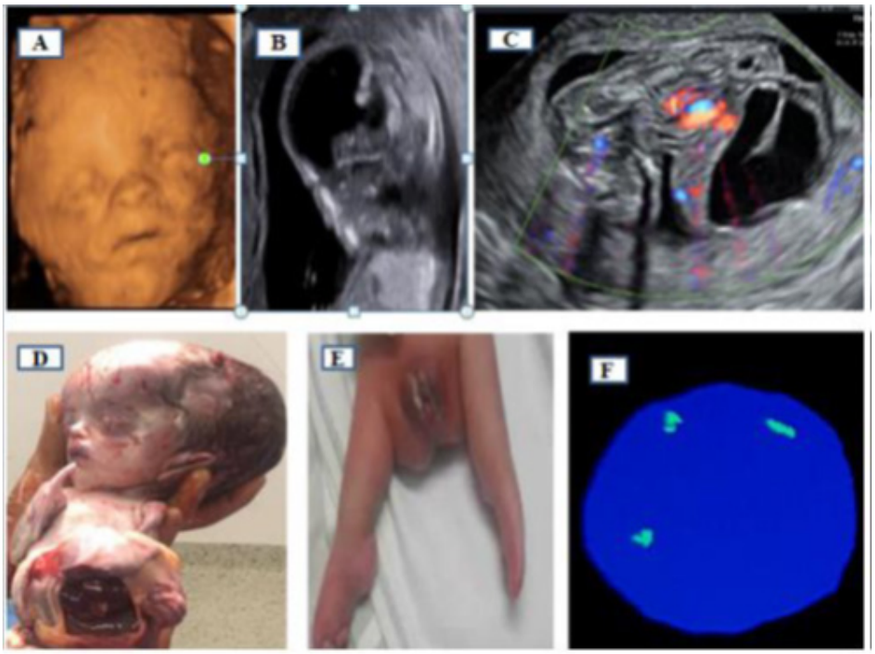

Fig. 7: Fetus with ABS in association with hydrocephalus, limb anomalies and and triploidy A)Threedimensional surface rendering mode of the fetal face demonstrating bilateral microphthalmia , midface hypoplasia and relative macrocephaly. B) Mid-sagittal view of fetal craniofacial region showing hydrocephalus and midface hypoplasia. C) Two dimensional transabdominal US image shows adherence of fetal abdominal structures to the placenta. D, E) Postmortem image confirms the presence of the above findings in addition to the presence of multiple limb reduction defects. F) FISH using centromere 2 spectrum green probe (MetaSystem) shows 3 signals (triploidy)

Table 1: Chromosomal aberration among fetuses with Ventral Wall Defects

Chromosomal aberration	Omphalocele N=121			Gastroschisis	Amniotic band syndrome	Ectopia cordis	Bladder exstrophy
	Not part of POC or OEIS complex N=110	Pentalogy of Cantrell N=6	OEIS complex N=5	N=63	N=12	N=2	N=2
Trisomy 18 N= 60 (63.4%)	N=49	_	N=1	N=10	_	_	_
Trisomy 13 N=21(22.5%)	N=18	_	_	N=3	_	_	_
Trisomy 21 N=5(5.37%)	N=5	_	_	_	_	_	_
45X0 N=4(4.3%)	N=2	_	N=1	_	_	N=1	_
Triploidy N=1 (1.07%)	_	_	_	_	N=1	_	_
Monsomy 21 N=1 (1.07%)	_	_	_	_	N=1	_	_
Structural aberrations (Ring chromosome 13) N=1 (1.07%)	_	N=1	_	_	_	_	_

Table 2: Associated anomalies detected prenatally classified by organ system among fetuses with Ventral Wall Defects

System affected	Omphalocele N=121			Gastroschisis	Amniotic band syndrome	Ectopia Cordis	Bladder Exstrophy
	Not part of POC or OEIS complex	Pentalogy of Cantrell	OEIS complex				
	N=110	N= 6	N= 5	N= 63	N=12	N=2	N=2
Cardiovascular system	N=20 (16.5%)	N=6 (100%)	_	N=7 (11.1%)	N=2 (16.6%)	N=2 (100%)	_
Ventricular septal defect	8	3		3	1	2	
Tetralogy of Fallot	5	2		2	1	_	
Hypoplatic left heart	3	1		1	_	_	
Ebstein anomaly	1	_		1	_	_	
Other	3	_		_	_	_	
Central nervous system	N=9 (7.4%)	_	_	N=3 (4.7%)	N=10 (83%)	_	_
Acrania	_			_	3		
Holoprosencephaly	2			_	3		
Ventriculomegaly	3			1	_		
Dandy Walker malformation	1			1	_		
Encephalocele	1			_	_		
Neural tube defects	2			1	4		
Facial anomalies	N=5 (4.5%)	_	_	N=2 (3.1%)	N=9 (75%)	N=1 (50%)	_
Anophthalmia/microphthalmia	2			1	3	_	
Cleft lip/palate	2			_	5	1	
micrognathia	1			1	1	_	
Congenital contractures	N=8(6.6%)	_	_	N=18(28.5%)	N=4(33%)	_	_
Limb anomalies	N=14 (12.7%)	N=1 (16.6%)	_	N=3 (4.8%)	N=12 (100%)	_	_
Radial ray defect							
Amelia							
Syndactyly/ectrodactyly							
Genitourinary anomalies	N=13 (10.7%)	_	N=5(1000%)	N=6(9.5%)	N=3(25%)	_	N=2(100%)
Hydronephrosis/hydroureter	5		2	2	1		_
Vesico-ureteral reflux	3		1	2	_		_
Multicystic dysplastic kidney	4		_	2	1		_
Ambiguous genitalia	1		2	_	1		2
Cystic hygroma/ hydrops fetalis	N=7(6.36%)	N=2 (33.3%)	_	N=3(4.7%)	_	_	_

Pregnancy characteristics and outcome

During the study period a total of 200 fetuses with VWDs were included in this study. There were 108 males and 92 females with a M:F sex ratio of 1.8:1 showing male predominance. Six fetuses (3%) were part of a dichorionic diamniotic twin pregnancy without in *vitro* fertilization (IVF) treatment. No history of exposure to teratogens or infections was reported. Consanguinity was present in 72 cases (36%). The mean maternal age in cases of gastroschisis (20.5 ± 5.0 years) was significantly lower than in cases of omphalocele (27.2 ± 5.5 years) ($P < 0.01$). The mean gestational age at time of diagnosis by ultrasound was 20 weeks ± 5 days (range 13-26 weeks).

In 148 cases (74%) the parents opted to terminate the pregnancy for associated chromosomal abnormalities and structural malformations, and there was 21 (10.5%) intrauterine fetal death (IUFD); in those cases, the parents refused autopsy. Only 31 (15.5%) fetuses were born alive between 36 and 38 weeks.

Classification of VWD

Among the 200 cases of VWDs; 121 (60.5%) cases were diagnosed at ultrasound with omphalocele, 63 with gastroschisis (31.5%), 12 cases (6 %) with body stalk anomaly ; 2 cases (1%) with ectopia cordis and 2 cases (1%) with bladder exstrophy.

Out of the 121 cases with omphalocele; 6 cases (4.9%) and 5 cases (4.1%) out of the 121 fetuses were part of POC and OEIS complex respectively.

Chromosomal analysis

Chromosomal analysis was performed in 188 (94%) fetuses. In 8 cases, amniocentesis was not performed or unsuccessful owing to amniotic bands (n = 3) or anhydramnios (n = 5). In 4 cases karyotyping failed due to IUFD. Chromosomal abnormalities were detected in 93 fetuses with an overall incidence of 49.4 %. Trisomy 18 was the most common aberration and was detected in 60 cases (64.5 %), of which 49 cases had omphalocele, 10 had gastroschisis and 1 case had OEIS complex. Trisomy 13 was detected in 21 cases (22.5%) of which 18 had omphalocele; 3 gastroschisis while trisomy 21 was detected in 5 cases (5.37%) with omphalocele. 45, X karyotyping was detected in 4 cases (4.3%) 2 with omphalocele, one with ectopia cordis and one with OEIS complex. Triploid karyotyping was detected in a case with body stalk anomaly associated with hydrocephalus and limb anomalies. Finally, one cases

(1.07%) with body stalk anomaly and saccrococcygeal teratoma had monosomy 21; and one case (1.07%) with POC had a de novo ring chromosome 13 karyotyping.

Patterns of Anomalies Associated with VWDs

Major structural anomalies were detected prenatally in 104 cases (86%) with omphalocele and 22 cases (34.9%) with gastroschisis. Structural cardiac defects were detected in 20 (16.5%) omphalocele cases; 7 (11.1%) gasrtroschisis cases; 2 cases with (16.6%) body stalk anomaly, and all the 6 cases (100%) with POC. CNS anomalies including acrania; holoprosencephaly; ventriculomegaly, Dandy walker malformation, encephalocele, neural tube defects with or without scoliosis were observed in 9 cases (7.4%) with omphalocele, 3 cases (4.7%) gastroschisis cases; 10 cases (83%) body stalk anomaly cases. Facial anomalies including anomphthalmia, microphthalmia, cleft lip/palate and micrognathia were detected in 5 cases (4.5%) of omphalocele; 2 (3.1%) gastroschisis cases, 1 case (50%) with ectopia cordis and 9 cases (75%) with body stalk anomaly. Limb anomalies including radial ray defects, amelia, syndactyly, ectrodactyly and sirenomelia were observed in 12 cases (100%) with LBWC; 14 (12.7%) omphalocele cases; 3 (4.8%) gastroschisis cases, 1 case (20%) of OEIS complex.

Genitourinary anomalies including hydronephrosis, hydroureter, vesico-ureteral reflux (VUR), multicystic dysplastic kidney, absent/small kidney, and ambiguous genitalia were detected in 13 (10.7%) of omphalocele cases and 6 (9.5%) gastroschisis cases, 3 (25%) of LBWC cases and all 5 cases (100%) with OEIS complex. Cystic hygroma, fetal ascites and hydrops fetalis were detected in 7 (6.36%) omphalocele cases and 3 (4.7%) cases of GS.

Finally, congenital contractures and arthrogryposis multiplex were detected in 18 cases (28.5%) with gastroschisis and in 8 (6.6%) omphalocele cases.

DISCUSSION

VWD are frequently associated with other congenital malformations; however; it is not well-established if gastroschisis and omphalocele and are associated with distinct patterns of associated malformations[3]. In the current study, we elucidate the prenatal imaging findings of a cohort of 200 fetuses with VWDs. Prenatal studies of VWDs usually report a higher frequency of associated anomalies than that reported in population based studies postnatal where associated malformations for omphalocele ranged from 27% to 63%, and for gastroschisis from 5% to 27%. This could be explained by the expected larger percentage of chromosome disorders in fetal and stillbirth cases[14,15,16]. We observed a significant difference in the prevalence of total associated anomalies between the omphalocele and gastroschisis cases (86% vs. 34.9%, $P<0.001$).

In the present study; the frequency of associated malformations with omphalocele was 86 % and 67 fetuses (61.1%) among them were associated with abnormal karyotyping which was in accordance with other prenatal studies documenting that chromosomal abnormalities are detected in 38 to 67% of the omphaloceles[4,17,18]. On the other hand; the proportion of gastroschisis cases with associated malformations (34.9%) was higher than those observed in previous studies with chromosome aberrations surprisingly accounting for 22.2% of fetuses with gastroschisis[11,19].

As previously reported in other studies; the most frequently encountered chromosomal aberrations in this study were trisomy 18 (64.5%) and trisomy 13 (22.5%). Data collection of the karyotyping abnormalities from literature gives the average incidence of 77.2% for trisomy 18 and of 11.4% for trisomy 13, in accordance with the published data. Other less frequent chromosomal aberrations that can be rarely identified at a relatively very low frequency include Trisomy 21, monosmy X; triploidy, and structural chromosomal aberrations[4,18,20].

Trisomy 21 was detected in 5.37 % of fetuses with abnormal karyotyping. The association between Trisomy 21 and VWD is largely controversial; Torfs *et al*[21] described one trisomy 21 case among 2,979 stillbirths and live births with omphalocele and concluded that trisomy 21 in not considered a predisposing risk factor for omphalocele. However, Mastroiacovo *et al*[22] reported seven cases of trisomy 21 among 8,560 VWD fetuses with an incidence higher than that general population and concluded that trisomy 21 predisposes to a higher risk for omphalocele.

VWD can also be associated with abnormalities in the sex chromosomes such as 45,X , and 47,XXY. In our study we reported the prenatal diagnosis of concomitant cystic hygroma and VWD in 4 fetuses (4.3%) with 45X karyotyping. Goldstein and Drugan proposed that the occurrence of VWD in Turner syndrome may be due to the denial of X chromosome inactivation[23]. OEIS is a polymalformative syndromes with omphalocele being an integral component[3,4]. OEIS complex can be associated with genetic syndromes including Goltz syndrome, Opitz G/BBB syndrome, frontonasal dysplasia, oculoauriculovertebral syndrome, trisomies 13, 18 and

21, triple X syndrome suggesting a genetic etiology[24] In our cohort we described the prenatal features of 5 cases of OEIS complex.

POC is another omphalocele associated polymalfomative syndrome detected in 6 fetuses in our study. Interestingly, in the present study, one case (4%) with POC in association with microcephaly, AVSD, scoliosis, and limb anomalies had the extremely rarely reported ring chromosome 13 karyotyping which is reported to be associated with microcephaly, congenital heart disease, hands and feet anomalies, and genital abnormalities. This case which in addition to the previously few reported cases encompassing the association between POC and limb malformations suggest a possible syndrome involving the genes responsible for fusion of the sternum and limb morphogenesis[24,25].

Interestingly; our study included two cases with Ectopia Cordis; one of them was associated with midline cleft lip and palate in association with 45, X karytyping. Associated intracardiac defects and craniofacial anomalies are frequently observed with this rare anomaly[26].

Our study also included 12 cases of body stalk anomalies in association with gastroschisis; among them were three fetuses of dichorionic diamniotic pregnancy discordant for the anomaly. There are only a few reports in the literature about body stalk anomalies in multiple gestations, and fewer about twin pregnancies in which only one fetus was affected[27]. Adjuvant 3D ultrasound was of considerable utility in revealing the striking combination of abdominal wall defects of variable severity in association with thoracic defect with herniation of heart in 5 cases (50%); craniofacial abnormalities in 3 cases (56%); spinal deformities including scoliosis in 6 cases (77%), limb abnormalities in 7 cases (95%). Moreover, amniotic bands and short umbilical cord were noted in 4 cases (40%). These findings were in accordance with those noted in previous series of fetuses with body stalk anomalies[27,28]. The broad criteria proposed for defining body stalk anomalies include multiple birth defects seen in common chromosomal trisomies, especially trisomy 18,[28] however; none of our cases had Trisomy 18 karyotyping.

Interestingly, one of the fetuses had a triploid karyotyping; representing a very rare occurrence of triploidy in a fetus with large defect in association with hydrocephalus, genital and limb malformations. Additionally, gastroschisis is not usually associated with sacrococcygeal teratoma; in the present series we report a very rare case of body stalk anomaly with extracorporeal liver associated with sacrococcygeal teratoma, limb anomalies and a monosomy 21 karyotyping is described in monochrionic monoamniotic twin; this association was not previously reported and subsequently requires further research.

In the present series we report similar frequencies in a set of congenital anomalies suggesting that VWD predisposition arise within shared antero-posterior and dorso-ventral developmental fields within the 3-week embryo. Therefore, cardiac, CNS, craniofacial and limb anomalies had parallel but relatively higher frequencies in omphalocele cases in comparison to gastroschisis (16.5% vs 11.1%); (7.4 vs 4.7%), (4.5% vs 3.1%), (12.7% vs 4.8%), respectively. The preponderance of cardiac, CNS, and limb anomalies associated with both VWD is in agreement with results of prior studies[4,19,22]. Similarly, genitourinary anomalies including hydronephrosis, hydroureter, vesico-ureteral reflux and anomalies of the reticuloendothelial system including cystic hygroma and fetal hydrops had relatively similar frequencies in both gastroschisis and omphalocele (10.7% vs 9.5%), (6.3% vs 4.7%) suggesting that secondary alterations of intra-abdominal pressure are similar for all types of VWDs.

Additionally; in our cohort the group associated anomalies that support thrombo-vascular disruption including arthrogryposis were more common in gastroschisis compared to omphalocele (28.5% vs 6.6%). On the other hand anomalies related to failure of lateral folding/ventral wall fusion including bladder exstrophies were detected only in association with omphalocele as depicted by similar patterns observed in previous studies[19,29,30].

A limitation of the current study is that further chromosomal microarray and exome sequencing were not performed for the euploid fetuses which would further elucidate the genetic pathogenesis of the associated findings. Additionally; most of the parents declined fetal MRI and postmortem autopsy which is considered another limitation.

CONCLUSION

In conclusion, this study highlights the clinical and genetic heterogeneity of VWDs especially the severe forms of this spectrum as well as demonstrating the extremely rare cases with triploidy, monosomy 21 and ring chromosome 13.

CONFLICT OD INTERESTS

There are no conflicts of interest

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