Table 1 Continued

Gene	Variant	Inheritance	Ultrasound findings in addition to NIHF
PTPN11	NM_002834.4:c.854T>C [p.Phe285Ser]	de novo	Mild ventriculomegaly, suspected aortic coarctation, absent DV, biventricular hypertrophy, pelviectasis, hepatomegaly, polyhydramnios
KRAS	NM_033360.3:c.220A>C [pThr74Pro]	de novo	VSD, left SVC draining into coronary sinus, SUA, polyhydramnios
KRAS	NM_033360.3:c.204G>C [p.Arg68Ser]	de novo	Absent CSP, cardiomegaly, hepatomegaly, clubbed feet, placentomegaly
BRAF	NM_004333.5:c.1741A>C [p.Asn581His]	de novo	FGR, echogenic bowel, SUA
RIT1	NM_006912.5:c.245T>G [p.Phe82Cys]	de novo	CNS malformation, congenital heart defect

Abbreviations: CNS, central nervous system; CSP, cavum septum pellucidum; DV, ductus venosus; FGR, fetal growth restriction; SUA, single umbilical artery; NIHF, nonimmune hydrops fetalis; SVC, superior vena cava; VSD, ventral septal defect.

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OP052

Genetic etiology of prenatally detected isolated moderate to severe ventriculomegaly

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Introduction: Ventriculomegaly (VM) is identified on prenatal ultrasound in 0.3-2.0 per 1000 pregnancies and is categorized into three groups based on measurement at the atrial level: mild (≥10-<12mm), moderate (≥12-<15mm), and severe (≥15mm). The literature suggests that approximately 2 to 15% of fetuses with identified VM have an abnormal karyotype, with lower prevalence in isolated cases (1.5-12%) compared to cases with additional anomalies (9.5-36%). Infectious etiologies and clotting disorders are causal in some. Isolated VM has been associated with many types of chromosomal anomalies, the most common being trisomy 21. Other chromosomal abnormalities (trisomy 18, trisomy 13, monosomy X, and triploidy), large deletions and duplications (1q dup, 7p dup, 5p del, and 4p del), microdeletion syndromes (22q11.2 del, 15q11.2 microdel, 16p13.11 microdel and microdupl, 1p36 microdel) and single gene disorders (*L1CAM, AP1S2, MPDZ, CCDC88C, EML1, WDR81, NSD1*) have also been reported. The objective of this study was to describe the genetic differences seen in our cohort of fetuses prenatally diagnosed with isolated moderate to severe VM.

Methods: This was a retrospective cohort study of patients that were referred for VM between April 2016 to August 2021. Patients were evaluated by high resolution ultrasound and fetal neuro MRI and offered genetic counseling and testing. A total of 144 patients were identified of which 50 went on to have postnatal neurology evaluation. 54 pregnancies resulted in terminations and 13 pregnancies were delivered but lost to follow up.

Results: Of the 131 patients identified, 70 had isolated VM and 61 had additional structural anomalies that excluded them from the analysis. In isolated cases, 67% (47/70) had genetic testing and 40% (19/47) of those had abnormal results (Table 1). 74% (35/47) had cytogenetic testing including karyotype and microarray. 11% (4/35) of patients who underwent cytogenetic testing had abnormal microarray, all of which were thought to be causative of the prenatal findings. 40% of patients (19/47) had single gene next generation sequencing and of those 31.5% (6/19) had positive test results, all of which were thought to be causal. 30% (14/47) of patients had Exome Sequencing (ES). 64% (9/14) had positive results, 67% (6/9) of which were felt to be contributory to disease, with an additional variant of uncertain significance and two pathogenic findings that were unrelated to VM but did impact clinical management. One patient had CMV infection and another had Neonatal Alloimmune Thrombocytopenia.

Conclusion: Advances in genetic testing have allowed us to identify etiologies of VM that were previously unknown. As technology has improved, patients with VM have gained more meaningful test results as evidenced by our ES findings. Our 30% diagnostic rate does not represent the full genetic potential of this cohort as barriers to genetic testing still exist such as cost, timing, and understanding of testing strategy. A portion of this population was lost to follow up, declined prenatal testing, or had work up that included only cytogenetic testing. This cohort represents the need for a standardized approach to testing strategy in those with prenatally detected isolated moderate to severe VM. A proposed testing strategy for cases of prenatally identified moderate or severe VM should include 1) diagnostic testing for chromosomal abnormalities with a karyotype and microarray, 2) Infectious PCR Testing and Neonatal Alloimmune Thrombocytopenia work up, 3) L1CAM gene sequencing for affected males, and 4) consideration of exome sequencing (ES).

Type of Testing	Positive	Negative	Genetic alteration
Single Gene	31.5% (6/19)	68% (13/19)	L1CAM COL4A1 CCCND2
Exome Sequencing	64% (9/14)	36% (5/14)	TRIM37 CHD7 FANCA TUBA1 GRIN2B GLI3 KIRREL3 OCA2 (incidental) KCNB2 (incidental)
Miscellaneous	100% (2/2)	0% (0/2)	CMV Infection, Neonatal Thrombocytopenia

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OP053

Barriers to completion of expanded carrier screening in an inner city population

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Introduction: The American College of Medical Genetics and Genomics emphasizes the need for a "consistent and equitable approach for offering carrier screening to all individuals during pregnancy or preconception" in order to facilitate informed reproductive decisions. At our academic center, publicly insured patients obtaining prenatal care underwent universal Expanded Carrier Screening (ECS) to promote equitable access and care. We evaluated barriers to timely ECS completion, namely, receipt of genetic counseling, partner screening, and ability to act on diagnostic testing results.
Methods: A descriptive retrospective cohort study was performed from 2018-2021 where patients were offered an ECS panel consisting of 283 recessive and X-linked pathogenic variants. Women who were found to be heterozygous for recessive pathogenic variants were contacted by genetic counselors (=/ > 5 attempts), for education on the finding and for partners to receive a test kit. Prevalence of patients who were heterozygotes and rates of genetic counseling, partner screening, diagnostic procedures and time to follow up were assessed.
Results: There were 987 first prenatal visits and 643 women underwent ECS. Median gestational age at ECS was 12 weeks and 3 days. Results were abnormal in 462 women (71.8%), who were heterozygous for a median of 2 pathogenic variants (recessive or X-linked). Genetic counseling occurred in 326 women (70.6%) with abnormal results, and 136 women (29.4%) did not have further follow up. Two hundred twenty-two partners (48%) obtained screening, with a median of 32 days from patient to partner result. There were 21 couples who were found to be heterozygous for the same recessive pathogenic variant, of which 13 (62%) were variants for recessive diseases that would not be detected by New York State's newborn screen. 3 women pursued diagnostic testing, with 1 fetus affected leading to termination.
Conclusion: ECS offers useful information, however, our data suggests there are significant barriers to follow up in our diverse population. The prevalence of heterozygotes on ECS in our population was higher than expected, which lead to strains on our system, causing delays in follow up. There were also suboptimal patient follow up and low partner screening rates, possibly due to lack of time to counsel and educate. Future directions include assessing disparities and implementing quality measures to ensure couples' completion of ECS.

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OP054

Chromosomal microarray analysis for open neural tube defect: The prevalence of significant results and implications on in utero repair

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Introduction: Open neural tube defects (ONTD) are the second-most-common major congenital anomaly, and have been associated with environmental insults or genetic factors. Prenatal screening and diagnosis are widely available, and in utero repair has demonstrated superior outcomes for eligible patients. The Management of Myelomeningocele Study (MOMS) required a normal karyotype as one of the eligibility criteria for in utero repair. However, current guidelines