

BACKGROUND

- Mirror syndrome (MS), is a rare life-threatening condition in which a pregnant person develops edema, “mirroring” that of their hydropic fetus.
- Data on genetic testing in affected pregnancies is limited.

OBJECTIVES

- Primary outcome: diagnostic yield of genetic testing.
- Secondary outcome: genetic testing rates, compared between hydrops with vs without MS.

METHODS

- Retrospective cohort of 200 fetuses with a prenatal diagnosis of hydrops between 2012–2023 at Texas Children’s Hospital, Houston TX USA.
- MS defined as: fetal hydrops + new/worsening maternal hypertension + significant edema.
- Diagnostic genetic testing performed pre- or postnatally: karyotype, chromosomal microarray (CMA), gene panels, exome sequencing (ES).
- A case was considered solved if a pathogenic or likely pathogenic variant explained the hydrops phenotype.
- Compared testing rates, diagnostic yield, and genetic conditions between MS and non-MS groups.

Table 1. Genetic findings in pregnancies affected by hydrops with and without mirror syndrome.

	Hydrops only n=168 (%)	Mirror Syndrome n=32 (%)	P-value
Genetic Testing			
Diagnostic genetic testing			
Yes	122/168 (72.6)	25/32 (78.1)	0.52
No	46/168 (27.4)	7/32 (21.9)	
Type of genetic testing			
Karyotype	82/168 (48.8)	13/32 (40.6)	0.40
CMA	107/168 (63.7)	23/32 (71.9)	0.37
Exome/Genome	33/168 (19.6)	15/32 (46.9)	0.001
Panel testing	3/168 (1.8)	3/32 (9.4)	0.053
Genetic Diagnosis (solved cases)			
Aneuploidy	18/120 (15.0)	1/24 (4.2)	0.20
Trisomy 21	10/120 (8.3)	1/24 (4.2)	0.69
Trisomy 18	1/120 (0.8)	0/24 (0)	0.99
Trisomy 13	1/120 (0.8)	0/24 (0)	0.99
Monosomy X	6/120 (5.0)	0/24 (0)	0.59
Copy-number variants	6/120 (5.0) 4q34.1q35.1 LOSS Unbalanced translocation 46,XY,der(13)t(13;17)(q34;q25) Partial trisomy 5p Unbalanced chr4 rearrangement Trisomy 16p Mosaic trisomy 22q	0/24 (0)	0.59
Single-gene disorders	10/36 (27.8) PIK3CA (Somatic overgrowth) JAG1 (Alagille) MYH7 (Cardiomyopathy) WDR19-related disorder PTPN11 (Noonan) EVC (Ellis-Van Creveld) TTN (Cardiomyopathy) RAPSN (Fetal akinesia deformation sequence 2) SPTA1 (Pyropoikilocytosis) RIT1 (Noonan)	5/18 (27.8) RAF1 (Noonan) HRAS (Costello) ZIC2 (HPE5) PTPN11 (Noonan) TPM1 (LVNC cardiomyopathy)	0.99

RESULTS

- 200 hydrops cases analyzed; 147 (73.5%) had diagnostic genetic testing.
- ES was more common in the MS group: (46.9% vs 19.6%, $p=0.001$).
- The rate of solved cases was the same between MS and non-MS cases (24.0% vs 27.9%, $p=0.69$).
- Similarly, there was no difference in the rates of aneuploidy, copy-number variants, and single-gene disorders.
- Single-gene conditions among both groups were enriched for cardiovascular and lymphatic disorders.

CONCLUSIONS

- The rates and types of genetic diagnoses were similar between hydrops cases with and without concomitant mirror syndrome.
- Mirror syndrome is likely driven less by a particular molecular mechanism and more by maternal vascular endothelial dysfunction resulting from high-risk fetal pathology.
- These data aid in counseling parents in the setting of hydrops and mirror syndrome.