EXPANDED CARRIER SCREEN RESULTS AND THEIR IMPACT ON IVF OUTCOMES

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PURPOSE & OBJECTIVES

During in-vitro fertilization (IVF), expanded carrier screen (ECS) testing is offered to identify risk for transmitting autosomal recessive (AR) or X-linked disorders to offspring [1,2].Most of the tested disorders are asymptomatic in the heterozygous carrier, heterozygous status of some AR disorders can present with phenotypes, some of which can impact fertility [3].

The objective was to determine if positive carrier status of disorders tested in the expanded carrier screen (176-gene panel) impacts IVF cycle characteristics and clinical outcomes.

MATERIAL & METHODS

A retrospective analysis was performed using primary IVF clinic data collected by our institution. All female patients undergoing first autologous cycles from July 2019 to July 2022 with ECS, both with or without male partner ECS, were included. Outcomes of first transfer cycles through July 2023 were included.

Primary outcome was the live birth rate following the first transfer cycle using either fresh or frozen embryos.

Secondary outcomes included total oocytes retrieved, fertilization rate, total number of embryos frozen or transferred, implantation rate, and miscarriage rate.

Models were run using the number of positive results on the carrier screen as a continuous variable.

Subanalysis of couples with positive ECS for disorders in which carriers are known to be at risk for symptoms, as reported by Myriad, was performed.

Odds and rate ratios (OR/RR) were calculated for the number of positive ECS results and adjusted for age. Fischer's exact and t-test were used for subanalysis.

During IVF, patients are offered Expanded Carrier Screens to identify risk for transmitting AR or X-linked disorders to their offspring. Heterozygous status of some AR disorders can present with phenotypes, some of which can impact fertility.

In this study we did not find evidence that carriers of AR or X-linked recessive disorders on our 176-gene ECS have impacted IVF outcomes.

RESULTS

A total of 217 females were found to be undergoing ECS at the time of their first IVF autologous cycle from July 2019 to July 2022. Of those, 184 had partners that also underwent ECS.

We did not find a relationship between the number of positive results on the female ECS, or cumulative positive results of a couple, and IVF outcomes (Table). Adjustment for female age did not impact findings.

Subanalysis did not find an effect of carrier status on our study population.

CONCLUSIONS

In this study we did not find evidence that AR or X-linked recessive disorders on ECS impact IVF outcomes.
This is the first study looking into carrier status of disorders tested in ECS and its impact on IVF outcomes.

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RESULTS

Table 1. Outcomes by # of mutations detected in female carrier screening

	# Positive Results in Female ECS				
	0	1	≥ 2	OR/RR	95% CI
Patients (n)	98	82	37		
Mean Total Oocytes Retrieved	15.6	17.1	15.5	1.01	0.97 – 1.05
Fertilization Rate (%)	70.8	71.9	70.7	0.99	0.63 – 1.56
Mean Embryos (frozen or transferred)	4.4	4.5	3.8	0.94	0.88 – 1.01
Number of Embryo Transfers (n)	91	69	31		
Implantation Rate (%)[1*]	55.0	62.3	53.2	1.02	0.83 – 1.26
Miscarriage Rate (%)[2*]	11.3	13.0	18.8	1.16	0.66 – 2.04
Live Birth Rate per Retrieval (%)*	45.7	48.1	36.4	0.95	0.70 – 1.29

Statistic presented for binary outcomes is odds ratio. Statistic presented for count and rate outcomes is rate ratio.
*Live birth, clinical pregnancy, implantation rate, and miscarriage are all for the 1st transfer cycle. Patients who had embryos frozen but did not have a transfer (n=11) were excluded from live birth, clinical pregnancy, implantation rate, and miscarriage outcomes. Patients who did not have any embryos transferred or frozen (n=10) were excluded from implantation rate and miscarriage outcomes.
1 implantation rate calculated with formula = fetal heartbeats on US/embryos transferred. Only those who had a transfer included: No mutations in carrier screening (n=20), 1 mutation (n=41), 2 mutations (n=31), 3 mutations (n=18), 4 or more mutations (n=9).
2 denominator is number of clinical pregnancies.

Table 2. Outcomes by # of cumulative mutations detected in couple carrier screening

	# Positive Results in Couple ECS						
	0	1	2	3	≥ 4	OR/RR	95% CI
Couples (n)	25	62	51	34	12		
Fertilization Rate (%)	72.1	70.8	69.2	72.5	75.6	0.98	0.67 – 1.44
Mean Embryos (frozen or transferred)	3.6	4.3	4.1	4.9	3.3	1.02	0.96 – 1.08
Number of Embryo Transfers (n)	23	55	44	30	10		
Implantation Rate (%)*	56.5	60.0	58.0	58.3	30.0	0.95	0.79 – 1.14
Miscarriage Rate (%)	14.3	8.8	11.5	16.7	0.0	1.01	0.58 – 1.78
Live Birth Rate per Retrieval (%)	45.8	52.7	42.0	46.9	27.3	0.89	0.68 – 1.15

Statistic presented for binary outcomes is odds ratio. Statistic presented for count and rate outcomes is rate ratio.
*Live birth, clinical pregnancy, implantation rate, and miscarriage are all for the 1st transfer cycle. Patients who had embryos frozen but did not have a transfer (n=11) were excluded from live birth, clinical pregnancy, implantation rate, and miscarriage outcomes. Patients who did not have any embryos transferred or frozen (n=10) were excluded from implantation rate and miscarriage outcomes.
1 implantation rate calculated with formula = fetal heartbeats on US/embryos transferred. Only those who had a transfer included: No mutations in carrier screening (n=20), 1 mutation (n=41), 2 mutations (n=31), 3 mutations (n=18), 4 or more mutations (n=9).
2 denominator is number of clinical pregnancies.

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