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Complications and Outcomes of Pregnancies Screening Positive for Microdeletions 22q11.2, 15q11.2, 1p36, 4p, or 5p

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Background

- Pregnancy complication types and rates have not been well described among those who screened positive for certain microdeletions.

OBJECTIVE: We aimed to characterize ultrasound findings and pregnancy complications and outcomes in pregnancies screening positive for microdeletions 22q11.2, 15q11.2, 1p36, 4p, or 5p on a prenatal cell-free DNA (pcfDNA) test using insurance claims data.

Methods

- Patients who received Prequel[1] (Myriad Genetics, Inc.), a whole genome sequencing-based pcfDNA screen that incorporates fetal fraction amplification, between July 2020 and January 2023 were linked to the Komodo Healthcare Map™ insurance claims database[2] using Datavant tokenization[3] **(Figure 1)**.
- Included patients were ≥18 years with singleton pregnancies and no other known abnormal pcfDNA screening results **(Figure 1)**.
- Diagnosis codes, procedure codes, and pharmacy fills during pregnancy were used to assess outcomes.
- Outcomes of microdeletion screen-positive (MDS+) patients were compared to microdeletion screen-negative (MDS–) patients using logistic regression with adjustment for health insurance type and history of high-risk pregnancy.

Conclusion

Microdeletion screen-positive pregnancies had higher rates of ultrasound abnormalities, including polyhydramnios and intrauterine growth restriction, and experienced higher rates of pregnancy loss and preterm birth compared to screen-negative pregnancies.

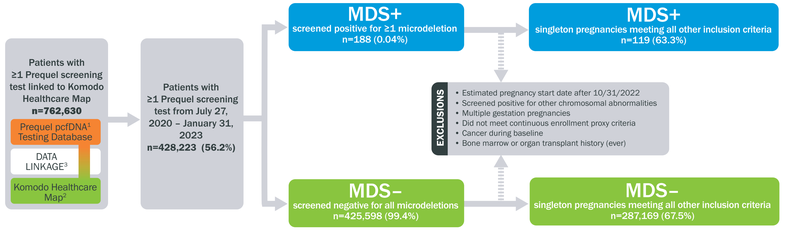
References: 1. Myriad Genetics, Inc., Salt Lake City, UT. Prequel® Prenatal Screen. https://myriad.com/womens-health/patient-prequel/. **2.** Komodo Health, Inc. https://www.komodohealth.com/healthcare-map. **3.** Datavant. https://www.datavant.com/.

Disclosures: All authors were employees of Myriad Genetics, Inc. at the time of this study and received salaries and stock as compensation.

Results

- The study population included 119 MDS+ patients and 287,169 MDS– patients **(Figure 1; Table 1)**; the frequency of each microdeletion is shown in **Figure 2**.

Figure 1. Cohort diagram



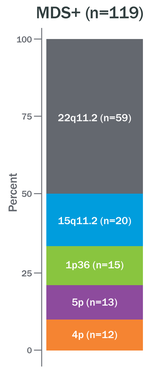
Other chromosomal abnormalities included monosomy or trisomy results for any autosomal chromosomes (1-22) or any sex chromosome abnormalities. In the MDS+ group, patients screening positive for >1 microdeletion were also excluded. The continuous enrollment proxy required: 1) at least one medical or pharmacy claim from 2 years prior to the estimated pregnancy start date (baseline period) to 8 weeks after the estimated pregnancy start date, 2) at least one medical or pharmacy claim +/- 4 weeks around Prequel test date, and 3) at least one pregnancy-related claim from the estimated pregnancy start date to 42 weeks after the estimated pregnancy start date (follow-up period). This was to ensure most claims occurring during the study period were captured.

Table 1. Cohort characteristics

Characteristics	MDS-	MDS+
Total N	**287,169**	**119**
Maternal age at expected delivery (years)		
Mean (SD)	30.9 (5.8)	30.9 (5.6)
Median (Q1 - Q3)	31.0 (27.0 – 35.0)	32.0 (26.5 – 35.0)
Age ≥35 (n, %)	201,650 (29.4)	34 (28.6)
Payer, n (%)		
Commercial	200,493 (69.8)	>59 (>49.6)
Medicaid	80,742 (28.1)	38 (31.9)
Medicare	1,690 (0.6)	<11 (<9.2)
Other	4,244 (1.5)	<11 (<9.2)
Ethnicity, n (%)		
African or African American	35,868 (12.5)	15 (12.6)
Ashkenazi Jewish	2,386 (0.8)	0 (0)
Asian/Pacific Islander	13,430 (4.7)	<11 (<9.2)
European	28,420 (9.9)	12 (10.1)
French Canadian or Cajun	376 (0.1)	0 (0)
Hispanic	32,529 (11.3)	18 (15.1)
Middle Eastern	2,197 (0.8)	<11 (<9.2)
Native American	1,304 (0.5)	0 (0)
Other/Mixed White	100,811 (35.1)	>31 (>26.1)
Unknown	69,848 (24.3)	21 (17.6)
Pregnancy history, n (%)		
Previous pregnancy	157,750 (54.9)	67 (56.3)
Pregnancy loss	49,506 (31.4)	20 (29.9)
Elective termination	6,110 (3.9)	0 (0)
Preeclampsia	10,647 (6.7)	<11 (<16.4)
Gestational diabetes	12,291 (7.8)	<11 (<16.4)
High-risk pregnancy	133,101 (84.4)	63 (94.0)
IUGR	16,370 (10.4)	11 (16.4)
Previous delivery	110,551 (38.5)	56 (47.1)
Preterm birth	7,917 (7.2)	<11 (<19.6)
Gestational age at pcfDNA testing (weeks)		
Mean (SD)	13.0 (3.7)	14.3 (5.0)
Median (Q1 - Q3)	12.0 (10.9 – 13.4)	12.6 (11.0 – 15.3)
Include microdeletion report results, n (%)	38,960 (13.6)	38 (31.9)

IUGR = intrauterine growth restriction; Q = quartile; SD = standard deviation.
Patient numbers <11 were masked to preserve patient privacy.

Figure 2. Frequency of microdeletions



- During pregnancy, MDS+ patients were more likely to have abnormal ultrasound findings including polyhydramnios and intrauterine growth restriction compared to MDS– patients, but did not have higher odds of gestational diabetes or preeclampsia **(Figure 3)**.
- Among patients with observed pregnancy outcomes, MDS+ patients were significantly more likely to experience pregnancy loss, undergo pregnancy termination, and deliver by caesarean section than MDS– patients.
- Among patients with a live birth, MDS+ patients were more likely to have a preterm delivery.

Figure 3. Association between microdeletion screen status and pregnancy complications and outcomes

Pregnancy Complications & Outcomes	MDS- n (%)	MDS+ n (%)	Adj. OR (95% CI)	p
Total Cohort	287,169	119		
Ultrasound findings				
Suspected fetal congenital anomaly	55,898 (19.5)	65 (54.6)	4.9 (3.4, 7.1)	***
Suspected fetal chromosome abnormality	8,047 (2.8)	32 (26.9)	12.6 (8.2, 18.7)	***
Hydrops fetalis	112 (0.0)	<11 (<9.2)	20.7 (1.2, 94.3)	**
Abnormal ultrasonic findings	12,902 (4.5)	20 (16.8)	4.2 (2.5, 6.6)	***
Inconclusive fetal viability	42,980 (15.0)	17 (14.3)	0.9 (0.5, 1.5)	
Decreased fetal movements	28,003 (9.8)	12 (10.1)	1 (0.5, 1.8)	
Abnormal heart rate/rhythm	32,133 (11.2)	18 (15.1)	1.4 (0.8, 2.3)	
Other/unspecified fetal problems	5,768 (2.0)	<11 (<9.2)	4.4 (2.2, 8)	***
Cohort observed to ≥20 weeks GA	268,605	108		
Complications				
Gestational diabetes	28,874 (10.7)	11 (10.2)	0.9 (0.5, 1.6)	
Preeclampsia	15,200 (5.7)	<11 (<10.2)	0.6 (0.2, 1.5)	
Polyhydramnios	9,073 (3.4)	20 (18.5)	6.3 (3.8, 10.1)	***
Oligohydramnios	6,472 (2.4)	<11 (<10.2)	1.5 (0.5, 3.7)	
IUGR	28,002 (10.4)	24 (22.2)	2.4 (1.5, 3.7)	***
Cohort observed to pregnancy end	232,317	100		
Outcomes				
Elective termination	680 (0.3)	<11 (<11.0)	22.2 (8.6, 46.8)	***
Loss	5,740 (2.5)	<11 (<11.0)	3.1 (1.3, 6.3)	**
Live birth	197,766 (85.1)	68 (68.0)	0.4 (0.2, 0.6)	***
Preterm birth	30,365 (15.4)	17 (25.0)	1.8 (1.0, 3.0)	*
Unspecified end[a]	28,627 (12.3)	>10 (>10.0)	1.7 (1.0, 2.7)	*
Vaginal delivery	124,348 (53.5)	34 (34.0)	0.4 (0.3, 0.7)	***
C-section	66,393 (28.6)	39 (39.0)	1.6 (1.1, 2.4)	*

Adj. OR=adjusted odds ratio; CI=confidence interval; IUGR=intrauterine growth restriction. *Indicates p<0.05, ** indicates p<0.01, *** indicates p<0.001. Odds ratios adjusted for payer type and history of high-risk pregnancy. Cell sizes <11 masked to protect patient privacy. Blue ORs and CIs correspond to outcomes with significantly higher odds in MDS+, green ORs and CIs correspond to outcomes with significantly higher odds in MDS–, and grey ORs and CIs correspond to outcomes that did not have significantly different odds for either group. a. Pregnancies with a delivery code indicating an end to the pregnancy, but without specific evidence of an outcome such as live birth or loss.