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Cell-Free DNA Results Indicating Mosaic Monosomy X of Likely Maternal Origin: Impact on Genetic Counseling Practices and Patient Experiences

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ABSTRACT

Objective: To investigate the current genetic counseling practices involving a cfDNA result indicating mosaic monosomy X of likely maternal origin, and to better understand the perspectives of patients who have received this result.

Method: A total of 60 prenatal genetic counselors completed surveys about their experiences with this result, cfDNA consenting practices, and management practices. In addition, qualitative interviews were conducted with 5 patients to gain insight into their experiences with result disclosure and follow-up care.

Results: 95% of genetic counselors reported feeling prepared to counsel on these results. However, responses to current practices varied. Of the genetic counselors surveyed, 62% state that their approach to management does not differ if the patient is symptomatic. Responses indicated 95% of genetic counselors ordered a karyotype for maternal diagnostic testing, and 30% ordered a chromosomal microarray. Interviews of patients found that 100% were not aware of the possibility of receiving an incidental finding from cfDNA. Patients reported feeling surprised, confused, and worried when they received their results.

Conclusion: The majority of genetic counselors report feeling confident in counseling these results, but their current practices vary. Patients who receive these results are found to have a difficult time adapting due to feeling surprised and confused. Based on these findings, we believe professional practice guidelines are needed to establish clear management recommendations, which in turn would hopefully decrease patient and provider stress.

1 | Introduction

Cell-free DNA screening (cfDNA), also known as non-invasive prenatal testing, is a form of prenatal screening that has the highest sensitivity and earliest detection of the most common aneuploidies [1]. Pregnant individuals often pursue cfDNA testing to learn the sex or health status of their fetus [2]. However, cfDNA can expose incidental findings or results that may be unrelated to the original reason for ordering the screen [3]. The screening method samples cell-free DNA of placental

Summary

- What's already known about this topic?
  - Mosaic monosomy X can present with a broad phenotypic spectrum, and mildly affected individuals may reach adulthood without awareness of their chromosomal status.
  - Incidental ascertainment of suspected mosaic monosomy X via cell-free DNA screening during pregnancy can generate surprise and confusion.
- What does this study add?
  - There is limited literature related to genetic counseling management or patient perspectives of this cfDNA maternal incidental finding.
  - This study identified gaps that may benefit from clarification in future clinical practices.

origin from the maternal bloodstream and detects maternal malignancies or maternal chromosome aneuploidies, such as trisomy X, mosaic monosomy X, and some copy number variants, is possible [4].

Maternal findings incidentally detected on cfDNA, such as monosomy X, can be associated with health concerns that require surveillance, especially during pregnancy. Genetic counseling practices do not consistently report discussing the possibility of these incidental findings or following up on the results with appropriate referrals, even though these counseling points are recommended [5, 6]. Additionally, patients may receive pre-test counseling from another provider, such as an obstetrician, who may not discuss the possibility of incidental findings during pre-test counseling.

Monosomy X (45, X) is the most frequent karyotype associated with Turner syndrome. Turner syndrome is defined as the complete or partial absence of the second sex chromosome in some or all somatic cells. Complete absence of an X chromosome is detectable on cell-free DNA screening, although the positive predictive value of this finding is thought to be around 14.5% [7]. A diagnosis of Turner syndrome is typically confirmed by a peripheral blood 30-cell karyotype [8, 9]. There are several X chromosome variations, with approximately 40%–50% of individuals exhibiting a complete monosomy X in all cells, while 15%–25% display mosaic monosomy X characterized by two different cell lines: 45, X and 46, XX. Individuals with mosaicism can have a wide range of symptoms, from asymptomatic to severe. Some individuals at the milder end of this phenotypic spectrum may remain undiagnosed into adulthood [10]. Therefore, individuals who are unaware of their mosaic monosomy X status and seek cfDNA for pregnancy-related information may unexpectedly receive incidental results regarding their own chromosomal status [6].

Management of Turner syndrome is complex and requires lifelong multidisciplinary care [9]. Adults with Turner syndrome may have health concerns such as insulin resistance and type 2 diabetes, hypertension, nonalcoholic fatty liver disease, hyperlipidemia, thyroid disease, and risks of aortic dissection [8]. Management recommendations for mosaic monosomy X are described in less detail than those for fully affected individuals. With a lack of clear management guidelines, we suspect inconsistent management of this diagnosis across genetic counseling practices.

A UTHealth Houston Turner Syndrome Society of the United States survey highlighted practice discrepancies related to counseling about the cfDNA result of mosaic monosomy X of likely maternal origin. Only 35% of patient participants who had received this result completed diagnostic testing. Individuals with short stature, hearing loss, or a history of growth hormone treatment were more likely to complete diagnostic testing than those who did not present with clinical features related to Turner syndrome. However, the study did not assess whether diagnostic testing was offered to all participants [11]. A more recent study found that 62% of patients chose to pursue diagnostic testing [12]. Additionally, interviews of Australian patients who received a maternal sex chromosome aneuploidy result from prenatal cell-free DNA screening revealed that patients did not feel prepared to make decisions on these unexpectedly complex results [13].

To investigate the current genetic counseling practices before and after a cfDNA result indicating mosaic monosomy X of likely maternal origin, we surveyed genetic counselors about their experience disclosing and counseling these types of results. In the absence of clinical guidelines, we hypothesize that genetic counseling practices for patients with suspected mosaic monosomy X may vary considerably, leading to increased confusion and anxiety for patients. Therefore, we interviewed patients who have received this type of result to ascertain their perspectives and feedback. The results of this study may promote future recommendations for genetic counseling and follow-up after a cfDNA result indicating monosomy X of likely maternal origin.

2 | Methods

This study utilized quantitative surveys of prenatal genetic counselors and qualitative interviews of patients. The study was reviewed by the University of Alabama at Birmingham and UTHealth Houston Institutional Review Boards and determined to be exempt (IRB #300010624).

2.1 | Survey Participants

Genetic counselors were recruited through the National Society of Genetic Counseling Student Research listserv from September 13th of 2023 to October 27th of 2023. Eligible participants were English-speaking prenatal genetic counselors who had experience with patients whose cell-free DNA results reported monosomy X of likely maternal origin. Participants were prompted to read and agree to the informed consent statement upon clicking the survey link. A total of 68 surveys were submitted and 60 were considered complete for data

analysis. 17 survey participants were randomly selected to receive a $20 gift card.

2.2 | Survey Instrumentation

The survey instrument was developed in the REDCap Database, a secure web survey application. Survey questions were developed by the research team, which consisted of a genetic counseling graduate student, two certified genetic counselors, and two medical geneticists. A total of 14 questions were asked within three themes: demographics, clinical experiences, and follow-up care (see the full survey in Supporting Information S1). Question types included multiple choice, select all that apply, and open response questions.

2.3 | Interview Participants

Eligible participants were English-speaking adults who had previously participated in a study conducted by UTHealth Houston, which surveyed participants about the health implications of receiving a maternal sex chromosome aneuploidy result from cell-free DNA screening (Roberts et al., 2023). Study participants who consented to be recontacted for further research were contacted by email and telephone calls for recruitment. Participants were read aloud an informed consent statement and verbally agreed to participate in this study. Five of the 11 eligible individuals completed interviews for this study. Each interview participant was provided a $20 gift card for completing the interview.

2.4 | Interview Instrumentation and Procedures

A genetic counseling student (A.M.) conducted 5 virtual interviews on Zoom video conferencing using a semi-structured interview guide (see interview guide in Supporting Information S1) from August 2023 to December 2023. The interview guide was developed by the same research team that created the survey. The discussion was focused on the emotional impact of cell-free DNA results reporting monosomy X of likely maternal origin and the patient experiences with follow-up medical care. Interviews ranged from 27 to 33 min with an average length of 31 min. Interviews were recorded, transcribed, and de-identified to protect participant confidentiality.

2.5 | Data Analysis

Descriptive statistics were calculated to summarize the study data. Open responses were included to provide context to closed ended survey responses of "sometimes". Associations between years of experience as a genetic counselor, practice setting, clinical experiences, and follow up care were assessed using Fisher's exact tests with p-values < 0.05 being considered statistically significant.

3 | Results

3.1 | Genetic Counselor Survey Results

3.1.1 | Survey Participant Characteristics

A total of 4718 NSGC members received the NSGC Research Survey listserv, and 69 members participated in the survey. Eligibility criteria required survey participants to be prenatal genetic counselors who have had experience seeing patients with a cfDNA result indicating mosaic monosomy X of likely maternal origin. Nine survey responses were incomplete and removed from the study, resulting in 60 evaluable surveys. The majority of participants (57%) reported having less than 5 years' experience as a genetic counselor, which is consistent with NSGC membership in 2023 (NSGC, PSS, 2023). About half (52%) of participants work in a university hospital setting. Detailed participant characteristics are summarized in Table 1.

3.1.2 | Experiences With cfDNA Result of Mosaic Monosomy X of Likely Maternal Origin

When asked how many patients were seen with a cfDNA result indicating mosaic monosomy X of likely maternal origin, participants most frequently selected 9+ (32%), followed by 3–4

TABLE 1 | Survey participant characteristics.

Characteristics	*N* (%)
Years practicing as a genetic counselor	
< 5	32 (53%)
6 to 10	10 (17%)
11 to 20	11 (18%)
21+	7 (12%)
Region[a] practicing in	
Midwest[b]	17 (28%)
Southeast[c]	16 (27%)
West[d]	10 (17%)
Northeast[e]	8 (13%)
Southwest[f]	7 (12%)
Multiple regions	2 (3%)
Practice setting	
University hospital	31 (52%)
Non-university hospital	21 (35%)
Other setting	8 (13%)

[a]There were no responses received from provinces of Canada.
[b]North Dakota, South Dakota, Nebraska, Kansas, Minnesota, Iowa, Missouri, Wisconsin, Illinois, Indiana, Michigan, and Ohio.
[c]Arkansas, Louisiana, Mississippi, Kentucky, Tennessee, Alabama, Georgia, West Virginia, Virginia, North Carolina, South Carolina, and Florida.
[d]Washington, Oregon, California, Idaho, Nevada, Utah, Montana, Wyoming, Colorado, Hawaii, and Alaska.
[e]Pennsylvania, New York, Maryland, Delaware, DC, New Jersey, Vermont, New Hampshire, Massachusetts, Connecticut, Rhode Island, and Maine.
[f]Arizona, New Mexico, Texas, and Oklahoma.

(27%) (Table 2). Nearly every participant (95%) selected that they feel prepared to counsel patients about this result. Less than half of the participants (43%) reported discussing the possibility of maternal incidental findings with patients during pre-test counseling (Table 2). Listed below are some responses of those who answered 'sometimes' in response to discussing maternal incidental findings with patients in pre-test counseling:

TABLE 2 | Survey participant's result experience responses.

Result experience	*N* (%)
Number of patients seen with this indication	
1 to 2	13 (21.6%)
3 to 4	16 (26.7%)
5 to 6	8 (13.3%)
7 to 8	4 (6.7%)
9+	19 (31.7%)
Feel prepared to counsel for these result	
Yes	57 (95%)
Sometimes	3 (5%)
No	0
Counsel on the possibility of maternal incidental findings	
Yes	26 (43%)
Sometimes	24 (40%)
No	10 (17%)
Discuss the medical impacts of these results	
Yes	55 (92%)
Sometimes	2 (3%)
No	3 (5%)
Suspicious of age-related loss of the X chromosome	
Yes	17 (28%)
Sometimes	32 (53%)
No	11 (18%)
Suspicious of twin fetus demise	
Yes	10 (16%)
Sometimes	20 (33%)
No	30 (50%)
Approach to management differs depending on the patient's symptoms	
Yes	20 (33%)
Sometimes	3 (5%)
No	37 (62%)
Use of practice guidelines to manage these cases	
Yes, clinical practice [14]	18 (30%)
Yes, care of [15]	9 (15%)
Yes, not listed	12 (20%)
No	21 (35%)

> Often patients are referred to my clinic after they have already received [cell-free DNA], so we were not able to discuss prior to it being ordered.

> Honestly, sometimes the session is focusing on so many other things that I forget to mention it, or it is a quick consent session after finding an abnormal and I don't get into that information while we are focusing more on the potential diagnosis.

> Almost never but it has happened at least once when patients are particularly interested in every detail.

A slight majority of participants (53%) selected that they are "sometimes" suspicious of age-related loss of the X chromosome as an explanation for this result (Table 2). In the open responses of those who selected "sometimes," many responses state that maternal age and other clinical features (or lack of features of monosomy X) impact their suspicion of age-related loss of the X chromosome. Half (50%) of participants selected "no" to being suspicious of twin fetus demise (Table 2). Of those who selected "sometimes" to this question, they stated that factors impacted their suspicion of twin fetus demise include if an ultrasound has not yet been performed, if there is a known fetus loss, and if there are any concerning ultrasound anomalies or medical history. The performing laboratory's platform (SNP vs. quantitative technology) is another factor mentioned by several participants that impacts their suspicion. When asked if their approach to management differs if the patient is symptomatic, more than half of the participants (62%) selected "no" (Table 2). Listed below are the responses of those who selected 'sometimes':

> I may talk with them about the risks differently if they are symptomatic - for example I might talk about how their symptoms could be consistent with mosaic 45, X which could increase the risk.

> (I) would make cardiac/renal recommendations regardless, but fertility can be dependent on their individual circumstances. Typically, it is not a concern since they are pregnant, and most have reported no problems conceiving.

3.1.3 | Follow-Up Practices for cfDNA Result of Mosaic Monosomy X of Likely Maternal Origin

Almost all participants (95%) recommended a karyotype for diagnostic testing (Table 3). When asked if they recommend fetal diagnostic testing, the majority of participants (63%) selected "yes" (Table 3). The second most selected response (32%) was 'sometimes' for this question. Some factors that these participants state may change their recommendations for fetal diagnostic testing include the presence of fetal anomalies, availability of the performing lab to discuss the case, and patient interest.

TABLE 3 | Survey participant's result follow-up responses.

Result follow-up	*N* (%)
Which diagnostic testing method do you recommend?	
Karyotype	57 (95%)
Chromosomal microarray	18 (30%)
Fluorescence in situ hybridization	8 (13%)
Other	1 (2%)
Do you recommend fetal diagnostic testing?	
Yes	38 (63%)
Sometimes	19 (32%)
No	3 (5%)
Which barriers have you faced in ordering diagnostic testing?	
Patient interest	45 (75%)
Insurance coverage	34 (57%)
Difficulty with compliance	10 (17%)
Lack of recommendations	6 (10%)
No barriers	5 (8%)
OB not feeling comfortable	1 (2%)
Other	1 (2%)
Which specialties do you refer these patients to?	
Cardiology	47 (78%)
Adult genetics	38 (63%)
Endocrinology	18 (30%)
Nephrology	16 (27%)
Other	5 (8%)
What resources do you give these patients?	
Website	36 (60%)
Condition handout	28 (47%)
Advocacy group information	25 (42%)
No resources	8 (13%)
Other	4 (7%)

Additionally, several participants felt that "recommend" was too strong of a word and that they would offer fetal diagnostic testing to anyone with atypical cfDNA results. Participants most commonly report that patient interest is a barrier to ordering diagnostic testing, followed by insurance coverage (57%) (Table 3). When asked which specialties genetic counselors refer these patients to, the majority (78%) report referring to cardiology and more than half (63%) report referring to adult genetics (Table 3). Most participants (60%) reported directing their patients to an online resource (or Supporting Information S1 online) following disclosure of these results (Table 3).

3.1.4 | Survey Data Analysis

Survey responses on participants' experiences with this result and their follow up practices were compared to their reported number of years practicing as a genetic counselor using Fisher's exact test with a p-value < 0.05. There were two statistically significant findings. When asked about barriers faced when ordering diagnostic testing, genetic counselors who reported having been practicing for 21+ years were more likely to select "no barriers" ($p = 0.02$). When asked what resources the participants provided their patients, genetic counselors who reported that they had been practicing for < 5 years were more likely to select "a handout/fact sheet" ($p = 0.0343$).

3.2 | Patient Interview Results

3.2.1 | Patient Interview Characteristics

A total of 11 patients were contacted with an invitation to participate in an interview, and 5 participated. The patients' average age at delivery was 33 years, ranging from 25 to 36 years.

3.2.2 | Results Disclosure Experiences

All patients ($n = 5$) stated that pre-test counseling for cfDNA was performed by their OB, rather than by a genetic counselor (Table 4). Patients were asked about why they chose to pursue cfDNA and representative quotes are listed in Table 5. Several patients mentioned it being common practice at their OB's practice to offer the testing to every patient. Two patients said that the recommendation for cfDNA testing was related to advanced maternal age. One patient elected to pursue the testing because they wanted to learn the sex of their baby. All patients ($n = 5$) reported that they were not aware of the possibility of maternal findings (Table 4). The most frequent initial reactions to receiving the abnormal results were surprise and worry (Table 5). Most patients ($n = 3$) reported that the waiting time was the most challenging aspect of this experience (Table 5).

3.2.3 | Follow-Up Care Experiences

Most patients elected to pursue maternal diagnostic testing ($n = 3$) (Table 4). One participant said they had Fluorescence in situ Hybridization (FISH), one had a microarray, and one had a karyotype. The patients who did not pursue diagnostic testing stated that the primary reason was the financial burden of additional testing. Most of the patients elected not to pursue fetal diagnostic testing (Table 4) primarily because they chose to pursue diagnostic testing for themselves first (and then testing baby if the mother's results were normal) or because the fetal ultrasound showed no apparent anomalies. Most patients ($n = 3$) did visit specialists after receiving this result (Table 4). Three patients were evaluated by cardiologists and underwent echocardiograms. One patient was identified to be at risk for aortic dissection. One patient was referred to a Turner Syndrome specialty clinic and underwent evaluations by specialists in cardiology, endocrinology, and nephrology. Two patients were referred to specialists but elected not to follow through with the referrals because they identified no features or symptoms in themselves related to Turner syndrome. When reflecting on their experiences, three patients identified complete disclosure and education about the result as the most important

TABLE 4 | Interview participant's (P) responses.

Interview question	P1	P2	P3	P4	P5
Was pre-test counseling performed by a genetic counselor?	No	No	No	No	No
Did participant know of the possibility of maternal incidental findings?	No	No	No	No	No
Had participant previously heard of Turner syndrome/monosomy X?	No	Yes	Yes	No	Yes
Did participant have an accurate understanding of mosaicism?	No	Yes	No	No	Yes
Would participant pursue cfDNA again if they could go back?	Yes	Yes	Yes	No	Yes
Did participant have diagnostic testing?	Yes	Yes	No	No	Yes
Did participant have fetal diagnostic testing?	No	No	No	No	Yes
Did participant see any specialists? (Cardio, Endo, etc.)	Yes	Yes	Yes	No	No

TABLE 5 | Representative patient quotes.

Topic	Representative quote(s)
Influences in decision to pursue cfDNA	"I think they offer it to anyone over 35...as like a standard test."—P1
	"So, I'll be honest, it was strictly because I wanted to know the gender of my baby as soon as possible."—P4
Reaction to results	" Yeah, it was pretty surprising, and I was worried, you know because well first I was like okay I don't know what that means (the atypical result). So of course, I spiraled and was looking into it online and there wasn't much to find."—P1
	"I was really surprised. I Had no clue that could even be a possibility. And I think I was more confused because the genetic counselor that I talked to that was giving me the results and everything was kind of brushing it aside."—P2
Most challenging aspect of results	"I think it's been overwhelming, especially at first because I was in a situation where I'm in my third trimester of pregnancy. I'm finding out I have a genetic problem that can have a lot of health consequences."—P2
	"I think the uncertainty." — P3
	"I think that just finding out at the beginning and waiting, like the waiting time for getting the appointment for the genetic counselor."—P5
Advice for healthcare professionals	"Don't be so quick to dismiss things. And if you have something that looks suspicious, just investigate it more. Because being dismissive can have detrimental effects. If I wouldn't have investigated all this, I could've had a vaginal delivery with my son and ended up with an aortic dissection. It could have been fatal"—P2
	"I really think like making sure like there's an understanding of the information because it's a lot of information..."—P3
	"Maybe just giving people a little bit more information about it.... just to manage the sort of stress of the situation and whatnot, just like having a bit more information"—P5

elements of counseling. Additional reflections reported by participants are listed in Table 5.

4 | Discussion

The purpose of this study was to investigate prenatal genetic counseling practices for a cfDNA result indicating monosomy X of likely maternal origin, and to recognize the perspectives of patients who have received this result. Through surveys of genetic counselors, we found that most genetic counselors felt prepared to counsel on this result. However, the responses on their current practices vary. Patient interviews revealed that this result causes confusion, surprise, and worry. Our results align with observations by Roberts et al. that many patients do not complete maternal diagnostic testing after receiving this result (Roberts et al., 2023). The findings from our study suggest this decision may be influenced by patient interest, which refers to the individual's willingness and desire to engage in diagnostic testing, as well as the cost of pursuing further testing. Patient interviews indicate that patient interest in completing maternal diagnostic testing may be reduced if they believe they have no symptoms that align with the cell-free DNA result. It is a well-established concept that the cost of genetic testing and insurance coverage of the test impacts genetic testing uptake within cancer and pediatric genetics and is likely applicable to other areas of genetic testing such as prenatal and adult genetics [16, 17].

Survey data reveal that most genetic counselors have seen more than nine patients for this type of cfDNA result, which may explain why most of our participants reported feeling prepared to counsel this indication. However, we identified significant disparities in counseling topics related to potential maternal mosaicism for monosomy X, with marked variation in the frequency that counselors mention possibly maternal incidental findings, potential detection of age-related X chromosome loss or twin fetal demise, and their approach to management differing based on patient symptoms. These observations highlight a gap in current clinical guidelines and an urgent need to clarify best practices related to genetic counseling for cfDNA results with maternal incidental findings.

Although genetic counseling practices were variable, the differences between practices were not attributable to the number of years the participants had been working as a genetic counselor. This finding suggests that there are other factors altering genetic counselor's practices outside of the number of years they have been working, such as their clinic's recommendations for counseling this result, the amount of communication with labs, or their familiarity with the result. Additionally, survey results indicate that some genetic counselors are basing their management and result follow up practices on the patients' reported symptoms. This practice may be unreliable as patient reports cannot replace a clinician's evaluation, and there is the possibility of health concerns that present asymptomatically until an adverse health event (i.e., aortic dilation).

Surveys by Roberts et al. found that only 35% of patients with this cfDNA result completed diagnostic testing. In the present study, three of the five interviewed participants completed diagnostic testing. The two participants who declined diagnostic tests met with a genetic counselor to discuss this result and were counseled about additional options. Both of these participants identified the cost of further testing as a barrier for them, and one patient reported that she felt that she was healthy and did not believe that additional tests were relevant. The interview data describing why some patients may not pursue diagnostic testing complement the genetic counselor survey results reporting that patient interest and insurance coverage are the most common barriers for ordering diagnostic testing.

Each of the patient participants stated they were surprised by this result, which aligns with literature reporting that individuals with mosaic monosomy X may remain unaware of their chromosomal aneuploidy throughout their lives. Most individuals with mosaic monosomy X retain some degree of ovarian function, and other symptoms may not be detected [10]. However, latent risks for adverse health events may be increased. This topic was particularly salient to one interview participant who was determined to be at risk for aortic dissection. Knowledge of her mosaic monosomy X status changed management recommendations for her pregnancy and delivery to reduce this risk. Those who continue to remain unaware of their exact chromosome aneuploidy by not pursuing diagnostic testing could be unknowingly facing similar health risks, which may be particularly impactful during pregnancy.

Several interview participants stated that they felt confused after receiving this abnormal maternal incidental finding. This response may be caused by a lack of thorough pre-test counseling for cfDNA, as all participants stated that they did not recall being informed about the possibility of maternal incidental findings from cfDNA prior to testing. Three of the interview participants explicitly requested more information about cfDNA testing in general, and about the implications of their particular results. These findings support a prior study that found that patients pursuing cfDNA want to receive as much information as possible [2]. Although patients seem to be information-seeking, this does not seem to be a motivating factor for pursuing diagnostic testing. This result also supports the utility of pre-test counseling with a genetic counselor, as they are trained in educating patients and obtaining informed consent for testing. However, the genetic counseling workforce is too small to provide pre-test counseling for every prenatal patient. Possible solutions to this gap in care include educating other providers in appropriate and thorough pre-test counseling or utilizing other healthcare models such as educational videos or group counseling sessions.

Less than half (43%) of genetic counselors said they counseled on maternal incidental findings for cfDNA during pre-test counseling. Many participants explained that they typically only receive patient referrals after abnormal cfDNA results were already returned to patients, suggesting that another healthcare provider is providing cfDNA pre-test counseling. Patient interview responses complement this idea, as each participant stated that it was not a genetic counselor who consented them for cfDNA testing. Prior studies state that counseling on maternal incidental findings for cfDNA is recommended [5, 6]. The findings from our research suggest that most patients are not receiving thorough pre-test counseling for cfDNA. To eliminate the patients' feelings of surprise, worry, and confusion from receiving a maternal incidental finding from cfDNA, informed consent practices need to be more consistent by both genetic counselors and other obstetrics providers.

4.1 | Study Limitations

The results of this study were limited by not collecting all demographic data of the participants. It is possible that there are other factors influencing genetic counselor's practices with this result, such as the amount of support they receive within their practice setting or how much of the practice decisions are influenced by the obstetrics specialists they work with. Additionally, it is possible that patients' decisions to pursue diagnostic testing and to schedule appointments with appropriate referrals are impacted by factors such as compounding health concerns, socioeconomic status, or their own beliefs about genetic testing. The use of interpretive description is beneficial in understanding common experiences among patients who have received this cfDNA result. However, the experiences of the patients who participated in these interviews are limited in their generalizability and may not apply to all patients who receive this type of result. Additionally, with such a specific result, the patient population eligible to participate in interviews is niche. The interviews had a small sample size, which also contributed to limited generalizability of results.

4.2 | Practice Implications

The results of this study indicate the need for professional practice guidelines from the American College of Obstetricians and Gynecologists (ACOG), the society for Maternal Fetal Medicine (SMFM), and the American College of Medical Genetics and Genomics (ACMG) on cfDNA maternal incidental findings, including mosaic monosomy X. Clarification on counseling recommendations, including distinguishing true germline mosaicism versus age-related mosaicism, may alleviate some of the current counseling inconsistencies.

The findings emphasize the importance of discussing the possibility of maternal incidental findings during pre-test counseling for cfDNA. The patient interview data highlighted patients' surprise and confusion in receiving this type of result after they had not been counseled on the possibility of maternal incidental findings.

The results also highlight the need for a longitudinal cohort study of patients who receive a cfDNA result indicating monosomy X of likely maternal origin. Following these patients over several years could clarify the medical intervention needs they may have and could inform practice guidelines on appropriate counseling topics and referrals to place after receiving this result. Furthermore, both genetic counselors and patients mentioned the need for resources to assist in patient understanding of cfDNA maternal incidental findings.

5 | Conclusions

This study provides insight into current prenatal genetic counseling practices for a cfDNA result indicating monosomy X of likely maternal origin, and the perspectives of patients who have received this result. The results indicate that the majority of genetic counselors feel confident in counseling these results, but their current practices vary. Patients who receive these results are found to have a difficult time adapting due to feeling surprised and confused. These findings suggest that practice guidelines for this indication may be helpful in providing consistency among genetic counselor practices and alleviating the stress of results disclosure for patients.

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Ethics Statement

Approval was obtained from the University of Alabama at Birmingham and UTHealth Houston Institutional Review Boards and determined to be exempt (IRB #300010624). The study was conducted in accordance with the Helsinki Declaration.

Consent

All participants were provided with a written or verbal consent and agreed to participate in this research study.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available upon request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.