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Shifting Paradigms: Twin Gestations in the Age of Cell-Free DNA

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I. Background

Prenatal screening options for aneuploidy changed significantly with the introduction of cell-free DNA (cfDNA) based screening tests. These cfDNA options have dramatically shifted the testing paradigm in aneuploidy evaluation during pregnancy. Given the unique biological factors in twin pregnancies such as zygosity and chorionicity, there are some known limitations related to any testing method. Despite these limitations, screening and diagnostic options are still typically discussed with patients who have twin pregnancies. The current study evaluates patient decisions regarding screening and diagnostic options in twin pregnancies before and after the introduction of cfDNA.

II. Methods

This study includes patients with twin gestations who were referred for genetic counseling during two time periods: 1,802 patients in the time period of 2009-2010 and 1,603 patients in 2014-2016. Patients who had previously had aneuploidy screening or diagnostic testing performed were excluded. The 2009-2010 patients were offered, at their physician's direction, both the option of maternal serum screening (MSS) and diagnostic testing such as chorionic villus sampling and amniocentesis, based on gestational age. The 2014-2016 patients were offered, at their physician's direction, all options including MSS, cfDNA, and diagnostic testing based on gestational age. During the course of the pretest genetic counseling discussion, patients were informed of their risks for aneuploidy based on risk assessment and twin gestation and were offered information about any potential benefits, risks, and limitations about their testing options, including any unique factors of testing in twin pregnancies. All statistical analyses employed two-sample, one-sided proportional z-tests to compare the 2009-2010 and 2014-2016 patient cohorts.

III. Results

Testing decisions were documented for each time period and compared (**Figure 1**). For the patients seen during 2009-2010, 47% of patients had MSS and declined diagnostic testing at the time of counseling. 20% of patients chose diagnostic testing while 2% wanted both tests. During this time period, 17% of patients declined all testing offered. The remaining 14% of patients wanted to follow-up with their physician prior to making a decision about MSS or diagnostic testing.

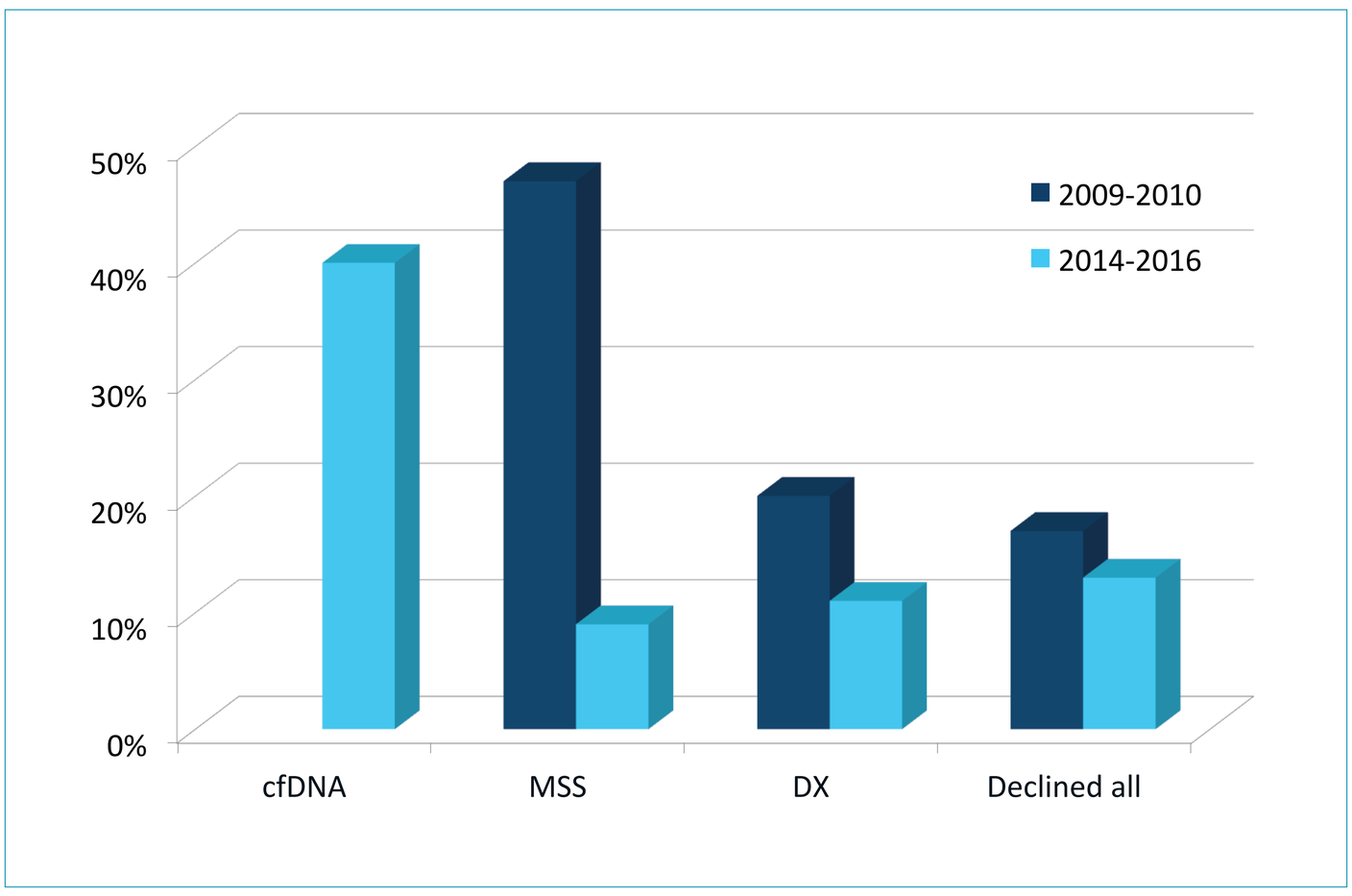
For the patients seen during 2014-2016, 9% of patients had MSS while 40% of patients chose cfDNA. 11% of patients chose diagnostic testing. Overall, 13% of patients declined all testing while 7% wanted a combination of tests. The remaining 20% of patients wanted to follow-up with their physician prior to making a decision about MSS, cfDNA, or diagnostic testing.

With the introduction of cfDNA, there were several notable changes in the testing decisions of patients with twin pregnancies (**Figure 2**). There was a significant decrease in the uptake of MSS ($p<0.001$) and diagnostic testing ($p<0.001$) from the 2009-2010 patient population compared to the 2014-2016 patient population. This shift can be attributed to the percentage of women (40%) who chose cfDNA in 2014-2016. Also of note was the significant decrease in the percentage of women who declined all testing once cfDNA became available ($p=0.001$).

Figure 1. Patient testing decisions

	2009-2010	2014-2016
cfDNA	N/A	40%
MSS	47%	9%
DX	20%	11%
Both / Multiple tests	2%	7%
Declined all	17%	13%
Follow-up with OB	14%	20%

Figure 2. Shift in decision making



IV. Conclusion

Twin pregnancies have historically been more challenging in regards to aneuploidy screening when considering both screening and diagnostic testing options. These challenges have included decreased detection rates for aneuploidy screening and potentially increased risks for losses related to diagnostic options, when compared to singleton pregnancies. The 2016 ACOG Practice Bulletin: Screening for Fetal Aneuploidy[1] noted that aneuploidy screening in twin gestations is not as accurate as singleton gestations and that limited prospective data or evidence is available for either MSS or cfDNA in twin pregnancies. Studies presented subsequent to this 2016 ACOG practice bulletin have provided evidence of the screening efficacy of cfDNA in twin pregnancies.[2] Our study clearly demonstrates that the vast majority of patients with twin pregnancies, when counseled about screening compared to diagnostic testing, prefer to pursue screening options first. Furthermore, once cfDNA became available as a screening option, there was a significant shift towards cfDNA and away from both MSS and diagnostic testing. The provision of clear information to patients considering all screening and diagnostic options is critical, especially with twin gestations, in order to support effective decision making and informed consent.

V. References

1. Practice Bulletin No. 163: Screening for Fetal Aneuploidy. *Obstet Gynecol*. May 2016, Volume 127, Issue 5.

2. Over a Half Million Noninvasive Prenatal Tests: A Clinical Laboratory Experience Khanna Adity MS LCGC; Almasri, Eyad PhD; Boomer, Theresa MS; CG/MB(ASCP), CGC; Wardrop, Jenna MS, LCGC; McCullough, Ron PhD; Cacheris, Phillip MD, PhD. *Obstet Gynecol*. May 2017.

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