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Response to Sahoo *et al*.

To the Editor: We thank Dr Sahoo et al.[1] for their letter highlighting important issues related to the detection of segmental aneuploidies and microdeletions by noninvasive prenatal testing. Many women, clinicians, and counselors are under the impression that cell-free DNA testing (noninvasive prenatal testing; NIPT) provides highly accurate results and are choosing noninvasive screening to avoid invasive diagnostic testing. In a follow-up to our case report,[2] Dr Sahoo and colleagues now document a high false-positive rate for microdeletion syndromes in a significant cohort of pregnant women, using tests offered by commercial companies. Moreover, due to incomplete coverage of the genome, other structural rearrangements and/or pathogenic genomic imbalances can be missed. Positive cell-free DNA findings require extensive invasive diagnostic testing to rule out genomic fetal pathology, as well as counseling and follow-up procedures to exclude possible maternal chromosomal alterations and gynecological and cancer disorders that can exist in pregnant women with a normal fetal karyotype.[3,4] Currently, five to seven chromosomal regions are targeted by various providers for cell-free DNA microdeletion screening, but these yield highly discordant results. Clearly, the magnitude of the problem will increase dramatically when commercial companies start offering genome-wide deletion and duplication testing. As previously noted by us and expanded on by Dr Sahoo et al., the inconclusive cell-free DNA results for microdeletion testing are confusing, thereby adding unnecessary stress and anxiety to the expectant mother and her health-care providers. Clinical validation for cell-free DNA microdeletion testing has been sacrificed in a commercial race to expand indications for noninvasive testing. Although there is considerable optimism about noninvasive screening for submicroscopic chromosome aberrations associated with clinically significant disorders,[5] the reliability and accuracy of NIPT for detection of such conditions have not been subjected to the rigor necessary to make this a valid clinical test. We recommend that additional research studies be completed and results followed up in academic institutions with appropriate diagnostic testing before clinical noninvasive testing for segmental aneuploidies and microdeletions is offered in clinical practice.

DISCLOSURE

The authors declare no conflict of interest.

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