

Distribution of Abnormal Karyotypes among Positive Maternal Serum Screening Results

Elaine Chen¹, Gila Muskin², Naomi Nakata¹, Sucheta Bhatt¹, Neil S. Silverman², Lawrence D. Platt² ¹Genzyme Genetics, Los Angeles, CA, United States, ²Center for Fetal Medicine and Women's Ultrasound, Los Angeles, CA, United States

Maternal serum screening has been an effective tool for prenatal risk assessment of Down syndrome and trisomy 18. We analyzed 1,061 samples positive for Down syndrome and/or trisomy 18 through Genzyme Genetics' first trimester, integrated, or sequential prenatal serum screening from July 1, 2006 through June 30, 2009 that were subsequently found to have abnormal karyotypes. We determined the percentage with karyotypes other than Down syndrome or trisomy 18, and the distribution of these karyotypes among the different screening results. Overall, 310 cases (29%) were found to have a karyotype other than Down syndrome (DS) or trisomy 18 (T18): 54 (17%) had trisomy 13; 46 (15%) had Turner syndrome; 47 (15%) had 47,XXX or 47,XXY; 47 (15%) had another autosomal trisomy; 25 (8%) had triploidy; and 91 cases (29%) were found to have other chromosome abnormalities, including deletions or duplications, marker chromosomes, and structural rearrangements. Among the different subgroups, 210/677 cases (31%) positive for DS only had karyotypes other than DS; 39/91 cases (43%) positive for T18 only had karyotypes other than T18; and 61/293 cases (21%) double positive for DS and T18 had karyotypes that were neither DS nor T18. A karyotype of Turner syndrome accounted for 12% of all cases positive for T18, compared to 4% of cases positive for DS and 3% of the double positive cases ($p=0.0007$). Triploidy accounted for 14% of all cases positive for T18, compared to 1% of cases positive for DS and 1% of the double positive cases ($p<0.0001$). 47,XXX and 47,XXY accounted for 6% of all cases positive for DS, compared to 1% of cases positive for T18 and 2% of double positives ($p=0.0074$). Other chromosome abnormalities (excluding trisomy 13 and other autosomal trisomies) accounted for 12% of all cases positive for DS, compared to 4% of cases positive for T18 and 2% of double positives ($p<0.0001$). Among women less than 35 years of age, 19/27 cases (70%) positive for T18 had a karyotype other than T18. These data support previous findings that 30-40% of cases ascertained through positive maternal serum screen will have a chromosome abnormality other than DS or T18. The data further reveal that the distribution of karyotypes differs depending on screening result. These findings suggest that prenatal maternal serum screening for DS and T18 is not only an effective screening tool for other aneuploidies, but may also be helpful in identifying pregnancies with other chromosomal rearrangements. Ultrasound findings may help to delineate the underlying chromosome abnormality. Genetic counseling should include a discussion of these other possibilities, as they may affect patients' decisions regarding invasive testing.