PROOF OF CONCEPT AND CLINICAL VALIDATION OF TRISOMY TEST® IN DETECTION OF VARIOUS SUBCHROMOSOMAL ABERRATIONS OVER THE WHOLE GENOME

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Introduction: Whole genome approach used in non-invasive prenatal testing enables detection of various subchromosomal aberrations. According to published data, the most critical parameters for detection are fetal fraction, size, position of particular aberration and local coverage. Due to the low frequency and high variability of subchromosomal aberrations, there is a lack of clinical validation data.Aim: To test the clinical utility of TRISOMY test® for various microaberrations detection across the whole genome.Materials and Methods: Artificially prepared DNA samples originated from clinically affected male probands or Corriel Repository biobank with known microdeletions were used in the proof of concept study. Aberrations from 0.9 Mb to 21 Mb and targeting fetal fractions from ~ 5% to ~ 20 % with at least 10 million reads were analyzed.Plasma samples from pregnant women carrying fetuses with different subchromosomal aberrations previously detected by invasive procedure were blinded and used in the validation study. Aberrations from 1 Mb to 52 Mb and fetal fraction ranging from 6.3% to 30.1% with more than 10 million reads were analyzed.Trisomy test® based on whole genome scan utilizing in-house bioinformatic pipeline was used for microaberrations detection.Results: Regarding proof of concept study aberrations events with size bellow 1 Mb, 3 Mb and above 5 Mb were detected at fetal fractions 12%, 8.7%, and 7.3%, respectively. Validation study results were in concordance with proof of concept study when aberrations with size 1 Mb was detected at fetal fraction 12.63%, aberrations bellow 3 Mb were not detected in case fetal fraction was less than 8.3%. Larger events were detected in samples having fetal fraction above 10.19%.Conclusion: We have shown the feasibility of whole genome based TRISOMY test® to detect various subchromosomal aberrations.