Objective
We sought to investigate the utility of chromosomal microarray analysis (CMA) for prenatal diagnosis of oral clefts, as compared with traditional chromosome analysis, for improved prenatal genetic counseling and discovery of a potential correlation between genotype and oral cleft.

Methods
This retrospective analysis encompassed 270 prenatal oral cleft cases with documented detailed ultrasound findings and CMA results from four referral centers. Detection rates for pathogenic copy-number variants (CNVs) were calculated and compared with cases for which chromosome analysis was also performed.

Results
The overall detection rate was 14.8% (40/270) for pathogenic CNVs by CMA, 7.2% (9/125) for the nonsyndromic cases, and 21.4% (31/145) for the syndromic cases. Of the nonsyndromic cases with ultrasound soft markers, 20% (5/25) were identified with pathogenic CNVs. CMA showed an improved detection rate of 15.3% (29/190) compared with 10.5% (20/190) for chromosome analysis.

Conclusion
This study not only highlights the improved detection of chromosomal defects by CMA in prenatal oral clefts but also deepens our understanding of oral clefts. The results suggest that CMA is highly recommended in prenatal invasive genetic testing not only for syndromic oral cleft cases but also for nonsyndromic cases with soft markers. Candidate genes including CRKL, AKAP8, SYDE1, BRD4 are worthy of further investigation regarding their role in human palatogenesis.