Population-based prevalence of 22q11 deletion syndrome and other chromosome abnormalities in a combined prenatal and postnatal cohort

Hui, L., Poulton, A., Kluckow, E., Lindquist, A., Hutchinson, B., Pertile, M., Bonacquisto, L., Gugasyan, L., Kulkarni, A., Harraway, J., Howden, A., McCoy, R., Da Silva Costa, F., Menezes, M., Palma-Dias, R., Nisbet, D., Martin, N., Bethune, M., Poulakis, Z., Halliday, J.

Introduction

- CMAs are now the gold standard of chromosome assessment in prenatal diagnosis and paediatrics.
- The expanding role of CMAs in reproductive medicine has not been comprehensively evaluated in a population-based cohort spanning both pregnancy and infancy.
- We have recently formed a research group of screening and diagnostic units in the Australian state of Victoria, called the *Perinatal Record Linkage (PeRL) collaboration*, which captures all instances of prenatal and postnatal chromosome testing performed in the state.
- The aim of this study was to create and analyse a population-based dataset of genomic tests performed on miscarriage, fetal, and infant samples in a state with > 73,000 annual births.

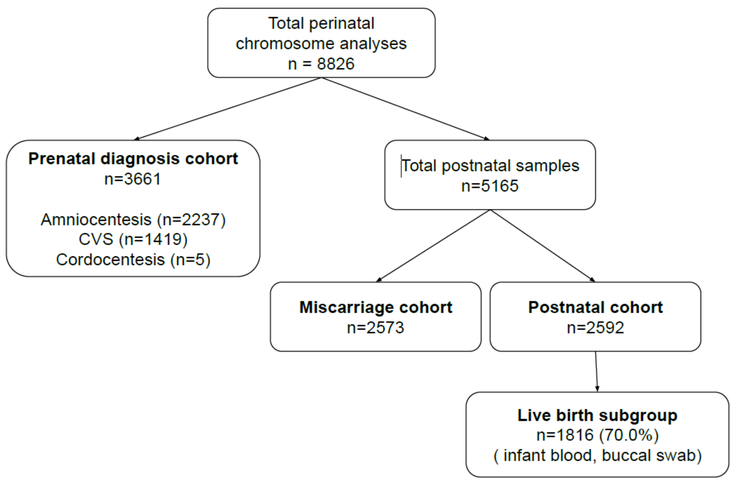
Methods

- Victoria, Australia has 73,000 births p.a, and median maternal age 31.5 years.
- Analysis of state-wide chromosome testing performed from Jan 2015 to Dec 2016.
- Data included all samples obtained via invasive prenatal diagnosis, and postnatal samples from pregnancy tissue and infants up to 12 months of age for the entire state.
- We analyzed our dataset for:
  1. The numbers and types of chromosome abnormalities in miscarriage, prenatal diagnosis and postnatal specimens.
  2. Trends in types of chromosome abnormalities with advancing development.
  3. The state-wide prevalence of the 22q11.2 deletion syndrome

Results

- 8826 perinatal samples were obtained**,** including 5165 miscarriages, 3661 prenatal, and 2592 postnatal samples (Figure 1).
- The majority (91.2%) were performed with chromosomal microarray.

Figure 1. Sample cohorts



- The frequency of chromosomal abnormalities declined significantly with increasing developmental stage, with the highest abnormality rate observed in miscarriage samples (50.9%) and the lowest rate in livebirths (13.4%).
- Conversely, the frequency of pathogenic copy number variants (CNVs) increased with developmental stage, from 1.9% of miscarriages to 6.0% of livebirths.
- The prevalence of 22q11 deletion syndrome was 1 in 4558 births; more than one third were diagnosed during pregnancy.

Figure 2 a and b. Results of chromosome testing in miscarriage and prenatal diagnosis cohorts, 2015-2016.

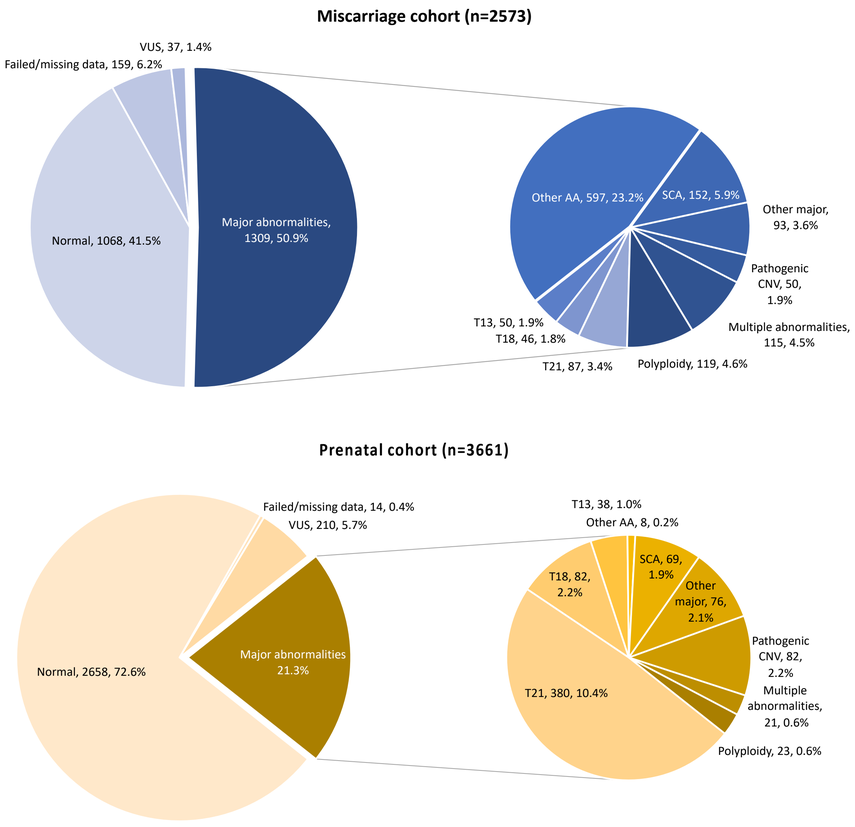
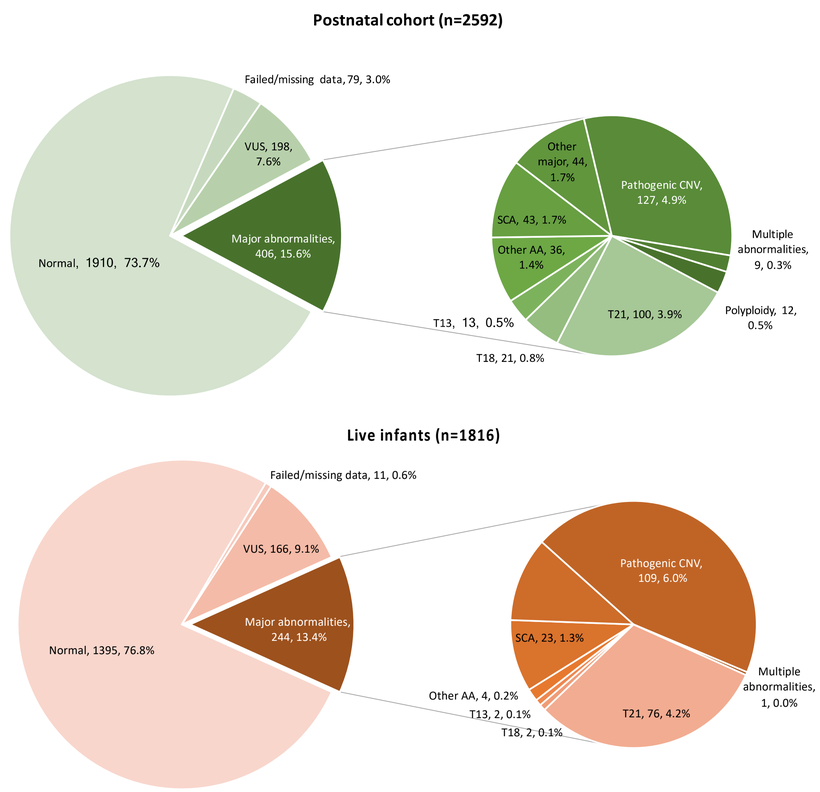


Figure 3 a and b. Results of chromosome testing in the postnatal cohort and live infant subgroup, 2015-



Conclusion

- CMA is now the standard method of diagnostic testing in reproductive and perinatal medicine.
- With advancing development, overall diagnostic yield declines, but pathogenic CNVs assume greater clinical importance.
- Integration of prenatal and postnatal diagnostic datasets provides important opportunities for estimating the prevalence of clinically important congenital syndromes.

Acknowledgements

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