Brazilian cohort-based structural variant profiling: insights for clinical interpretation

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INTRODUCTION AND OBJECTIVES

Structural variants (SVs), including deletions and duplications, contribute significantly to human phenotypic diversity and population variability. However, SVs remain less explored than single nucleotide variants, mainly due to their interpretative complexity and limited population studies. This study aimed to describe the frequency of clinically and non-clinically relevant SVs in a Brazilian admixed clinical population, highlighting the most frequent clinically significant SVs and the distribution of common polymorphisms.

METHODS

Following clinical evaluation, including prenatal, developmental, family history, and anthropometric data, microarray analyses were performed in 5,420 individuals to identify causative SVs.

RESULTS AND DISCUSSION

We identified the most common SV polymorphisms present in this Brazilian cohort, providing a detailed picture of their distribution and frequencies within this admixed population. For instance, at the region 6p21.32-p21.33 we have detected a variant allele frequency (VAF) for deletions events of 0.3101 vs. 0.3514 in dbVar and a VAF of 0.1145 vs. 0.2755 for duplications events. At 14q11.2, loss VAF was 0.1881 (vs. 0.095) and gain VAF 0.0953 (vs. 0.0994); 16p11.2 had a loss VAF of 0.1581 (vs. 0.0714) and gain VAF of 0.0673 (vs. 0.0414). In 1q31.3, loss VAF was 0.1225 (vs. 0.3289) and gain VAF 0.0090 (vs. 0.1822); 10q26.3 showed gain VAF 0.0645 (vs. 0.0288). The most commonly observed clinically significant SVs in our cohort included losses at 16p11.2 (0.39%), 7q11.23 (0.31%), 22q11.21 (0.30%), 1p36 (0.28%), 2q37 (0.28%), and 15q11.2 (0.28%).

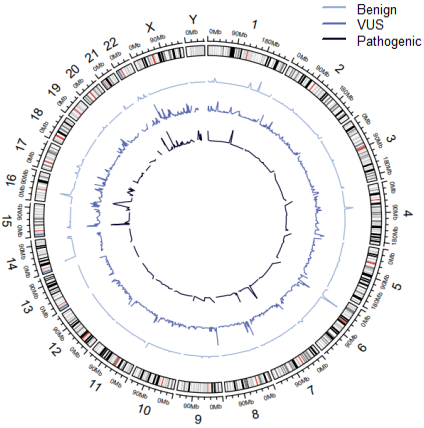

Figure 1 – Circosplot showing genomic distribution of SV across all chromosomes.

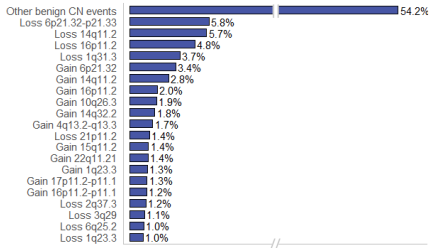

Figure 2 – Proportion of the most frequent CN benign events.

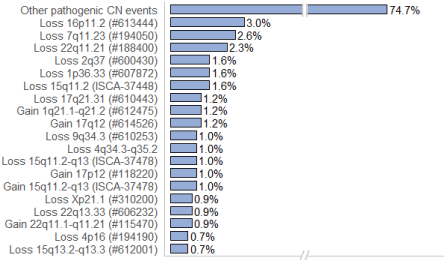

Figure 3 – Proportion of the most frequent CN pathogenic events.

CONCLUSION

Our findings highlight the unique distribution of SV polymorphisms in the Brazilian population, with frequencies that often differ from global databases. Loci such as 14q11.2 and 16p11.2 showed higher frequencies in our cohort, while 1q31.3 and 4q13.2-13.3 showed lower frequencies. These differences underscore the importance of regional studies for refining variant interpretation and pathogenicity assessments.

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