

A RETROSPECTIVE REVIEW OF CHROMOSOMAL INSTABILITY ASSESSMENTS IN A TERTIARY CARE HOSPITAL

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INTRODUCTION

PERIPHERAL BLOOD KARYOTYPING FOR CHROMOSOME INSTABILITY (CIN) RESEARCH IS USED TO DETECT CHROMOSOMAL ABNORMALITIES IN SUSPECTED CASES OF SYNDROMES SUCH AS FANCONI ANEMIA (FA), BLOOM SYNDROME, AND ATAXIA-TELANGIECTASIA. THE TEST ASSESSES CELLULAR SENSITIVITY TO CLASTOGENIC AGENTS, SUCH AS DIEPOXYBUTANE AND BLEOMYCIN, WHICH INDUCE CHROMOSOMAL BREAKS, GAPS, RING CHROMOSOMES, DICENTRICS, TRANSLOCATIONS, AND RADIAL FIGURES THAT ARE CHARACTERISTIC OF THESE SYNDROMES.

OBJECTIVE

TO DESCRIBE THE PROFILE OF CIN TEST RESULTS PERFORMED BY THE MEDICAL GENETICS SERVICE (SGM) OF THE HOSPITAL DE CLÍNICAS DE PORTO ALEGRE (HCPA) AND TO CORRELATE THESE RESULTS WITH THE MAIN CLINICAL INDICATIONS FOR WHICH THE TESTS WERE REQUESTED.

METHODOLOGY



A RETROSPECTIVE CROSS-SECTIONAL STUDY WAS CONDUCTED BY REVIEWING CIN TESTS PERFORMED BY THE PRENATAL DIAGNOSIS AND TISSUE CULTURE LABORATORY OF THE SGM/HCPA BETWEEN 2017 AND 2024. FOUR BLOOD CULTURES WERE PREPARED FOR EACH CASE: WITH AND WITHOUT THE DRUG, FOR BOTH THE CONTROL AND THE INDEX CASE. THIRTY METAPHASES FROM EACH CULTURE WERE ANALYZED. DATA WERE EVALUATED USING DESCRIPTIVE STATISTICAL ANALYSIS.

RESULTS AND DISCUSSION

THE MAIN CLINICAL INDICATIONS FOR PERFORMING THE TEST WERE BONE MARROW APLASIA (N = 39; 33.9%), SUSPECTED FA (N = 37; 32.17%), SUSPECTED ATAXIA-TELANGIECTASIA (N = 9; 7.8%), PANCYTOPENIA (N = 8; 6.96%), MYELODYSPLASTIC SYNDROME (N = 5; 4.35%), AND OTHER CONDITIONS (N = 17; 14.78%). AMONG THE 115 CIN TESTS PERFORMED DURING THE STUDY PERIOD, 5 (4.35%) WERE POSITIVE FOR CHROMOSOMAL BREAKS, 85 (73.92%) SHOWED NO SIGNIFICANT ABNORMALITIES, AND 25 (21.73%) YIELDED AN INSUFFICIENT NUMBER OF METAPHASES FOR CYTOGENETIC ANALYSIS.

THE LOW POSITIVITY RATE REFLECTS NOT ONLY THE RARITY OF CHROMOSOMAL INSTABILITY SYNDROMES BUT ALSO THE TECHNICAL LIMITATIONS INHERENT TO CELL CULTURE, PARTICULARLY IN PATIENTS WITH BONE MARROW FAILURE. GIVEN THESE CONSTRAINTS, THE IMPORTANCE OF INCORPORATING COMPLEMENTARY METHODS, SUCH AS MOLECULAR ANALYSES, TO ACHIEVE A DEFINITIVE DIAGNOSIS AND TO GUIDE CLINICAL MANAGEMENT MORE EFFECTIVELY IS UNDERSCORED. NEVERTHELESS, CIN TESTING REMAINS THE GOLD STANDARD FOR THE INITIAL SCREENING OF THESE SYNDROMES, REINFORCING THE RELEVANCE OF INTEGRATING CLASSICAL CYTOGENETIC APPROACHES WITH EMERGING GENOMIC TECHNOLOGIES IN THE DIAGNOSTIC SETTING.

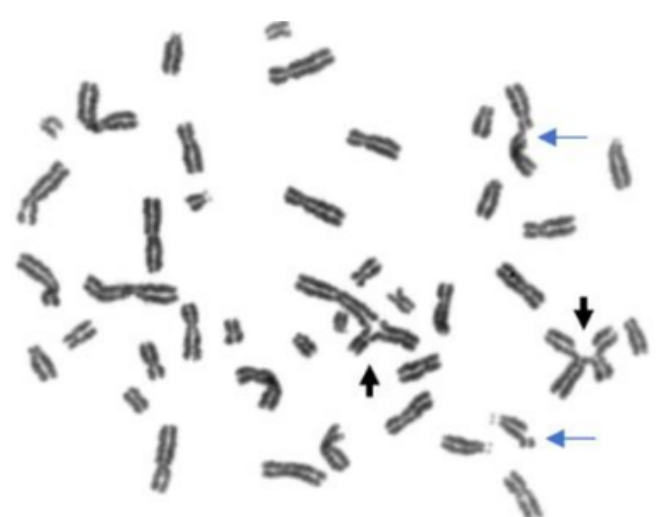


FIGURE 1. METAPHASE WITH STRUCTURAL CHROMOSOMAL ABNORMALITIES. BLUE ARROWS INDICATE CHROMATID BREAKS, AND BLACK ARROWS INDICATE RADIAL FIGURES.

CONCLUSION:

CIN TESTING IS CONSIDERED THE GOLD STANDARD FOR DETECTING CHROMOSOME INSTABILITY SYNDROMES SUCH AS FA. HOWEVER, IT CAN BE CHALLENGING TO PERFORM DUE TO THE NEED FOR SPECIALIZED LABORATORIES, THE USE OF TOXIC SUBSTANCES, AND THE COMPLEXITY OF THE ANALYTICAL PROCESS. ADDITIONALLY, CELL CULTURE FAILURE IS COMMON —PRIMARILY DUE TO THE LOW VIABILITY OF LYMPHOCYTES RESULTING FROM BONE MARROW FAILURE AND THE HIGH SENSITIVITY OF CELLS TO BREAK-INDUCING AGENTS. IN SUCH CASES, MOLECULAR TESTS SUCH AS NEXT-GENERATION SEQUENCING (NGS) PANELS, MULTIPLEX LIGATION-DEPENDENT PROBE AMPLIFICATION (MLPA), AND WESTERN BLOTTING ARE ESSENTIAL FOR CONFIRMING THE DIAGNOSIS, IDENTIFYING THE GENETIC SUBTYPE, AND GUIDING GENETIC COUNSELING FOR THE FAMILY.

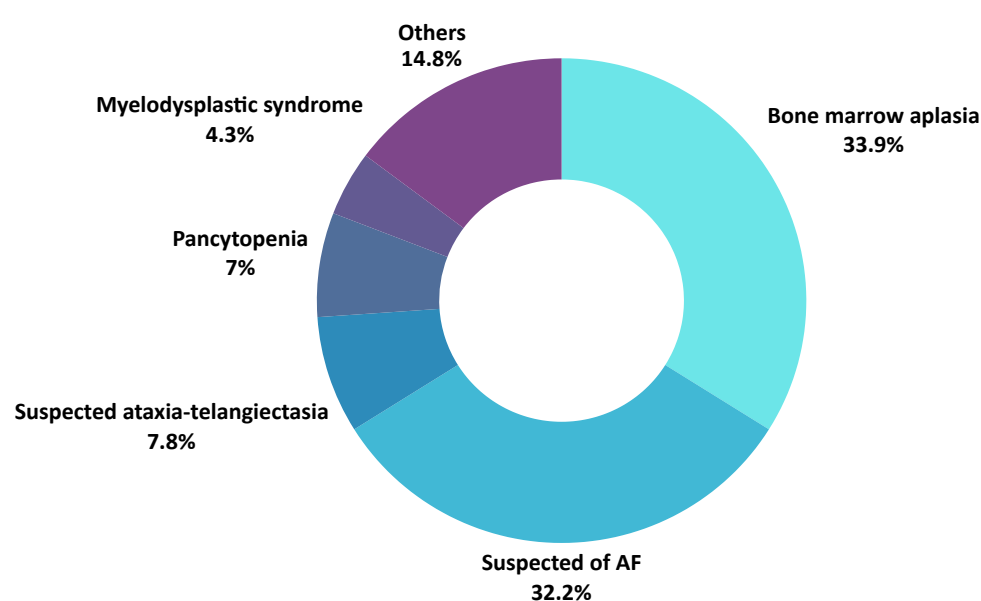


FIGURE 2. MAIN CLINICAL INDICATIONS FOR CHROMOSOMAL INSTABILITY TESTING.

REFERENCES

GARCÍA-DE-TERESA B, RODRÍGUEZ A, FRIAS S. CHROMOSOME INSTABILITY IN FANCONI ANEMIA: FROM BREAKS TO PHENOTYPIC CONSEQUENCES. GENES. 2020; 11(12):1528. [HTTPS://DOI.ORG/10.3390/GENES11121528](https://doi.org/10.3390/GENES11121528)

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