A spectrum and frequency of *CHEK2* variants in breast cancer in Latvia, initial results and literature review

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Abstract

Background: While *BRCA1/2* gene mutational spectrum and clinical features are widely studied, there is limited data on breast cancer-predisposing non-*BRCA* pathogenic/likely pathogenic variants (PV/LPVs) in Latvia. According to previous studies, *CHEK2* is the most frequent moderate-risk breast cancer predisposition gene. The study aimed to analyse the frequency and mutational spectrum of *CHEK2* PV/LPVs in Latvia and perform a literature review on the subject data in neighbouring countries.

Methods: *CHEK2*, *BRCA1*, *BRCA2*, *PALB2* testing with next-generation sequencing (NGS) was carried out in selected breast cancer cases. **Results:** In breast cancer affected cohort from Latvia 6 *CHEK2* variants classified as PV/LPVs were observed (6/105; 5,7%), including recurrent ones c.470T>C (1.9%) and del5395(ex9-10del) (1.9%), as well as single ones – c.1100delC (1%) and c.444+1G>A (1%). For the literature review altogether, 49 PubMed articles were found, 23 of which were relevant, representing *CHEK2* PV/LPVs in the population of interest. Ten publications are from Poland, eight from Russia, three from Latvia and two from Belarus. **Conclusions:** This study is the first report on complete *CHEK2* PV/LPVs screening in selected breast cancer affected cases in Latvia. The initial results are in line with other studies that *CHEK2* PV/LPVs frequency is around 5 to 6% of selected breast cancer cases. This is also the first report on c.1100delC and c.444+1G>A pathogenic variants from the Baltic States. High 8,6% population frequency of c.470T>C continues to question the variant's pathogenicity in particular populations. Other findings are concordant with previous reports from Latvia and neighbouring populations.