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Short Communication

Insights of Mitochondrial Genetics in Breast Cancer

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ABOUT THE STUDY

Caucasian women have a higher incidence and prevalence of breast cancer. Although changes in the mitochondrial genome are likely to play a role in carcinogenesis, the evidence is ambiguous and inconclusive. The goal of this study was to determine the frequency of polymorphisms associated with breast cancer by examining mitochondrial sequences of clinical cases diagnosed from various origins and reusing data from the public free access database GenBank.

For more than a decade, breast cancer has been the leading cause of death from malignant neoplasms in women, primarily affecting age groups between the fourth and sixth decades of life and affecting all socioeconomic levels. In the last five decades, the mortality rate for this neoplastic disease has increased significantly [1]. Between 1955 and 1960, the rate was around two to four deaths per 100,000 women, steadily rising in adult women of all ages, but with a greater impact after the age of 30. Breast cancer is a multifactorial disease with modifiable and non-modifiable risk factors, according to the evidence. The most important modifiable factors are obesity, menopause, smoking, and physical inactivity. Inherited genetic autosomal mutations have been linked to 10% of all breast cancer cases [2].

There are significant regional differences in incidence and prevalence in Latin America, with a higher frequency of breast cancer in areas with the highest socioeconomic incomes compared to indigenous areas with lower socioeconomic incomes. This evidence is consistent with the epidemiology of breast cancer worldwide, where it is more prevalent in developed countries and has a lower incidence and prevalence rate in third-world populations. Several authors have mentioned the relationship with the genetics of different human populations, with special attention to the different mitochondrial haplo-groups, as being more than a socioeconomic or environmental component [3]. There is, however, no evidence linking mitochondrial haplogroups to sporadic or familial hereditary breast cancer.

Because the control region D-loop of the mtDNA contains essential sequences for transcription and replication, some authors believe that Mitochondrial DNA (mtDNA) alterations play an important role in carcinogenesis. Previous research has suggested that polymorphisms in these non-coding regions of the control area may play an important role in breast cancer pathogenesis. These changes in the sequence can be linked to a specific phenotype and act as markers for the development of various cancers [4]. Some studies, however, suggest that different mitochondrial polymorphisms differ from one population to the next. Furthermore, some polymorphisms are more closely linked to the presence of breast cancer than others.

Many studies have concentrated on polymorphisms associated with regions involved in protein and RNA synthesis for mitochondrial metabolism. The A10398G polymorphism, associated with the synthesis of the protein NADH-ubiquinone oxidoreductase 3 (ND3), has been identified as a biomarker in various populations such as Polish, Indian, Chinese, and, most notably, Afro-descendant groups. This polymorphism has also been linked to metabolic syndrome and mental disorders in Asian populations. In a meta-analysis, however, it was discovered that there is no association when analyzing this polymorphism individually, without correlating with other mitochondrial polymorphisms in women with this cancer [5]. Although the *A10398G* substitution confers an increased risk of breast cancer in Caucasian American human groups of European descent, other polymorphisms with greater statistical significance, such as the *T16519C* located in the control region, have been identified.

Other research has concentrated on *T16519C*. In particular, the mutation in the D-loop associated with an increased risk of breast cancer, which can occur alone or in combination with other mitochondrial protein-coding gene alterations such as *A10398G*, *G13368A*, or *C14766T*. Furthermore, the combination of several variants produced a significant predictive breast cancer factor. *A10398G*, along with other mutations such as *T4216C*, *G9055A*, *A12308G*, and *T16519C*, is thought to increase the risk of developing breast cancer in women.

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The frequency of two novel D-loop polymorphisms, one at position 16290Tins and the other at position 16293Adel, was statistically significantly higher in breast cancer patients than in controls [6]. According to the findings, two novel polymorphisms in the D-loop could be candidate biomarkers for breast cancer diagnosis in Bangladesh women.

Despite these promising findings, and the fact that the majority of these mtDNA polymorphisms have functional consequences, associations between specific polymorphisms and cancer risk have been hotly debated. Several studies involving the association of specific polymorphisms with cancer risk have been thoroughly examined due to flawed experimental design, interpretation, and poor data quality. Many of these mtDNA variants may be inconclusive due to artefacts caused by genotyping errors or poor experimental design. However, because of its potential utility as a diagnostic tool, the mitochondrial DNA study and its relationship to cancer must remain an important focus of oncological biomarker research, with an adequate study design, population stratification, and independent replication of the results.

The goal of this study was to determine the frequency of polymorphisms associated with breast cancer by examining mitochondrial sequences of clinical cases diagnosed from various origins and reusing information from the public free access database GenBank.

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