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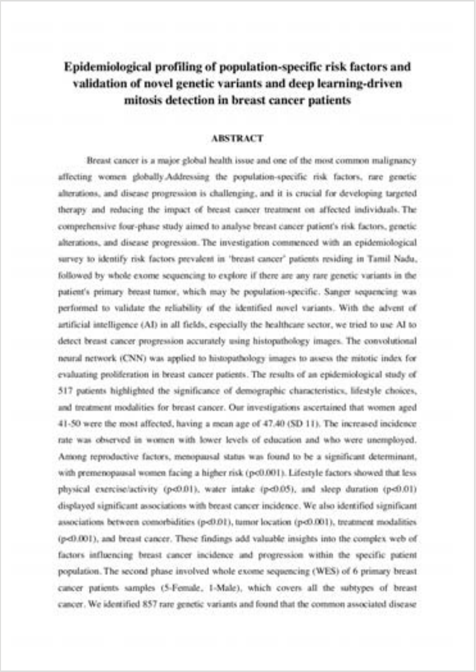

**Epidemiological profiling of population-specific risk factors and validation of novel genetic variants and deep learning-driven mitosis detection in breast cancer patients**

**ABSTRACT**

Breast cancer is a major global health issue and one of the most common malignancy affecting women globally.Addressing the population-specific risk factors, rare genetic alterations, and disease progression is challenging, and it is crucial for developing targeted therapy and reducing the impact of breast cancer treatment on affected individuals. The comprehensive four-phase study aimed to analyse breast cancer patient's risk factors, genetic alterations, and disease progression. The investigation commenced with an epidemiological survey to identify risk factors prevalent in 'breast cancer' patients residing in Tamil Nadu, followed by whole exome sequencing to explore if there are any rare genetic variants in the patient's primary breast tumor, which may be population-specific. Sanger sequencing was performed to validate the reliability of the identified novel variants. With the advent of artificial intelligence (AI) in all fields, especially the healthcare sector, we tried to use AI to detect breast cancer progression accurately using histopathology images. The convolutional neural network (CNN) was applied to histopathology images to assess the mitotic index for evaluating proliferation in breast cancer patients. The results of an epidemiological study of 517 patients highlighted the significance of demographic characteristics, lifestyle choices, and treatment modalities for breast cancer. Our investigations ascertained that women aged 41-50 were the most affected, having a mean age of 47.40 (SD 11). The increased incidence rate was observed in women with lower levels of education and who were unemployed. Among reproductive factors, menopausal status was found to be a significant determinant, with premenopausal women facing a higher risk ($p<0.001$). Lifestyle factors showed that less physical exercise/activity ($p<0.01$), water intake ($p<0.05$), and sleep duration ($p<0.01$) displayed significant associations with breast cancer incidence. We also identified significant associations between comorbidities ($p<0.01$), tumor location ($p<0.001$), treatment modalities ($p<0.001$), and breast cancer. These findings add valuable insights into the complex web of factors influencing breast cancer incidence and progression within the specific patient population. The second phase involved whole exome sequencing (WES) of 6 primary breast cancer patients samples (5-Female, 1-Male), which covers all the subtypes of breast cancer. We identified 857 rare genetic variants and found that the common associated disease