ABSTRACT

Introduction: Breast cancer ranks as the foremost prevalent cancer worldwide, and a rising burden has been associated with it for the past couple of years. In India, every year, approximately there are 100,000 new breast cancer diagnoses. A receptor for Vitamin D (VDR), belonging being a family of nuclear receptors for steroid hormones, contributes a key role in the biological function of calcitriol, an active form of vitamin D. Several Epidemiological studies have shown associations between breast cancer and the VDR gene polymorphisms, yet no conclusive results were obtained. Also, apart from these studies, the role of VDR gene polymorphisms in relation to steroid receptor (estrogen and progesterone) status is still limited.

Aim: The objective of this study is to identify the association of VDR FokI, ApaI, and BsmI genotypic distribution frequency with the risk of breast cancer and also across different prognostic variables.

Methodology: The case-control study consisted of 220 samples, including 110 breast cancer patients and 110 age-matched control women aged 30-70 years. PCR-RFLP genotyping was performed using DNA extracted from blood and assessment of serum levels of 25-hydroxyvitamin D.

Results: An analysis of the 5' FokI VDR variant revealed a significant association with increased breast cancer risk, with odds ratios of 5.49 (FF) and 6.00 (Ff), both demonstrating statistical significance ($P < 0.05$), and a chi-square value of 0.006. The 3' VDR polymorphism BsmI sequence showed minimal association with breast cancer risk. The bb genotype had a significantly lower odds ratio of 0.056 ($P < 0.05$). Conversely, the BB and Bb genotypes exhibited no statistically significant associations with odds ratios of 1.76 (95% CI: 0.36–8.54; $P > 0.05$) and 1.30 (95% CI: 0.27–6.25; $P > 0.05$), respectively. Furthermore, the Fok1 FF polymorphism and

ER had statistically significant interactions with a significant p-value of 0.024 with an odd ratio of 2.53 (95% CI: 1.163, 5.514). Also, ApaI AA polymorphism and ER show statistically significant interactions leading to a statistically significant p-value of 0.017 with an odd ratio of 1.26 (95% CI: 0.592, 2.70). In neither case did the Fok1 polymorphism or ApaI polymorphism have statistically significant interactions with PR or Her2. The BsmI genotype, besides, did not show a significant correlation with ER, PR, or Her2 status. Additionally, The p-value for serum Vitamin D levels was found to be highly significant at 0.000, indicating that the levels were significantly lower in individuals newly diagnosed with breast cancer compared to those in the healthy control group.

Conclusion: Our study found a notable link between breast cancer risk and VDR (FokI) polymorphism FF and Ff genotypes, with minimal impact observed for (BsmI) polymorphism bb genotype that is possibly a susceptible risk factor for the development of breast cancer. Also, ApaI AA and FokI FF polymorphism and ER had statistically significant interactions. This implies that certain genetic variations, especially in the FokI polymorphism of the vitamin D receptor gene, are associated with an elevated risk of breast cancer. In addition, vitamin D levels showed a potential link connecting vitamin D deficiency and an increased risk of cancer of the breast, signifying a statistically significant difference between the two groups.

Keywords: Breast Cancer, Vitamin D, Vitamin D receptor, gene polymorphisms, FokI SNP, ApaI SNP, BsmI SNP, Steroid receptor status.