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PTPH1 immunohistochemical expression and promoter methylation in breast cancer patients from India: A retrospective study

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Abstract

Protein Tyrosine Phosphatase H1/Protein Tyrosine Phosphatase Non receptor Type 3 (PTPH1/PTPN3) is upregulated and/or mutated in glioma, ovarian, gastric, and colorectal cancers. Previous studies have documented that PTPH1-associated breast cancers exhibit enhanced sensitivity to tamoxifen and tyrosine kinase inhibitors through dephosphorylation of ER and epidermal growth factor receptor, respectively. Owing to the key role that PTPH1 plays as a biomarker in predicting the response of chemotherapeutic drugs and lack of studies on Indian breast cancer patients, the present study investigated PTPH1 protein expression and its relationship to clinical features, ER/PR/HER2/neu statuses, and methylation of promoter in breast cancer tissues ($n = 67$) among Indian population by immunohistochemistry and methylation specific polymerase chain reaction. PTPH1 expression was upregulated in 58.21% (39/67) and downregulated in the rest of tumor specimens, and it correlated with ER, PR, and HER2/neu statuses with p values of <0.0001, 0.0113, and 0.0448, respectively. Additionally, we found that the 2 kb region upstream of *PTPH1* gene harbored CpG sites within, and was ubiquitously methylated in breast cancer ($n = 13$), colon cancer tissue ($n = 1$), uterine cancer tissue ($n = 1$), normal breast tissue ($n = 1$) in addition to Hela and MCF7 cell lines. In conclusion, our data showed a strong correlation of the PTPH1 status with the ER and ubiquitous nature of *PTPH1* promoter methylation at specific CpG sites irrespective of cancer types and protein expression. Our findings underscore the clinical relevance of PTPH1 expression in Indian patients and warrant additional studies to explore the importance of ubiquitously methylated promoter at specific CpG sites in upstream of the *PTPH1* gene.

KEYWORDS
breast cancer, epigenetics, PTPH1

1 | INTRODUCTION

Breast cancer is clinically and genetically heterogeneous. The classification and understanding of molecular regulators in breast carcinoma have evolved over decades not only to aid diagnosis but also for clinical decisions (Malhotra, Zhao, Band, & Band, 2010). In 2017, the estimated number of new cases of and deaths related to breast cancer in USA the was 2,52,710 and 40,610, respectively (https://seer.cancer.gov/statfacts/html/breast.html). In India, the Indian Council of Medical Research has reported breast cancer to be the most common cancer among women with 1.5 lakhs new cases of breast cancer reported in year 2016

