BREAST TUMOR KINASE EXPRESSION AND ESTRADIOL LEVELS AMONG BREAST CANCER PATIENTS IN LAGOS, NIGERIA

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BY

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A DISSERTATION SUBMITTED TO THE SCHOOL OF POSTGRADUATE STUDIES IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE AWARD OF MASTERS OF SCIENCE (M.Sc) DEGREE IN BIOCHEMISTRY IN THE DEPARTMENT OF BIOCHEMISTRY, COLLEGE OF SCIENCE AND TECHNOLOGY, COVENANT UNIVERSITY, OTA, OGUN STATE, NIGERIA

AUGUST, 2024

ACCEPTANCE

This is to attest that this thesis is accepted in partial fulfillment of the requirements for the award of the degree of Master of Science (M.Sc)in Biochemistry in the Department of Biochemistry, College of Science and Technology, Covenant University, Ota, Nigeria.

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DECLARATION

I, NNAJI, FAITH CHINASAOKWU (**22PCP02385)** declare that this research was carried out by me under the supervision of Dr. Titilope M. Dokunmu of the Department of Biochemistry, College of Science and Technology, Covenant University, Ota Nigeria. I attest that the thesis has not been presented wholly or partially for the award of any degree elsewhere. All the sources of materials and scholarly publications used in the dissertation have been duly acknowledged.

NNAJI, FAITH CHINASAOKWU

Signature and Date

CERTIFICATION

I certify that this dissertation titled "**BREAST TUMOR KINASE EXPRESSION AND ESTRADIOL LEVELS AMONG BREAST CANCER PATIENTS IN LAGOS, NIGERIA**" is an original work carried out by **NNAJI, FAITH CHINASAOKWU** (**22PCP02385**) in the Department of Biochemistry, College of Science and Technology, Covenant University, Ota, Ogun State, Nigeria, under the supervision of Dr. Titilope M. Dokunmu. I have examined and found the work acceptable as part of the requirements for the award of a degree of Master of Science (M.Sc) in Biochemistry.

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Prof. Akan B. Williams
(Dean, School of Postgraduate Studies) **Signature and Date**

DEDICATION

I would like to dedicate this report to the Almighty God for his grace, strength, and power in carrying out this exercise. May His name be praised forever and ever, Amen

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LIST OF ABBREVIATIONS

BC	Breast Cancer
BRCA1	Breast Cancer gene 1
BRCA2	Breast Cancer gene 2
BRAF	B-Raf proto-oncogene, serine/threonine kinase
PALB2	Partner and localizer of BRCA2
TP53	Tumor Protein p53
ATM	Ataxia Telangiectasia Mutated
CHEK2	Checkpoint Kinase 2
BRIP1	BRCA1 Interacting Protein C-terminal Helicase 1
EGFR	Epidermal Growth Factor Receptor
ErbB1	Erythroblastic Oncogene B1
HER1	Human Epidermal Growth Factor Receptor 1
ErbB2	Erythroblastic Oncogene B2
HER2	Human Epidermal Growth Factor Receptor 2
ErbB3	Erythroblastic Oncogene B3
GPER1	G-protein-coupled Estrogen Receptor 1.
HER3	Human Epidermal Growth Factor Receptor 3
ErbB4	Erythroblastic Oncogene B4
HER4	Human Epidermal Growth Factor Receptor 4
Ras	Rat Sarcoma
Ras	Rapidly Accelerated Fibrosarcoma
MEK	Mitogen-activated protein Kinase
ERK	Extracellular Signal-Regulated Kinase
PI3K-Akt	Phosphoinositide 3-Kinase - Protein Kinase B
JAK/STAT	Janus Kinase /Signal Transducer and Activator of Transcription

ABSTRACT

Cancer is a major factor in global death rates and a significant challenge to improving life expectancy worldwide. Breast cancer (BC), typified by the unregulated growth of abnormal cells within breast tissue, arises from a combination of genetic mutations, environmental factors, hormonal influences, and lifestyle choices. Studies have shown that the presence of Breast tumor kinase (BRK) gene overexpression results in increased BC cell proliferation and enhanced cell migration. Studies have also revealed that the dysregulation of estrogen (a hormone responsible for the proliferation and growth of specific cells in the body, which is also responsible for the development of secondary sexual characteristics in women) modulates some molecular signaling pathways involved in breast tumor growth and progression. This observational study aims to evaluate the expression levels of BRK and estradiol levels in BC patients as a prognostic marker in breast tumorigenesis in Nigerian patients. A total of forty women, 20 BC patients who had been histologically diagnosed, and 20 healthy control participants were recruited for this study after informed consent was obtained. Venous blood samples (5ml) were drawn from the study participants into anticoagulant tubes and transported to the molecular biology laboratory for analysis. Total RNA was extracted using the TRIzol reagent method. RNA concentration, integrity, and purity were analyzed using a NanoDrop spectrophotometer. cDNA synthesis and quantitative analysis of the relative expression levels of BRK were done using a Reverse transcriptase real-time qPCR machine. From the estradiol, 25ul plasma was used for enzyme-linked immunosorbent assay (ELISA) detection of estradiol according to the manufacturer's instructions. Overall, mean BRK expression levels in BC was significantly higher (1.6 folds higher) than the expression levels of BRK in healthy control ($P < 0.05$). Mean estradiol level in BC *vs* healthy control was 330 ± 27.42 and 309 ± 27.41 pg/mL, showing no significant difference in estradiol levels between the 2 groups. For the first time, this study reports BRK expression levels in Nigerian BC and healthy control and identified BRK as a prognostic marker for monitoring BC progression, thereby providing a suitable target for aggressive cancers common in Nigerian population. This study provides deeper insights into genetic contribution to cancer progression and a biomarker guide for treatment modalities.

Keywords: BRK, Breast cancer, Nigeria, aggressive, estradiol