POLYMORPHISM AND CIRCULATING LEVELS OF IGF-1, IGF-1R, AND IGF-BP3 AMONG PROSTATE CANCER PATIENTS IN LAGOS STATE, NIGERIA

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AUGUST, 2024

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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 MASTER OF SCIENCE, (M.Sc.) IN BIOCHEMISTRY IN THE DEPARTMENT OF BIOCHEMISTRY, COLLEGE OF SCIENCE AND TECHNOLOGY, COVENANT UNIVERSITY, OTA, NIGERIA

AUGUST, 2024

ACCEPTANCE

This is to attest that this dissertation is accepted in partial fulfillment of the requirements for the award of a 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, **AGBETUYI-TAYO, PRAISE TOMIWA** hereby declare that I carried out this research work under the supervision of Dr. Oluwakemi A. Rotimi (Supervisor) of the Department of Biochemistry, College of Science and Technology, Covenant University, Ota, Ogun State. I attest that the dissertation has not been presented either wholly or partially for the award of any degree elsewhere. All sources of data and scholarly information used in this dissertation were duly acknowledged.

AGBETUYI-TAYO, PRAISE TOMIWA

Signature and Date

CERTIFICATION

We hereby, certify that this dissertation titled "**POLYMORPHISM AND CIRCULATING LEVELS OF IGF-1, IGF-1R, AND IGF-BP3 AMONG PROSTATE CANCER PATIENTS IN LAGOS STATE, NIGERIA**" is an original research work carried out by **AGBETUYI-TAYO, PRAISE TOMIWA** with matriculation number **(22PCP02375)** from the Department of Biochemistry, College of Science and Technology, Covenant University, Ota, Ogun State, Nigeria, under the supervision of DR. OLUWAKEMI A. ROTIMI. We reviewed the work and determined that it meets the requirements for the award of the degree of Master of Science (M.Sc.) in Biochemistry.

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DEDICATION

This dissertation is dedicated to God for his never-ending faithfulness and grace throughout the course of this project.

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LIST OF ABBREVIATIONS

PCa	Prostate Cancer
IGF-1	Insulin-Like Growth Factor 1
IGF-1R	Insulin-Like Growth Factor 1 Receptor
GF	Genotype Frequency
SNP	Single Nucleotide Polymorphism
GH	Growth Hormone
EDTA	Ethylenediamine tetraacetic acid
STAT3	Signal transducer and activator of transcription 3
ELISA	Enzyme-Linked Immunosorbent Assay
MAPK	Mitogen-activated protein (MAP) kinase pathway
AKt	Protein kinase B

ABSTRACT

Prostate cancer (PCa) is the most prevalent cancer in sub-Saharan Africa, with over 77,000 new cases annually, and Nigeria accounting for approximately 30,000 of these cases. The insulin-like growth factor (IGF) pathway, crucial for cellular proliferation and apoptosis, is implicated in cancer progression, including PCa. Elevated plasma IGF-1 levels are associated with PCa progression, whereas increased levels of IGF binding protein 3 (IGF-BP3) may reduce PCa risk. Genetic variations in IGF-1, such as the C-T haplotype, are linked to poorer survival in PCa patients with bone metastases. This study aims to examine single nucleotide polymorphisms (SNPs) in the IGF-1 and IGF-1R genes and their relationship to plasma levels of IGF-1, IGF-1R, and IGF-BP3, and the risk of PCa among men in Lagos State. The case-control study consisted of 75 PCa patients and 75 paired healthy controls. Plasma levels of IGF-1, IGF-1R, and IGF-BP3 were measured using enzyme-linked immunosorbent assay (ELISA), and SNP genotyping (IGF-1: rs6219, rs6220, rs5742694; IGF-1R: rs2229765) was performed using TaqMan assay. No overall statistical difference was found in plasma levels of IGF-1, IGF-BP3, and IGF-1R between cases and controls, although the IGF-1/IGF-BP3 molar ratio was higher in PCa patients (42.67) compared to controls (19.04), indicating increased level of bioavailable IGF-1 in PCa patients. Chi-square analysis revealed a strong positive association (OR: 9.1; p: 0.026) between the A/A genotype of IGF-1R SNP (rs2229765 (A/G)) and PCa, suggesting that individuals with this genotype are more likely to develop PCa. Significant differences in IGF-1R and IGF-1 levels were observed for specific genotypes of rs5742694 and rs2229765 SNPs. In conclusion, genetic polymorphisms in IGF-1R and IGF-1 are associated with differential protein levels in PCa cases versus controls, indicating potential risk and protective factors in Nigerian men.

Keywords: Prostate cancer, IGF-1, IGF-1R, IGF-BP3, SNPs, Genetic polymorphis