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ORIGINAL ARTICLE

Molecular Characterization of PTEN Gene Alterations in Men with Prostate Cancer in Osun State

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ABSTRACT

Prostate cancer is known to be the most common cancer in men and a slow-growing malignancy that primarily occurs in men over 50 years of age. The aim of this study was to determine the genomic alterations of PTEN genes amongst men with prostate cancer in Osun State. About 234 tissue blocks drawn from the archives of the Department of Histopathology at the Obafemi Awolowo University Teaching Hospital, Ile-Ife. This was an analytical experimental design. Previously processed and diagnosed prostate cancer blocks between the years of 2014 to 2019 were selected for this study. The corresponding reports were also sought for each selected paraffin wax block. DNA was extracted from the tissue using the Dellaporta DNA extraction protocol. PCR was carried out in a GeneAmp 9700 PCR System Thermal cycler with a PCR profile for each primer. The amplified DNA was sequenced using a Genetic Analyzer 3130xl sequencer from Applied Biosystems. The results revealed the occurrence of genomic alterations in the PTEN genes in the prostate cancer tissue. The PTEN gene was observed to have been altered on positions 220, 265 and 268 on the amino acid. In addition, C deletion was observed in position 220, the presence of G-T mutation was observed in position 265 and another C deletion was observed in position 268. Routine genomic screening of adult male above 45 years of age is advocated to detect early as well as manage and treat patients with prostatic cancer.

Keywords: Prostate Cancer; PTEN gene; DNA extraction; Mutations.

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1.0 INTRODUCTION

Prostate cancer is the fifth most common cause of cancer-related mortality among males worldwide and the second most common type of cancer overall (Bray et al., 2018). In about 84 nations, it is the most common cancer in men, and it is more prevalent in the industrialized world. In the developing world, rates have been rising. Due to a surge in PSA testing, detection rose dramatically in several locations between the 1980s and 1990s (Ferlay et al., 2020). According to Zlotta et al. (2013) study, between 30% and 70% of Russian and Japanese men over 60 years who had passed away from unrelated reasons had prostate cancer (Singh et al., 2022). Men are frequently affected by prostate cancer, which typically prevalent among men aged 50 years and older (National Cancer Institute, 2021). This condition causes the prostate to grow abnormally, multiply uncontrollably, and eventually develop into a tumor (Ferlay et al., 2020). The prostate is a gland of the male reproductive system that surrounds the urethra and contributes to semen production, which serves as the medium for sperm transport (Geybels et al., 2017). The majority of prostate tumors grow slowly. Prostate cancer may not cause any symptoms in its early stages, but in its later stages, symptoms may include back or pelvic pain, blood in the urine, or difficulty or pain when urinating (Truong et al., 2017). Prostate cancer risk factors include age, race, and family history. Other late signs include fatigue, which is caused by low red blood cell counts (Steinberg et al., 2021). The incidence of prostate cancer increases substantially with age, with the majority of cases diagnosed in men aged 50years and older (Steinberg et al., 2021). The risk is increased by two to three times if a first-degree relative has the illness. Other variables include eating a lot of red and processed meat, and while the risk of consuming a lot of milk products is unclear, there has been a correlation with gonorrhea, however no explanation for this relationship has been found (Ferlay et al., 2020). Tyrosine phosphatase and tensin homologous proteins Glioblastoma, breast cancer, and prostate cancer are all tumor suppressed by Phosphatase and Tensin Homolog (PTEN) (National Cancer Institute, 2021). Instructions for producing an enzyme that is present in practically every tissue in the body are provided by the PTEN gene. By preventing cells from expanding and dividing (proliferating) too quickly or uncontrollably, the enzyme functions as a tumor suppressor, which helps regulate cell division (Bray et al., 2018). The PTEN enzyme must first attach to another PTEN enzyme (dimerize) before binding to the cell membrane in order to function. The PTEN enzyme removes phosphate Groups, which are made up of clusters of phosphorus and oxygen atoms, from other proteins and fats (lipids). Phosphatases are enzymes that perform this action (Gkountakos et al., 2019). PTEN-corresponding genes are found in the majority of mammals whose whole genomes are available (Singh et al., 2022). PTEN's tumor-suppressive effects are thought to be primarily caused by its capacity to dephosphorylate phospholipids or proteins and block the phosphatidylinositol 3-kinase pathway. PTEN expression has been demonstrated to cause apoptosis, halt cell migration, induce a G1 (good one) arrest, and stop the cell cycle (Mashhadi et al., 2014). Numerous cancers, such as glioblastoma, lung cancer, breast cancer, and prostate cancer, are largely caused by gene mutations (Flicek et al., 2014). Numerous neoplasms, such as primary central nervous system,

breast, prostate, colon, and bladder cancers, glioblastoma, and non-Hodgkin's lymphoma, have also been linked to genetic changes at the PTEN locus (Feng et al., 2016; Jia et al., 2023; Wilson & Zishiri, 2024). PTEN loss of function as a tumor suppressor gene accelerates tumor angiogenesis, cell proliferation, and death (Wilson & Zishiri, 2024). Magdalena et al. (2022), claims that inactivating TGF-signaling in the prostate epithelium and deleting the PTEN tumor suppressor can encourage both locally aggressive malignancy and metastatic disease. The phosphatase and tensin homolog gene (PTEN), which is found on chromosome 10q23.3 and acts as a negative regulator of the PIK3/Akt survival pathway, is the tumor suppressor gene most frequently lost in prostate cancer (Álvarez-Garcia et al., 2019). Mutations cause the PTEN gene to accumulate, which is linked to Cowden syndrome and kindred conditions where patients experience various organ hyperplastic lesions (harmatomas) with a higher chance of malignant transformation (Jamaspishvili et al., 2018; Pilarski, 2019). Monoallelic loss of PTEN is present in up to 60% of locally advanced prostate cancers, and complete loss of PTEN in prostate cancer is linked to metastasis and androgen-independent progression (Bray et al., 2018). In research on the genomic status of PTEN in prostate cancer, the two-color fluorescence insitu hybridization (FISH) test was initially used to determine PTEN copy number in formalin fixed paraffin embedded tissue preparations (Steinberg et al., 2021). When paired with the identification of other significant genetic biomarkers for prostate cancer, such as ERG, androgen receptor, and MYC, the evaluation of PTEN genomic status has shown advantageous for patient classification and treatment. Although they are less frequent than allelic deletions, point mutations in the gene and epigenetic silencing are also known to contribute to the loss of PTEN function and ultimately the genesis of prostate cancer. All things considered, PTEN is clearly a useful biomarker for prostate cancer (Álvarez-Garcia et al., 2019; Steinberg et al., 2021). When employed as a companion diagnostic for new therapeutic medications, FISH analysis of PTEN is advancing human prostate cancer toward improved cancer management and treatments (Charalampos et al., 2021; Daly et al., 2023). It has been demonstrated that gene mutations play a crucial role in cellular reprogramming and disease onset especially cancers. Recurrent somatic mutations, copy number alterations, and oncogenic structural DNA rearrangements (chromosomal abnormalities) have been found in primary prostate cancer, metastatic prostate cancer, and metastatic castration-resistant prostate cancers (mCRPC) (Álvarez-Garcia et al., 2019; Ferlay et al., 2020; Daly et al., 2023). PTEN is the most often mutated gene in prostate cancer, according to the combined findings of multiple research, it has been revealed that it has clinical significance. About 70% of patients with prostate cancer have been reported to have decreased PTEN expression. PTEN is a multifunctional tumor suppressor (Robinson et al., 2015; Hendricks et al., 2021). According to Robinson et al. (2015), PTEN is a key tumor suppressor that regulates cell survival and proliferation primarily by inhibiting the phosphatidylinositol 3-kinase–protein kinase B (PI3K–AKT) signaling pathway. However, PTEN also exerts important biological effects through AKT-independent pathways, contributing to the regulation of cell proliferation and other cellular processes (Hendricks et al., 2021; Singh et al., 2022). PTEN is frequently changed in prostate cancer by copy-number loss as opposed to point mutation. Prior studies have examined the role of PTEN mRNA expression in the development and beginning of prostate cancer (Robinson et al., 2015; Pilarski, 2019). Furthermore, patients with PTEN mutations may have different essential cell signaling pathways and processes than patients with PTEN wild-type (Kmak et al., 2020; Hendricks et al., 2021). Different PTEN statuses can thereby affect the course, outcome, and treatment approaches of the disease, leading to inherently resistant conditions. The genetic changes involved in carcinogenesis may be present in the tumor genome alone or in the germline DNA. Prostate cancer is known to have a highly complex genetic composition, including somatic copy number variations, point mutations, structural rearrangements, and chromosomal number changes (Álvarez-Garcia et al., 2019; Kmak et al., 2020). Genetic changes accompany the carcinogenesis of prostate cancer. This study was aimed to assess PTEN gene alterations in prostate cancer patients.

2.0 MATERIALS AND METHODS

2.1 Study area

Obafemi Awolowo University Teaching Hospital, Ile-Ife (OAUTHC), Nigeria, was the site of this investigation. The hospital is a referral center for the treatment of cancer and a tertiary healthcare facility. Located in Ile-Ife, Osun State, in the Southwest region of Nigeria.

2.2 Study design

This was an analytical experimental design. The tissue blocks archive of the Histopathology Laboratory at the Obafemi Awolowo University Teaching Hospital in Ile-Ife, Osun State, provided the samples used in this investigation. Blocks that have already been processed and diagnosed with prostate cancer between 2014 and 2019 were chosen for this study. The laboratory surgery logbook and the patient's request form provided socio-demographic data.

2.3 Ethical approval

Ethical clearance to carry out this study was sought and obtained from Osun State Ministry of Health's Ethics and Research Committee (*Ref No: OSHREC/PRS/569T/439*)

2.4 Inclusion and exclusion criteria

2.4.1 Inclusion criteria

1. Archived formalin-fixed paraffin-embedded (FFPE) tissue blocks of patients with histologically confirmed prostate adenocarcinoma diagnosed between January 2014 and December 2019 at the Department of Morbid Anatomy and Forensic Medicine, Obafemi Awolowo University Teaching Hospitals Complex (OAUTHC), Ile-Ife.
2. Tissue blocks with adequate tumour tissue for DNA extraction and molecular analysis of the PTEN gene.
3. Tissue blocks accompanied by complete histopathological reports and relevant clinicopathological information, including age at diagnosis.
4. Tissue blocks that are well preserved and suitable for molecular analysis.

2.4.2 Exclusion criteria

1. Archived tissue blocks with a histopathological diagnosis other than prostate adenocarcinoma, including benign prostatic hyperplasia (BPH), prostatitis, prostatic intraepithelial neoplasia (PIN), or other non-malignant lesions.
2. Tissue blocks with inadequate tumour tissue or insufficient material for DNA extraction.
3. Tissue blocks with poor preservation, extensive tissue degradation, or DNA of inadequate quality for molecular analysis.
4. Tissue blocks lacking corresponding histopathological reports or essential clinicopathological information.
5. Duplicate tissue blocks obtained from the same patient for the same tumour, in which case only one representative block was included.

2.5 Sample size

Sample size of n = 234 samples used for this study was determined using the formula for sample size determination described by Naing et al. *(*2006).

$$n = \frac{Z^2P(1-P)}{d^2}$$

When n=Sample size,Z = level of confidence 95% (1.96), P = Estimated prevalence (0.1875), n = Required sample, D = Accepted error (0.05).

2.6 Histopathology analysis

To confirm the diagnosis of prostate cancer on the chosen paraffin wax blocks from laboratory archives, sections were cut at 3 µ using a rotary microtome. The sections were stained with Haematoxylin and Eosin (Avwioro, 2014). The pieces were hydrated in decreasing alcohol grades, dewaxed in two xylene changes, and then submerged in water. After 10 min of Coles haematoxylin staining, hydrated slices were washed with water and briefly distinguished in 1% acid alcohol. After being cleaned with water, the stained sections were blued for ten min in flowing tap water and counterstained for three min in 1% aqueous eosin. Stained sections were cleaned in two xylene changes, dehydrated in increasing alcohol grades, washed in water, and then mounted in DPX. The prior diagnosis was confirmed by microscopically examining the sections with X10 and X40 objectives.

2.7 Gene Extraction and analysis

2.7.1 DNA extraction

A sterile Eppendorf tube was used and 500 µL of extraction buffer was added. Each tissue was grounded in sterile mortal and pistil. 10 µL of 5 M potassium acetate was added, vortexed briefly, and centrifuged at 10,000 x g for 10 min at. About 33 µL of 20% sodium dodecyl sulphate (SDS) was then added, vortexed briefly, and incubated in a water bath at 65°C for 10 min, the lysate was centrifuged at to pellet the cellular debris. The clear supernatant was carefully transferred into a fresh 1.5 mL Eppendorf tube. Subsequently, 300 µL of cold isopropanol was added, stirred gently, and left at -20° C for 60 min. After centrifuging the mixture for 10 min at 13,000 x g, the supernatant was carefully decanted so as not to disrupt the DNA pellet. Following a 10-min centrifugation at 10,000 x g, the DNA pellet was washed with 500 µL of 70% ethanol. After the ethanol was decanted, DNA was allowed to air dry at ambient temperature until the tube showed no more ethanol, as confirmed by visual inspection. The pellet was then re-suspended in 50 µL of Tris EDTA buffer in order to preserve and sustain the DNA (Oba et al., 2022).

2.7.2 Polymerase chain reaction

For all PCRs, the PCR sequencing preparation cocktail included 25 µL of sterile distilled water, 15 µl of DNA template, 10 µL of 5 x GoTaq colorless reaction, 3 µL of 25 mM $MgCl_2$, 1 µL of 10 mM dNTPs mix, 1 µL of 10pmol per primer, and 0.3 units of Taq DNA polymerase (Promega, USA). With a PCR profile for every primer, PCR was performed in a GeneAmp 9700 PCR System Thermalcycler (Applied Biosystem Inc., USA).

Table **1**. Primers used in the study

Gene name	Primer name	Primer sequence	PCR profile
Pten	Pten-F	AAGGGACGAACTGGTGTAATG	An initial denaturation at 94°C for 5min; followed by 30 cycles consisting of 94°C for 30s, 46°C for 30s and 72°C for 30 seconds; and a final termination at 72°C for 10 mins
	Pten-R	AATGGGTAACATGTGCTAGTATGA	

2.7.3 Integrity

10 µL of a 5 x GoTaq colorless reaction, 3 µL of 25 mM MgCl2, 1 µL of a 10 mM dNTPs mix, 1 µL of each 10 pmol primer, and 0.3 units of Taq DNA polymerase (Promega, USA) were included in the PCR sequencing preparation cocktail for all PCRs. The total volume was 35 µL, which was made up of 15l of DNA template and fresh distilled water. The PCR procedure was carried out in an Applied Biosystem GeneAmp 9700 PCR System Thermalcycler (USA) using a PCR profile for every primer. After 45 min of electrophoresis at 120V, the gel was photographed and examined under UV trans-illumination. The sizes of the PCR products were determined by comparing the mobility of a 100 bp molecular weight ladder with experimental samples ran next to it in the gel **(**Ekpo et al., 2026**)**.

2.7.4 Purification of amplified product

Following gel integrity, the amplified fragments were ethanol filtered to remove the PCR chemicals. Each 40-l PCR amplified product was mixed with 240 µL of 95% ethanol and 7.6 µL of Na acetate 3 M in a fresh, sterile 1.5-l Eppendorf tube. After thoroughly mixing the mixtures with a vortex, the tubes were stored at -20°C for half an hour. Following a 10-min centrifugation at 13,000 x g and 4°C, the supernatant was poured off, and 150 µL of a 70% ethanol mixture was added to the 7,500 g and centrifuged for 15 min at 4°C to clean the pellet. The supernatant was aspirated and allowed to dry for 15 min at room temperature in the fume hood before to sequencing. The DNA pellet was kept at -20° C after being reconstituted in 20 µL of sterile distilled water. To verify the presence of the purified product, the purified fragment was tested on a 1.5% Agarose gel run at 110V for one hour and quantified using a Thermo Scientific Nanodrop model 2000.

2.7.5 Sequencing procedures and identification

As directed by the manufacturer, the amplified fragments were sequenced using an Applied Biosystems Genetic Analyzer 3130xl sequencer using the BigDye terminator v3.1 cycle sequencing kit. MEGA 6 and Bio-Edit tools were used for all genomic research (Usman et al., 2026). All PTEN partial sequences were between 99.69% - 100% identical to Homo sapiens clone BAC 46b12 PTEN (PTEN) gene, complete CoDing Sequences (cds) and the sequences obtained for Pten gene have been submitted to the NCBI gene bank and accession numbers allotted were (G1) OK357121-(G1)357127; (G2)357128-(G2)357134; (G3)357135-(G3)357141.

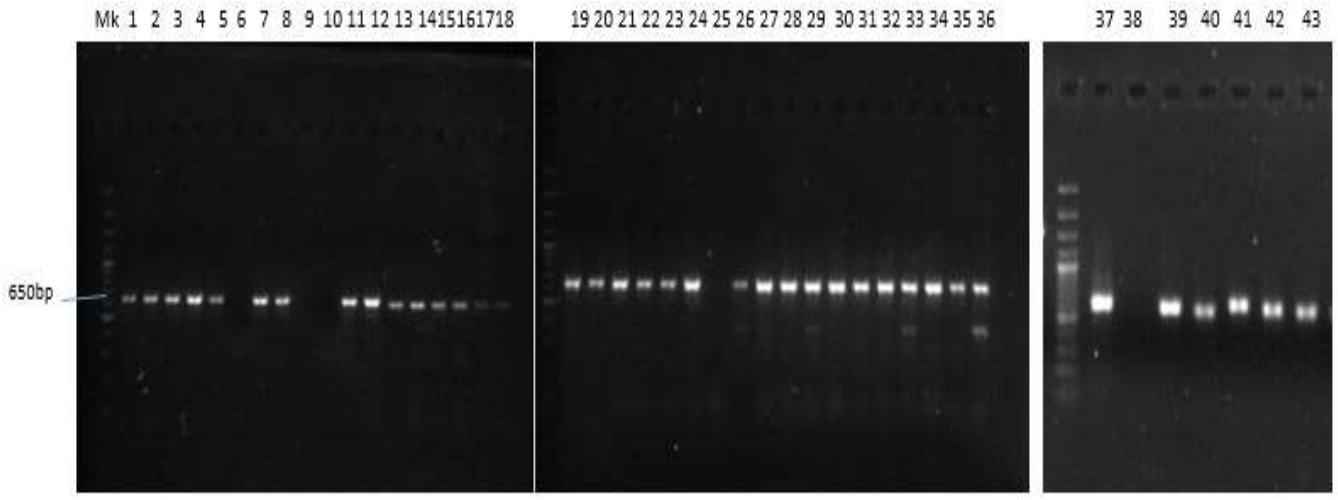

Plate **1**. Gel electrophoresis for PTEN gene region of prostate cancer tissue

3.0 RESULTS

3.1 DNA extraction outcome

Table 2 presents the DNA extraction outcomes by age Group. Only seven tissue samples from each age category yielded DNA of sufficient quality for molecular analysis, whereas most archived tissue blocks failed to produce amplifiable DNA. This low extraction success is likely due to DNA degradation and fragmentation commonly associated with long-term storage and formalin fixation of FFPE tissues.

Table **2**. DNA extraction success according to age

Age	Successful DNA extraction	Failed DNA extraction
50-59 years	7 (8.2%)	78 (91.8%)
60-69 years	7 (9.2%)	69 (90.8%)
>70 years	7 (9.6%)	66 (90.4%)

Table **3**. Relationship between age of subjects and mutation of PTEN genes

Gene	Effects	50-59 years	60-69 years	70+ years	X^2	*p*
PTEN	No mutation	6(85.7%)	6(85.7%)	3(42.9%)	4.200	0.122
	Mutation	1(14.3%)	1(14.3%)	4(57.1%)		

Significant at $p>0.05$

In this study, age of subjects did not significantly affect the mutations of PTEN genes ($p > 0.05$). Generally, PTEN mutations were more prevalent in the older age Group (70 years and above) (Table 3).

Table **4**. Gene alterations observed in prostate cancer tissue blocks.

Gene	Nucleotide position	Mutation type	Mutation effect
PTEN	220	C in-del	missense mutation
	265	G-T(3:19)	missense mutation
	268	C/A in-del	missense mutation

With only three putative SNPs along the analyzed segment, the PTEN partial gene sequence has more homologues. Two insertion-deletions were found at places 220 and 268 along the sequenced segments, and one possible mutation was found at position 265 on the matched sequence. At nucleotide position 220, an insertion-deletion (indel) occurred with a S frequency of four individuals having a C inert and eighteen individuals having a C delete. Group 1 individuals 36, 23, 1, 43, and Group 3 individual 19 had a C insert, whereas position 220 had a C delete for the remaining people. People with C deletion have a histidine deletion as a result of this C-indel mutation (Table 4).

3.2 PTEN Gene (Phosphatase Tensin Homolog Gene)

With only three putative single nucleotide polymorphisms (SNPs) along the analyzed segment, the PTEN partial gene sequence has more homologues. Along the sequenced fragments, two insertion-deletions were found at positions 220 and 268 and one possible mutation was found at position 265 on the matched sequence. With a S frequency of four people having a C inert and eighteen individuals having a C delete, an insertion-deletion (indel) took place at nucleotide position 220. Position 220 had a C delete for the remaining individuals, but Group 1 individuals 36, 23, 1, 43, and Group 3 individual 19 had a C insert. People with C deletion had a histidine deletion as a result of this C-indel mutation (Figure 1). The G-T mutation found at location 265 of the partially sequenced Pten gene. Three people had the G nucleotide and nineteen people had the T nucleotide in this missense G-T (glycine-threonine) mutation. While those with the T nucleotides translated to a stop code, those with the G nucleotide translated to the amino acid glycine (Figure 1). Ultimately, a C/A-indel mutation was found at position 268. According to amino acid translation study, samples 36, 23, and 1 of Group 1 individuals included the A nucleotide, which translated to methionine, whereas samples 43, 27, and 19 of Group 1 individuals contained the C nucleotide, which translated to lysine (Figure 1). Because they have few mutations, the Pten evolutionary tree is crowded together. Within the major cluster or branch, there is only one cluster but two branches: samples 43 and 1 branch off from the major beach, Samples 22 and 1 branch off from the major cluster or branch, and samples 4 and 3 form a minor cluster (Figure 2). Groups 2 and 3 were closely connected to each other along the PTEN gene, while Group 1 showed a genetic difference of 0. However, there is a 0.0008576301 genetic difference between Groups 2 and 1, and a 0.0007833059 genetic difference between Groups 3 and 1.

Table **5**. Pairwise genetic distance showing the level of sequence difference between any two Groups along the PTEN gene.

	Group 1	Group 2	Group 3
Gp 1			
Gp 2	0.0008576301		
Gp 3	0.0007833059	0.0000000000	

Along the PTEN gene, Group 2 and Group 3 were closely related compared to Group 1 recording a genetic difference of 0. However, Group 2 differs from Group 1 with a genetic difference of 0. 0008576301while Group 3 differs from Group 1 with a genetic difference of 0. 0007833059.

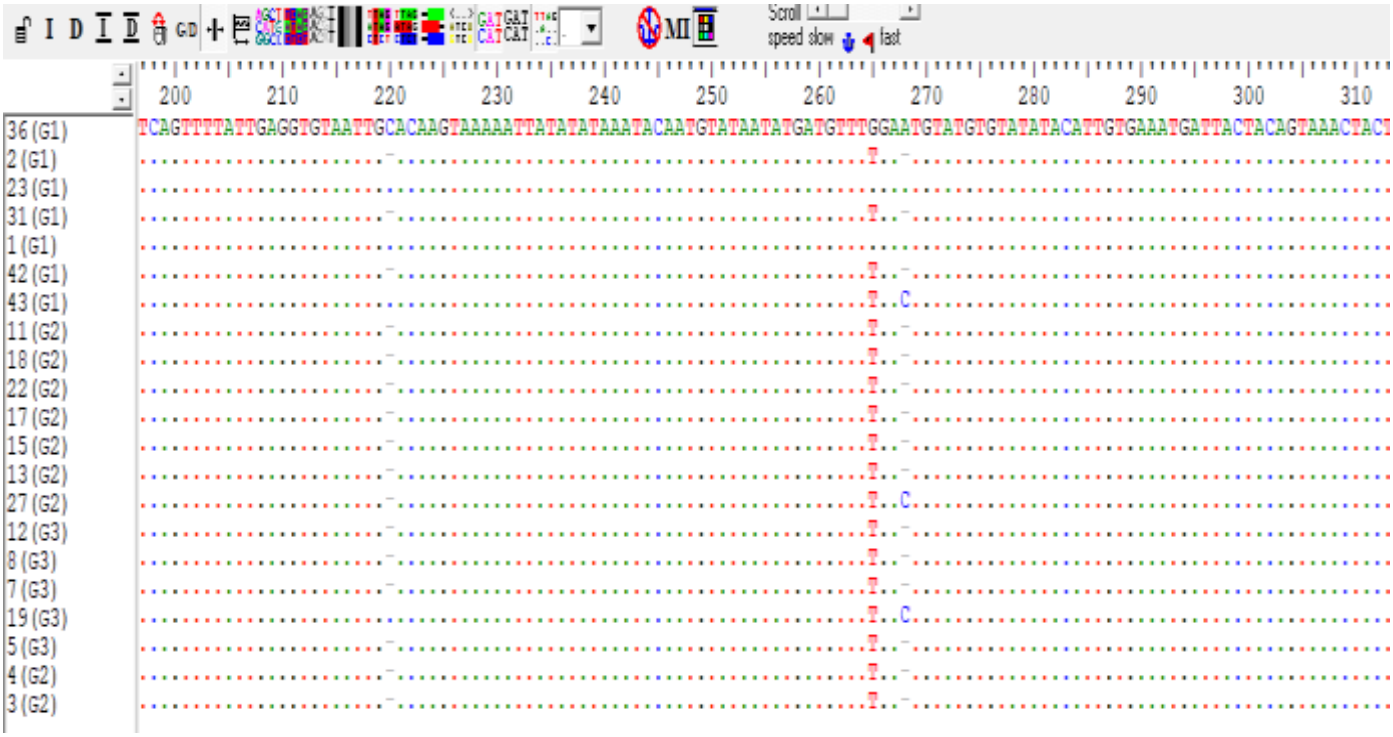

Figure **1.** Nucleotide alignment that showed the region of SNP mutations along the PTEN gene in tissue of prostate cancer patients

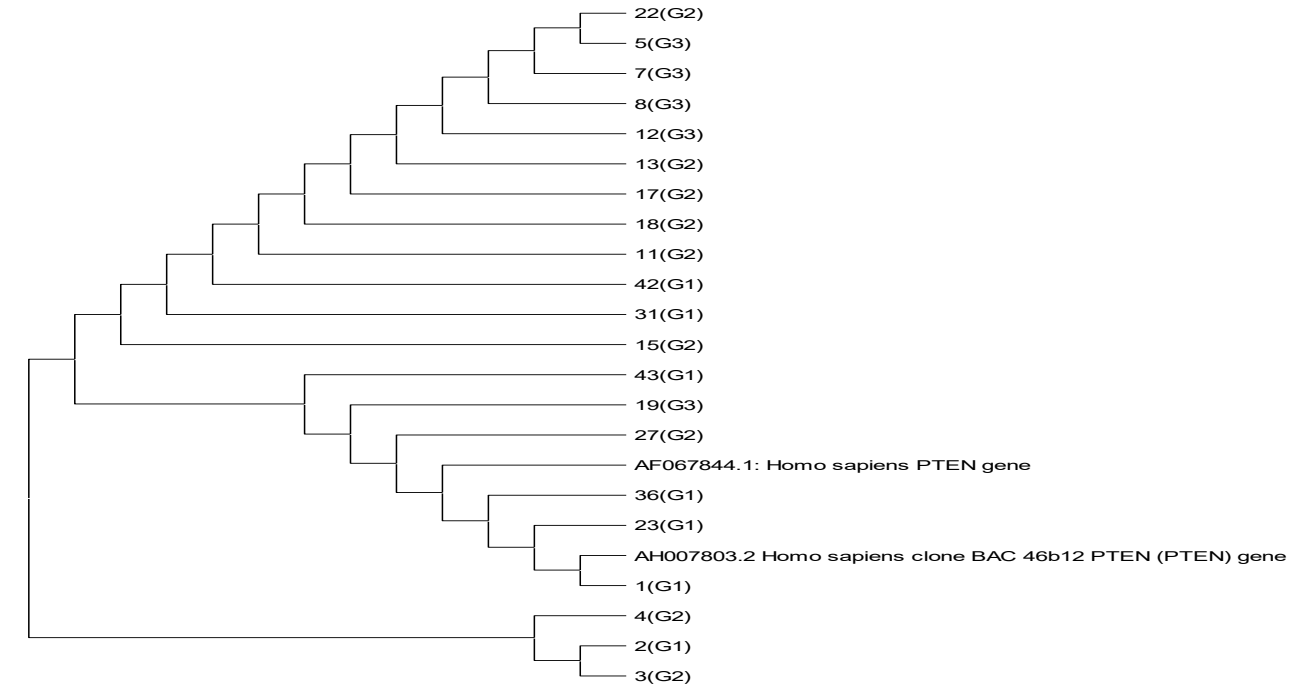

Figure 2: Phylogenetic Analysis

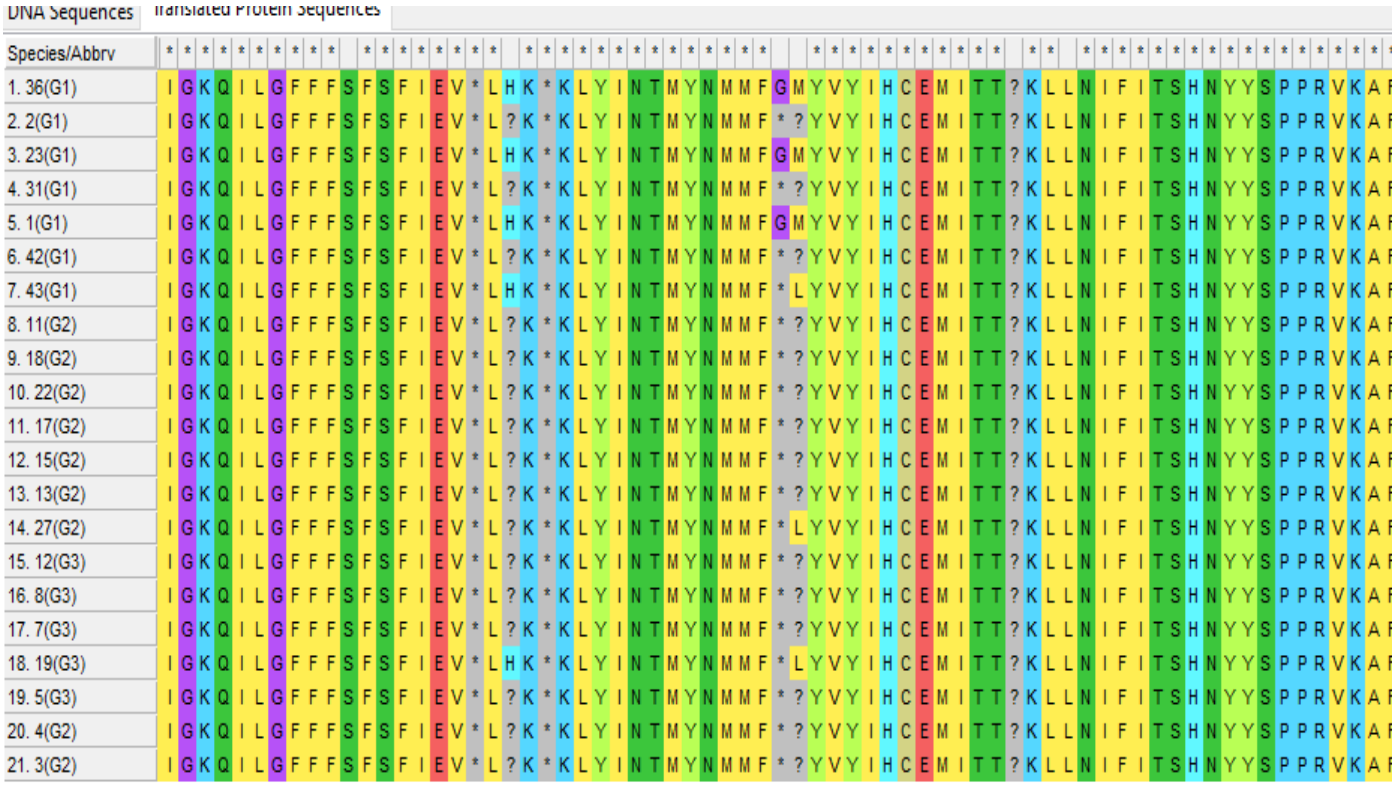

Figure **3**: Amino acid alignment showing the effect of potential SNPs on amino acid sequence along the sequenced PTEN gene

4.0 DISCUSSION

The present study investigated sequence variations within a partial region of the PTEN gene in prostate cancer tissue samples and explored their relationship with age and genetic diversity among study participants. Three sequence variants were identified within the analyzed PTEN fragment, consisting of a single nucleotide substitution (G>T) at nucleotide position 265 and two insertion/deletion (indel) variants at positions 220 and 268. Phylogenetic analysis further demonstrated a high degree of sequence conservation among the analyzed samples, indicating that only limited variation occurred within the sequenced region of the PTEN gene. According to Jin-Tang et al. (2001) and Jamaspishvili et al. (2018), prostate cancer is a clinically varied disease. While some patients have an aggressive disease with metastases and progression, others have an indolent disease with low chance of advancement. According to reports, breakthroughs in molecular technologies have accelerated our understanding of the genetic processes that contribute to the initial onset and progression of prostate cancer (Kmak et al., 2020; Wilson & Zishiri, 2024). The development of knowledge on the genetic, biochemical, and metabolic anomalies of prostate cancer at various phases of disease progression has made it easier to identify new potential therapy targets. This spurred research into innovative treatments for prostate cancer, where the use of novel drugs or biomarkers to determine which patients are best

suited for therapy reflects the novelty (Robinson et al., 2015). PTEN deficiency raises the risk of developing cancer, according to a wealth of research and reliable data on the protein's role in cancer (Gkountakos et al., 2019; Wilson & Zishiri, 2024). Given that PTEN was first discovered to be a tumor suppressor gene, this is not shocking. Numerous malignancies have been linked to PTEN deficiency, and PTEN-deficient animals make excellent carcinogenesis models (Ong et al., 2018). Adjacent normal tissue also exhibits PTEN reduction (Raffone et al., 2019). Many factors can cause PTEN expression to decline, but endometrial, gallbladder, colon, prostate, and breast cancers have all been linked to methylation that results in repression (Siddiqui et al., 2016; Yazdani et al., 2016; Tekcham et al., 2017; Ong et al., 2018). PTEN gene mutations involving methionine were found in Group 3, which includes patients aged 70years and above, with a statistical analysis report of 57.1%. In contrast, PTEN mutations involving lysine were found in both Group 2 (60-69 years) and Group 1 (50-59 years), with statistical analysis reports of 14.3% and 14.3%, respectively. This study differs with one carried out in Togo by Darré et al. (2022), which found that 0.7% of persons under 50years had prostate cancer. This could be because the population and age ranges used in this study differed. According to Bleyer et al. (2020), the incidence of prostate cancer in young adults is 4% among Asians and Australians, and 9% and 3% among Caucasians and black Americans respectively. The phosphatase and tensin homolog (PTEN) gene functions as a tumor suppressor by directing the synthesis of an enzyme found in nearly every bodily tissue. This enzyme aids in the regulation of cell division by stopping cells from reproducing excessively or uncontrolled (Nicola et al., 2020). The PTEN enzyme attaches (dimerizes) with another PTEN enzyme after initially interacting with the cell membrane (Jin-Tang et al., 2001). The PTEN enzyme modifies other proteins and fats (lipids) by removing phosphate Groups, which are composed of a cluster of phosphorus and oxygen atoms (Bray et al., 2018). Loss of PTEN due to mono- and biallelic deletions or mutations is one of the most prevalent genetic abnormalities in localized and metastatic prostate cancer (Magdalena et al., 2022). The main enzymatic function of PTEN is to dephosphorylate phosphatidylinositol-3,4,5-trisphosphate (PtdIns(3,4,5) P3), a potent activator of 3-phosphoinositidedependent kinase (PDK) and AKT (Wilson & Zishiri, 2024). The PTEN gene has mutations at amino acid sites 220, 265, and 268 according to this study. Additionally, a G-T mutation was found at position 265; a C deletion was found at position 220; and a second C deletion was found at position 268. This result is in line with a study by Geybels et al. (2017) in San Diego, California, USA, which found PTEN gene alterations in prostate cancer patients. Barbieri et al. (2012) revealed that the onset and spread of prostate cancer are linked to the loss of specific chromosome regions and suspected tumor suppressor genes, such as the deletion of the 10q and PTEN genes (Geybels et al., 2017; Wilson & Zishiri, 2024). Loss of PTEN activity results in the accumulation of PtdIns (3,4,5)P3 and subsequent activation of the PI3K/AKT signalling pathway, thereby promoting cell growth and survival. The phylogenetic tree with two branches a major branch with 18 samples and a minor branch with just 3 samples was calculated using edited sequences amplified using PTEN-specific primers. There are two sub-branches inside the main branch. Samples 22, 13, 17, 18, 11, 15 (from Group 2), 5, 7, 8, 12, (from Group 3), 42, and 31 (from Group 1) are closely related in the first sub-branch. In contrast to the other members of this cluster (samples 43 (Group 1), samples 27 (Group 2), and Samples 19 (Group 3), the second sub-branch is made up of samples 1, 23, and 36 (all from Group 1) that are closely related to one another and have a G:T mutation in position 265. There are just four samples in the minor branch: samples three, two, and four. It has an A:G mutation at position 2 on the matched nucleotide sequence, making it different from the primary branch. These results are in line with those of Geybels et al. (2017), who found PTEN gene alterations in prostate cancer patients in California, USA. In comparison to Group 1, which recorded a genetic difference of 0, Groups 2 and 3 were closely connected along the PTEN gene. However, there is a 0. 0008576301 genetic difference between Groups 2 and 1, and a 0. 0007833059 genetic difference between Groups 3 and 1.

Conclusion

This study identified three putative sequence variants within the analyzed PTEN gene fragment in prostate cancer tissues, comprising one G>T substitution and two insertion/deletion variants. The detected alterations were infrequent, and phylogenetic analysis demonstrated a high degree of sequence conservation among study samples, supported by very low genetic distances between Groups. Although PTEN mutations appeared more common among subjects aged 70 years and above, no statistically significant association between age and mutation status was observed. These findings suggest that sequence variation within the analyzed PTEN region is limited in this cohort and that PTEN alterations in prostate cancer may involve mechanisms beyond the nucleotide changes detected in this study. Larger studies incorporating comprehensive genomic and functional analyses are required to determine the biological and clinical significance of PTEN alterations in prostate cancer within African populations.

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Availability of data and materials

All data and materials that were collected during this study are available with the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

Consent for publication

Not Applicable

Authors' contributions

EEO and AFO conceived the idea. EEO and AFO designed the study methodology. EEO and AFO conducted the study. EEO, AAB and AFO analyzed the data. EEO, AAB and AFO interpreted the results. EEO, AAB and AFO wrote the draft manuscript. EEO, AAB and AFO revised and edited the final manuscript. EEO, AAB and AFO approved the manuscript.

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