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Genotype Factors and Mineral Status for the Expression of Prostate Cancer among Whites and Blacks Races

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ABSTRACT

Prostate cancer are more in number nowadays its third most frequently occurred cancer in the world. So prevalence of PC is necessary to reduce risk, mortality and morbidity. It has so many pre-disposing factors in that genetical variation are most important because genetical variation can be caused by may be due to chemical agents, hereditary, X -rays and etc… some essential vitamin can causes the prostate cancer and insulin induced factor are also involved .But in another way vitamin can cure the cancer at early stages of cancer.selenium is the one trace element induced the prostate cancer.

KEYWORDS: Races, Prostate Cancer, Genetics, Mineral Status

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INTRODUCTION

Prostate cancer is the second most frequently diagnosed disease and the sixth most common cause of cancer mortality in males globally. In 2020, it was predicted that there will have been 1,414,259 new cases of prostate cancer and 375,304 deaths related to it. In 20 of 47 Asian nations, prostate cancer was among the top three most common cancers in men, and it was most common in Israel, Lebanon, Kuwait, United Arab Emirates, Qatar, Oman, and Japan. [1]

The incidence in western nations has largely plateaued or is declining, in contrast to this trend. Suppression of AR signaling has historically been one of the main therapy goals for prostate cancer since the androgen receptor (AR) is a critical factor in the evolution of prostate cancer [2–3.]

Although prostate cancer mortality has dropped in recent years, it remains the most prevalent visceral malignancy in males in the United States, with 230 110 new cases and 29 900 fatalities (the second largest cause of cancer death) estimated in 2004. By 2025, it's anticipated that there would be more than 380 000 new cases annually. For Caucasian males, the estimated lifetime risks of developing prostate cancer and dying from it are 17.6% and 2.8%, respectively, while for African American men, the anticipated lifetime risks are 20.6% and 4.7%, respectively. In the entire world, African American men face the greatest risks. Men treated for localized disease typically face side effects despite earlier detection because to widespread prostate-specific antigen (PSA) screening and advancements in prostate cancer surgery and radiation therapy. Morbidity and treatment problems are common in males receiving treatment for localized illness .[4]

Consumption of P-carotene or provitamin A, in contrast to dietary retinol, has either been inversely related with or unassociated with risk of prostate cancer. P-carotene may have an impact on carcinogenesis in addition to being transformed into vitamin A by lowering free radical damage or boosting immune performance. More than 500 different kinds of carotenoids exist in nature, while research has mostly concentrated on p-carotene. Along with P-carotene, the most prevalent carotenoids are a-carotene, lycopene, lutein, and P-cryptoxanthin. Because values for amounts of carotenoids in foods have only recently become accessible, epidemiologic information for specific carotenoids (other than p*-carotene) and risk of prostate cancer is lacking. The prevalence of prostate cancer appears to be unrelated to dark green, leafy vegetables, which are the main sources of lutein and the vegetable class most consistently linked to lower risk of various malignancies.[5]

Prostate cancer risk may be correlated with vitamin D deficiency. They noted that a greater incidence of prostate cancer and vitamin D insufficiency appeared to be positively connected with black race, northern latitudes, and older age. They proposed that lower concentrations of pre-vitamin D,

which we get via exposure to sunshine, and 25 hydroxyvitamin D, which is created in the liver by hydroxylating pre-vitamin D, could affect 1, 25 D synthesis. Recent research has shown that 1, 25 D may be crucial for both the onset and advancement of prostate cancer. It inhibited the growth of primary generated prostate tumours as well as metastasis to the lungs.[6]

WHY AFRICAN AMERICAN MEN ARE MORE AFFECTED BY PROSTATE CANCER

Compared to white men, African American men have a higher incidence of prostate cancer and a higher mortality rate from the disease. Better screening in this cohort could help close the difference even though both physiological and social factors may be to blame. However, the Unequal Treatment: Confronting Racial and Ethnic Disparities in Health Care report from the Institute of Medicine in 2002 revealed evidence that minorities frequently receive lower-quality medical care than whites, "even when access-related factors, such as patients.

Genetic predisposition's function. Epidemiologic studies of males with similar genetic backgrounds show that there is a genetic component to the increased incidence and mortality rate in African American men. Men of African heritage in the Caribbean islands and the United Kingdom, for instance, as well as men in Nigeria and Ghana, have high prostate cancer incidence rates.[7]Chromosome 8q24 polymorphisms are more prevalent in African American men and have been linked in multiple studies to an increased risk of prostate cancer.[8]A number of studies have also revealed that African American men had greater rates of polymorphisms in tumor-suppressing genes such EphB2 and cell-apoptosis genes like BCL211.

According to the Surveillance Epidemiology and End Results (SEER) database, metastatic illness was more common in African American men across all age groups.[9] Doctors also need to be aware of ethnic variations in PSA levels and understand that PSA's ability to predict prostate cancer in African Americans and Whites may vary. PSA levels have been observed to be greater in black males, whether or not they have prostate cancer. African American males without prostate cancer had considerably higher mean PSA values than white men across all age groups, according to research by Kyle and colleagues37. Furthermore, African Americans with newly diagnosed localized prostate cancer had higher serum PSA levels than whites at diagnosis, according to Vijayakumar et al38. [10.11]

GENETICAL VARIANTS

Men of African ancestry had a 50% frequency of latent prostate cancer by the age of 60, men of White race by the age of 80, and men of Asian race by the age of 90.[12] The countries with the highest incidence rates are typically those in North America (73.7 cases/100,000 men), Western Europe (75.8 cases/100,000 men), Australia and New Zealand (86.4 cases/100,000 men), and Northern Europe (85.7 cases/100,000 men). Africa is home to some of the world's lowest prostate cancer incidence rates (Northern Africa: 13.2 cases per 100,000 men; Eastern Africa: 23.9 cases per 100,000 men; Western Africa: 31.9 cases per 100,000 men; Middle Africa: 35.9 cases per 100,000 men). [13] However, the prevalence of prostate cancer among non-Hispanic Black males in the United States is the highest in the world (172.6 cases/100,000 men). Non-Hispanic Black males in the United States have an incidence rate that is over 80% greater than non-Hispanic White men. When compared to non-Hispanic White men (17.8/100,000 men), non-Hispanic Black men have a death rate from prostate cancer that is more than twice as high (37.9/100,000 men). [14]

DIFFERENT GENES MUTATION INVOLVE IN PROSTATE CANCER:

1. Gene 8q24

Recent genome-wide scans of prostate cancer families in Iceland and an admixture scan of African Americans have shown the 8q24 region as a prostate cancer susceptibility locus. Additional research on 8q24 variants has revealed the presence of additional single nucleotide polymorphisms (SNPs) that increase the risk of prostate cancer, raising the potential that the illness may have variants in several locations. The 8q24 area has been identified as a prostate cancer susceptibility locus by a genome-wide linkage analysis of families with prostate cancer in Iceland.[15] There are several alleles in the area, particularly the -8 allele of the microsatellite marker DG8S737 and the A allele of the single nucleotide polymorphism (SNP) rs1447295. However, the latter study suggested that the association between DG8S737 and risk of prostate cancer may simply be due to the overall difference in allele frequencies between Caucasians and African Americans.[16] Numerous other SNPs in the 8q24 area have also lately been linked to prostate cancer risk, but less research has been done on them than the two original markers, DG8S737 and rs1447295.[17]SNPs from genome-wide association studies were used to map the 8q24 area precisely.[18]

Japanese Americans, Native Hawaiians, Latino Americans, and European Americans all showed a favorable connection with prostate cancer when DG8S737 and rs1447295 were specifically analyzed. Both the local 8q individual ancestry (LIA) and the global individual ancestry (GIA) results showed that West African ancestry was considerably greater among the PCa cases than controls. Of the genotyped SNPs, twenty-four correspond to human chromosome 8. The remaining 21 SNPs map to 8q24, whereas three SNPs map to 8p.

Two SNPs were eliminated: rs1668875 for being monomorphic in our population and rs10086908 for having a substantial divergence from Hardy Weinberg equilibrium.Minor allele frequencies ranged from 6% to 42%

in the African American controls. Allele frequencies for the remaining 22 SNPs are detailed. 8q24 is mapped by three SNPs.13, After adjusting for age and GIA, rs16901979 in our African American cohort seems to affect the chance of developing prostate cancer. African Americans have been found to have an increased risk of developing prostate cancer due to the 8q24 polymorphisms rs1447295 A allele, DG8S737-8 allele, rs16901979 A allele, and rs7008482 G allele.[19]

2 Gene

a) 10q11

, Recently, two genome-wide association analyses linked the risk of prostate cancer to an SNP at 10q11 (rs10993994) in the 50 region of the MSMB gene. We genotyped 16 tagging SNPs and imputed 29 additional SNPs in a 65 kb genomic region at 10q11 in a Swedish sample to find potential causative variants in the area.

We discovered proof of two distinct loci, separated by a recombination hotspot, linked to the risk of prostate cancer. The first SNP in locus 1, rs10993994, was the most significant of several significant SNPs. Importantly, we demonstrated that the risk allele of this SNP had only 13% of the promoter activity of the wild-type allele in a prostate cancer model, LNCaP cells, using an MSMB promoter reporter experiment. Curiously, the second novel locus, designated locus 2, was found in the gene NCOA4 (also known as ARA70), which is known to increase the transcriptional activity of the androgen receptor in prostate cancer cells. However, in one of the three additional study populations, its association was only marginally supported. Together, the facts that rs10993994 is the most strongly associated variant in the area and that its risk allele significantly affects the transcriptional activity of MSMB (microseminoprotein beta), a gene with previously described prostate cancer suppressor function, point to the T allele of rs10993994 as a potential causal variant at 10q11 that increases the risk of prostate cancer. , , The risk allele T of rs10993994 had significantly lower MSMB promoter activity when compared to the C allele in the LNCaP cell line model of prostate cancer, in addition to the outcomes that were related with it.The MSMB gene, which codes for -microseminoprotein (prostatic secretory protein 94), contains the most significant single-nucleotide polymorphism (SNP) marker known, rs10993994, which is located 57 base pairs centromeric of the first exon.[20]

b) 10q21

Human chromosome 10q21 has the annexin A7 (ANXA7) gene, which codes for a Ca2+-activated GTPase. This region is frequently damaged by chromosomal loss and is thought to contain tumor suppressor genes (TSG). ANXA7 expression was frequently lost in prostate cancer during the initial assessment of the gene as a potential 10q21 candidate, particularly in metastasis and local recurrences of hormone-resistant prostate cancer. Prostate cancer patients frequently have LOH at ANXA7. Restoration of ANXA7 expression in LNCaP and PC-3 prostate cancer cell lines greatly decreased colony formation and cell proliferation in functional experiments.[21]

3) **Hereditary mutate Gene**

a) RNASEL /HPC1(Hereditary Prostate Cancer)

To look into the phenotypic traits of families that may have a connection to the hereditary prostate cancer 1 (HPC1) locus on chromosome 1q24–25. If a first-degree relative has prostate cancer, there is a 2- to 3-fold increase in the risk of having the disease. Changes in the HPCl locus may raise the risk of prostate cancer in a variety of groups and ethnic backgrounds, as white families in Sweden and both white and African-American families in North America were possibly connected. It is not surprising because families with case patients whose diseases were diagnosed at a young age were given preference throughout the study's ascertainment of families. In the HPCl families, 41% of patients had stage (III or IV) illness at the time of their diagnosis. ,) where the prostatic capsule had been affected by the disease, resulting in a ratio of localized (organ-confined) to progressed disease (stages O-II/stages III-IV). [22]

Three genes, ELAC2/HPC2 at 17p (MIM 605367), 2V-5Voligoadenylate-dependent RNase L gene (RNASEL/HPC1) at 1q25, and macrophage scavenger receptor 1 gene (MSR1) at 8p22, have been found and characterized as hereditary genes for prostate cancer. A constitutively produced latent endonuclease called RNASEL is responsible for the IFN-inducible 2-5A system's antiviral and proapoptotic functions. According to reports, the two RNASEL mutations Met1Ile and Glu265X segregate with prostate cancer. Loss of heterozygosity of the wild-type allele was seen in microdissected prostate tumor DNA from prostate cancer patients carrying the Glu265X or 471delAAAG mutations, whereas Arg462Gln had considerably reduced RNASEL enzymatic activity than the wild-type protein. MSR1 belongs to a larger family of individuals.[23]

A second autosomal prostate cancer susceptibility locus at 1q42, known as PCAP, was suggested by the results of a genome-wide scan employing high-risk families from France and Germany. Initial findings point to population-based genetic variations in the prevalence of HPC genes. So far, the findings show that linkage to Chromosome 1q24 is more common in African Americans than in Whites. The proven relationship to chromosome Xq27 among whites has been abolished, but in this initial examination, no such linkage has been found among blacks. Additionally, investigations conducted on populations in France and Germany in Europe have identified a locus (linkage) for prostate cancer susceptibility at 1q42.[24]

b) Gene ELAC2/HPC2

One hereditary prostate cancer (HPC) family had a truncating mutation, although two missense variants, Ser217Leu and

Ala541Thr, had been linked to a higher incidence of PRCA in the general population. Linkage analysis has been used by numerous organizations to identify susceptibility genes for PRCA in order to investigate the genetic origins of the disease. Five potential loci have been identified: PCAP (1q42.2-q43; MIM 602759), HPC1 (1q24-q25; MIM 601518), HPCX (Xq27-q28; MIM 300147), CAPB (1p36; MIM 603688), and HPC20 (20q13; MIM 176807). Multiple sequence variants were found in the ELAC2/HPC2 gene, including the frame-shift mutation 1641 insG and the missense mutations Ser217Leu, Ala541Thr, and Arg781His. We first checked probands from 66 HPC families for mutations in the ELAC2/HPC2 gene's 24 exons.[25]Using the polymerase chain reaction (PCR) technology and the proper restriction enzymes.[26]researchers have linked the Ala49Thr and Val89Leu polymorphisms of the latter gene to prostate cancer in Turkish males. Using the Touch down polymerase chain reaction (Touch down PCR) technique, the ELAC 2 gene was amplified from the isolated genomic DNA of each study participant. Using the forward and reverse primers 5'GGCTGTCAGCTCACCTTGTG3' and 5'GCAGAGAATTAAGAAAACGCAAGC3', respectively, a 231 bp fragment containing the missense mutation (Ser217Leu) in exon 7 of ELAC2 was amplified. [27]

c) MSR1(Macrophage Scavenger Receptor 1)

African-American males are more likely to get prostate cancer when they have MSR1 mutations. A rising collection of molecular and genetic epidemiology evidence points to one or more genes crucial to the development of prostate cancer on the short arm of chromosome 8 (8p22-23). Most recently, an etiologic connection between germline changes in 8p and prostate cancer has been suggested, using the MSR13 gene. In comparison to Caucasian men, African-American men in the United States have a higher incidence and mortality rate from prostate cancer. Characterizing genetic risk factors in this patient population is an important public health initiative, and more research into a potential role for MSR1 is necessary. Four of these (Ser41Tyr, Asp174Tyr, Gly294Glu, and Pro36Ala) are missense mutations and an intron 7 [28] deletion/insertion of 3 bp. These mutations were either not seen or were shown less frequently in men without prostate cancer, according to further analysis of a group of individuals with non-HPC and unaffected men.The uncommon MSR1 mutations were found in 4.4% of white men, The Class A scavenger receptor MSR1 protein is a multidomain trimeric molecule made up of the same protein chains. A single 11-exon mRNA is alternate spliced to produce two functional isoforms (Type I and Type II) and one nonfunctional isoform (Type III). All or some of these mechanisms have been linked to the development of prostate cancer, despite the fact that the precise involvement of MSR1 in prostate carcinogenesis is uncertain. New evidence demonstrating that the degree the relationship between MSR1 and prostate cancer is strengthened by the finding that macrophage infiltration is related to the prognosis of the disease. An SNP in the promoter region (PRO3), a 15-bp insertion/deletion of "GAATGCTTTATTGTA" in intron 1 (INDEL1), an SNP in intron 5 (IVS5-59), a missense alteration in exon 6 (P275A), and a 3-bp insertion/deletion of "TTA" in intron 7 (INDEL7) are the five sequence variations genotyped in this work.[29] By screening a group of men with non-HPC (i.e., affected males without a family history of prostate cancer or with only one affected first-degree relative), as well as unaffected men, we were able to further assess the relationship between these mutations and prostate cancer. Once more, the nonsense mutation Arg293X was exclusively discovered in people of European ancestry and was noticed far more frequently. in people without HPC .[30]

Serum level

IGF-1* and *IGFBP-3

IGF-1, or insulin-like growth factor IGFs, which are regulated by binding proteins, proteases, and receptors, are crucial mediators of cell growth, differentiation, apoptosis, and transformation (2). Post-natal IGF-1 activity is increased The IGF-1 gene is found on chromosome 12, has 72 amino acid residues, two promoters, and multiple mRNA species that can be expressed in different tissues as a result of alternative splicing and transcriptional initiation. Insulin-like growth factor binding protein-3 (IGFBP-3) is a potent apoptosis inhibitor that also functions as a growth hormone mediator. Serum levels of IGF1 and IGFBP-3 have been connected to cancer risk. Here, we examine the connection between three prevalent IGF polymorphisms [a dinucleotide repeat (CA) and a C/T single-nucleotide polymorphism (SNP) (rs7965399)]. near the 2202 A/C SNP in the IGFBP-3 gene and the 5# regulatory region of the IGF-1 gene, respectively. Immunochemiluminometric test was used to determine the levels of IGF-1 and IGFBP-3. IGFBP-3 serum levels were substantially correlated with having at least one copy of the IGFBP-3 2202 C allele. Additionally, we found that Pca risk was two times higher in people who had the IGFBP-3 2202 C allele. That African-Americans' Pca risk and IGF serum levels may be affected by variance in the IGF-1 and IGFBP-3 genes' five untranslated regions. IGF-1 and IGFBP-3 blood levels are negatively correlated with aging, and this may be because GH synthesis is declining. IGF-1 and IGFBP-3 production can potentially be impacted by nutritional control. Red meat and other fat-based foods can raise IGF-1 serum levels; by contrast, foods high in carbs have the opposite effect. Consuming saturated fat also had the opposite effect on IGFBP-3 serum levels. IGF levels have also been demonstrated to dramatically vary by ethnicity; for example, African-Americans in the USA had lower serum concentrations of IGF-1 and IGFBP-3 than European Americans. To find out if variations in blood IGF levels and risk for Pca in African-American men were correlated with two polymorphisms inside IGF-1 and one single-nucleotide polymorphism (SNP) in the IGFBP-3 gene, we carried out a separate case-control analysis. The IGF-1 gene's rs7965399 (C/T) polymorphism and the cytosine-adenosine (CA)n

dinucleotide repeat, which are situated 17 and 1 kb upstream of the due to their prior associations with Pca risk and aggression (14,16,17), as well as the functional rs2854744 (202 A/C) SNP in the IGFBP-3 locus. We also looked at serum levels of IGF-1 and IGFBP-3 and Pca risk .[31]

SRD5A2

It is an androgen-dependent malignancy, and androgens have been shown to have a significant role in the disease's propensity. The SRD5A2 gene, which produces the human prostatic (or type II) steroid 5-reductase, regulates the metabolic conversion of testosterone to dihydrotestosterone. The outcome of this mis-sense substitution is the substitution of threonine (A49T) for an alanine residue at codon 49. Additionally, we overexpressed the enzyme in mammalian tissue culture cells and recreated this mutation in the SRD5A2 cDNA. The higher risk may be caused by an enhanced steroid 5-reductase enzyme-catalyzed conversion of testosterone to dihydrotestosterone. In the mentioned cohort, we looked into the association between three SRD5A2 gene polymorphisms and the chance of developing prostate cancer. The first is a repetition of the (TA)n dinucleotide in the 3' Untranslated region, sense substitution, V89L, which changes codon 89.7's valine to leucine. This polymorphism is particularly intriguing because it is very prevalent in low-risk Chinese and Japanese patients. These patients also have low serum levels of 3 alpha-androstanediol glucuronide, a key dihydrotestosterone metabolite, as well as an in-vivo index of steroid 5alpha-reductase activity.

The A49T mis-sense substitution, the third polymorphism in the SRD5A2 gene, is significantly different from the two previously reported polymorphisms. [32]We examined the relationships between four polymorphic markers in the SRD5A2 gene: the A49T (a substitution of threonine for alanine at codon 49), the V89L (a substitution of leucine for valine at codon 89), the R227Q (a substitution of glutamine for arginine at codon 227), and the aa (a substitution of adenine for alanine). The SRD5A2 gene, which is found on chromosome 2 (2p23), codes for the type II steroid 5-reductase enzyme. Over 40 kb of genomic DNA make up the SRD5A2 gene, which has 5 exons and 4 introns.

Vitamins Role in Prostate Cancer Americans and Africans

1. Serum carotenoid and retinol levels

Prostate cancer (PC) is a known risk factor for black males. Different black groups at risk have not been compared for carotenoids and retinol, which are connected to PC. We compared the amounts of retinol and carotenoid in serum between PC-free African-Caribbean (AC) Tobagonian males with increased serum prostate-specific antigen (PSA) levels (4 ng/ml) and African-American (AA) men with high PC risk (high-grade prostatic intraepithelial neoplasia, atypical foci, or recurrent abnormal PC screenings). By using isocratic HPLC, serum samples were examined for carotenoid (-carotene, -carotene, -cryptoxanthin, lutein/zeaxanthin, and lycopene) and retinol levels. In both the general population and among males with elevated serum PSA, quantile regression was employed to investigate the relationship between serum carotenoid and retinol levels and black ethnicity. African-Caribbean (AC) and African-American (AA) men Compared to other racial groups, are known to have the highest incidence rates of prostate cancer. Some fruits and vegetables include retinol and carotenoids, which are natural colours. Because of their antioxidant properties in lowering oxidative stress, a component thought to contribute to the development and progression of malignancies, studies suggest that certain micronutrients may influence prostate cancer risk and progression.-carotene, -carotene, -cryptoxanthin, lutein, lycopene, and zeaxanthin are the six main dietary carotenoids. Retinol, also known as provitamin A carotenoids, and its carotenoid precursors (-carotene, -carotene, and -cryptoxanthin) have been revealed to play a role in carcinogenesis-influencing processes like cell development, differentiation, and death .[33]

Consumption of P-carotene or provitamin A, in contrast to dietary retinol, has either been inversely related with or unassociated with risk of prostate cancer. P-carotene may have an impact on carcinogenesis in addition to being transformed into vitamin A by lowering free radical damage or improving immune function. More than 500 different kinds of carotenoids exist in nature, while research has mostly concentrated on p-carotene. Along with P-carotene, the most prevalent carotenoids are a-carotene, lycopene, lutein, and P-cryptoxanthin. Because values for the quantities of carotenoids in foods have only recently become accessible, there is a paucity of epidemiologic information regarding specific carotenoids (other than p*-carotene) with the risk of prostate cancer. The risk of prostate cancer was impacted by the specific food source for lycopene. Since lycopene is extremely lipophilic, micellar dispersion is necessary for intestinal absorption.[34]

Lycopene is the main circulating carotenoid in most Americans and ranks first among the major natural carotenoids in its ability to quench singlet oxygen and scavenge free radicals. A previous study of circulating lycopene levels in relation to prostate cancer reported a 50% lower risk for the highest versus the lowest quartile of serum lycopene.Theoretically, lipid-soluble antioxidants like carotenoids and tocopherols could lower the risk of cancer by preventing oxidation of targets including DNA and membrane lipids. Recent research shows that additional mechanisms, such as changes in intracellular signaling pathways or modulation of intercellular communication via gap junctions, may potentially be involved in their anticarcinogenic potential. Prior to randomization, we carefully looked at the plasma concentrations of all five major carotenoid types, including lycopene. Retinol, two different kinds of tocopherol (- and -tocopherol), and. Results pertaining to baseline -carotene levels as well as the effects of random assignment to active -carotene supplements are published elsewhere because the randomized trial

intervention included -carotene. We discovered a moderate degree of connection between plasma antioxidant concentrations and the carotene baseline associated with prostate cancer. In the case of lycopene, correlations (Spearman r) ranged from 0.43 with -carotene to 0.17 with -tocopherol, while correlations with -carotene ranged from 0.70 for -carotene to 0.01 for -tocopherol. Each carotenoid, with the exception of lycopene, showed a strongly inverse correlation with body mass index. The geometric mean concentration of lycopene was 424 ng/ml in control men under the age of 60 and 358 ng/ml in men over the age of 60. These concentrations were lower in older participants. Men who reported drinking more frequently and exercising little to no reported decreased plasma levels of carotenoids; these correlations were less pronounced for lycopene than other carotenoids. Because carotenoids are largely carried by lipoproteins in blood, their levels had substantial but minor relationships with plasma total cholesterol (r = 0.23 and 0.15 for lycopene and -carotene, respectively). [35]

2. Serum Vitamin D level

Over 90% of the circulating amounts of 25(OH) D are obtained from ultraviolet (UV)-B photons from sunlight. High levels of melanin, which are frequently found among ethnic groups with dark skin, including AA men, restrict the amount of UVB sunlight absorbed in the skin, lowering levels of 25(OH) D and raising the risk of developing vitamin D shortages. Only 16% of older AA participants in the Health, Aging and Body Composition Study had serum 25(OH) D levels over 30 ng/mL, compared to 44% of EA participants.Results from the Prostate Cancer Prevention Trial showed that AA males with higher vitamin D levels have a lower risk of developing high-grade illness, but vitamin D deficiency may be a problem for Afro-Caribbean men living in the Caribbean. Raise the risk of prostate cancer. Furthermore, molecular studies suggest that deficits in vitamin D over time may contribute to the development of prostate cancer from pre-clinical to clinically aggressive forms. [36]

Additionally, vitamin D deficiency is more prevalent in AAs than EAs, and the discrepancy in blood vitamin D levels may contribute to the explanation of the PCa differences. However, nothing is known about how vitamin D affects aggressive PCa in AAs. Studies have shown that 1, 25-dihydroxyvitamin D, the active form of vitamin D, reduces inflammation in prostate tissue by modulating the expression of genes relevant to the immune system. A considerable difference exists between AAs and EAs in the expression of immune-related genes in PCa tissues, and inflammation plays a significant role in the pathogenesis and development of PCa. There are numerous routes that have been investigated for how vitamin D influences PCa etiology and progression. 1,25-dihydroxyvitamin D [1,25(OH)2D], the active form of vitamin D, slows tumor cell growth and triggers apoptosis. Additionally, 1,25(OH)2D modifies immune-related gene expression in tissue of the prostate.Numerous genes with vitamin D response elements (VDREs), a section of DNA present in the promoter region of vitamin D target genes, are regulated by 1,25(OH)2D's binding to the vitamin D receptor (VDR). The synthesis of immune-related biomarkers may be impacted by the transcriptional regulation that 1,25(OH)2D and VDR provide. Additionally, inflammation is crucial for PCa pathogenesis, and AAs and European Americans (EAs) express immune-related genes in PCa tissues quite differently.[37] Because aggressive prostate cancer is more common in African-American males and is linked to lower vitamin D levels, our hypothesis is that African-American men may be vitamin D deficient (25(OH) D levels.[38]

Vitamin D $_3$:

The idea that vitamin D shortage over time may contribute to the progression from subclinical prostate cancer to clinical disease is raised by the fact that vitamin D stimulates the differentiation of prostate cancer cells. Our study team has just finished an open-label clinical experiment with participants with early-stage, low-risk prostate cancer to evaluate the security and possible effectiveness of vitamin D3 supplementation at 4000 international units (IU) per day for a year. Because of the improved outcome (a lower number of positive cores at repeat biopsy), the findings of this clinical study show that vitamin D3 supplementation at a dose of 4000 IU per day may be beneficial for patients with early-stage, low-risk prostate cancer who are under active surveillance. These scientific findings also imply that consistent and strong vitamin D3 Supplementation can help African-American men with prostate cancer live healthier lives, and widespread hypovitaminosis D in the African-American community is at least partially to blame for these health disparities.[39]

Selenium

According to estimates, Caucasian men (European men) had lifetime risks of developing prostate cancer of 17.6% and 2.8%, respectively, whereas African American men have lifetime risks of 20.6% and 4.7%, respectively. In the Prostate Cancer Prevention Trial (PCPT), a phase III randomized double-blind, placebo-controlled trial of finasteride for the prevention of prostate cancer, men who took the drug (which inhibits the enzyme 5-reductase and prevents testosterone from being converted to dihydrotestosterone) had a lower risk of developing the disease. Prostate cancer prevalence over a 7-year period was reduced by 25% relative (against placebo) by treating the major androgen in the prostate .[40, 41]

SELECT is a phase III randomized, placebo-controlled study that will examine the effectiveness of selenium (200 g/day from L-selenomethionine) and/or vitamin E (400 IU/day from all-rac-tocopheryl acetate) supplementation for the prevention of prostate cancer over a minimum of 7 years and a maximum of 12 years. For men to be eligible, they must be at least 50 years old (the age requirement was lowered for African American men due to their higher age-adjusted prostate cancer risk), have a serum PSA level under 4 ng/mL, and have a digital rectal examination (DRE) that is negative

for prostate cancer. The amount of selenium consumed daily in the United States typically ranges from 80 to 165 g. The suggested daily intake for an adult North American is 55 μg /day, and 400 g/day is thought to be the safe top dietary limit. The secondary results of the NPC trial, which was carried out in areas of the United States where daily selenium intake is low, provided the most support for assessing selenium in SELECT. [42-46] However, there were statistically significant decreases in the risks of some secondary cancer endpoints, including a 63% reduction in prostate cancer risk, a 46% reduction in lung cancer risk, a 58% reduction in colorectal cancer risk, and a 53% reduction in overall cancer risk. This is despite the fact that there was a nonstatistically significant association between selenium intake and an increased incidence of the primary endpoint, nonmelanoma skin cancer. Additionally, selenium showed no harmful consequences that were statistically (or clinically) significant, despite the correlation with nonmelanoma skin cancer [47.]

Vitamin E (α-Tocopherol)

Eight distinct forms of vitamin Eα-, β-, γ-, and -tocopherols and α-, β-, γ and δ-tocotrienols—have diverse activity and mechanism profiles that are important for the prevention of cancer.[48,49] The typical daily vitamin E consumption in the United States is around 10 mg for men and 7 mg for women of naturally occurring, or all-rac --tocopherol—levels that are much lower than the 15 mg advised by the Institute of Medicine Food and Nutrition Board for both men and women.[50] All vitamin E forms are absorbed, but only a few stereoisomers of -tocopherol are kept in the human blood and tissues. As a result, only -tocopherol is now thought to contribute to the advised daily intake of vitamin E. Tocopherol comes in eight stereoisomers. The most prevalent vitamin E supplement is synthetic -tocopherol all rac -tocopheryl acetate, which contains all eight stereoisomers.

The massive randomized, controlled ATBC Study's secondary analysis provided the greatest evidence in favor of vitamin E's potential to prevent prostate cancer. The goal of this trial, which was conducted in Finland by the National Public Health Institute of Finland and the U.S. NCI, was to see if all-rac-tocopheryl acetate (50 mg daily) and/or beta-carotene (20 mg daily) could lower the risk of lung cancer in 29 133 male smokers between the ages of 50 and 69.[51] In order to directly compare the ATBC Study with the SELECT participants' levels of -tocopherol, which can be replaced by -tocopherol, it was suggested that 50 mg of all-rac --tocopheryl acetate (the choice of this formulation is discussed below). However, this low dose was ultimately rejected for a number of reasons. First, it was found that males with higher baseline, and therefore total, -tocopherol levels had a bigger reduction in prostate cancer incidence after the -tocopheryl intervention in the ATBC Study. Second, people who receive supplements of as little as 30 mg/day of -tocopherol experience decreased plasma -tocopherol levels. [52,53]Therefore, it was decided that vitamin E as all-rac --tocopheryl acetate, which is present in vitamin supplements and was thought to potentially be more protective (than lower dosages) against prostate cancer [54] would be utilized in SELECT at a daily dose of 400 IU (equal to 400 mg).

Only one past cancer prevention experiment, the General Population experiment (GPT) of the Nutrition Intervention Trials in Linxian, China, had studied the combination of selenium and vitamin E therapeutically. According to the GPT, taking 50 g of selenium each day, 30 mg of tocopherol, and 15 mg of beta-carotene reduced overall mortality, cancer mortality overall, and the incidence and death of gastric cancer without having any negative side effects. Recent findings indicate that the active ingredients in the GPT combination, despite the presence of -carotene, were -tocopherol and selenium. [55,56]Prostate tumors rarely occur incidentally. Data from animal models of nonprostate cancer also indicated that the combination of selenium and vitamin E was effective in reducing carcinogenesis while avoiding negative interactions. In particular in animals on the edge of nutritional deficit for either drug, the combination decreased the level of oxidative DNA damage more than did each agent alone. [57, 58]

Omega fatty acids

Omega-3 fatty acids have been found to prevent PCa growth, however high levels of omega-6 fatty acids have been associated with an increased risk of prostate cancer. However, since both omega-3 and omega-6 are essential fatty acids and are a necessary component of a balanced diet, it is more important to identify the perfect ratio of the two so that patients can take advantage of the therapeutic effects of omega-3 fatty acids. Under hormone-deprivation circumstances, dietary-based ratios of omega-6 to omega-3 fatty acids were applied to LNCaP prostate cancer cells to examine the effects on several cellular functions. By inhibiting pathways implicated in the evolution of prostate cancer, such as the Akt/mTOR/NF-B axis, a low omega-6 to omega-3 PUFA ratio can slow the progression of cells toward castration-resistance. Additionally, it reduces cyclin D1 expression, and proapoptotic processes are induced as evidenced by the activation of caspase-3 and annexin V staining. All things considered, our data show that preserving a low omega-6 to omega-3 fatty acids ratio can improve the effectiveness of hormone ablation therapy. [59]

Incidence and mortality rates of prostate cancer are greater in Western nations than in Asian nations. [60,61] Omega-6 fatty acids, which are frequently found in red meats, refined vegetable oils, and highly processed diets, are linked to an increased incidence of prostate cancer mortality in Western nations. [62–64]Contrarily, omega-3 fatty acids, which have been found to be inversely linked with the development of prostate cancer. [67,68] are severely underrepresented in the average Western diet. [65,66]

According to epidemiological studies, Western nations have greater incidence and fatality rates for prostate cancer than Asian nations. Additionally, after moving to the United States, the incidence of prostate cancer in Asian males rises.

[69,70] suggesting an environmental rather than hereditary factor. It has been suggested that consumption of PUFAs contributes to this association. Studies have shown that while omega-3 fatty acids slow the spread of the disease, omega-6 fatty acids encourage the development of prostate cancer. We were, however, interested in figuring out the appropriate ratio of the two to support an anti-cancer environment because both omega-3 and omega-6 fatty acids are critical nutrients needed for regular physiological function. Studies examining human tissue and serum samples reveal that patients with benign hyperplasia had greater ratios of omega-6 to omega-3 fatty acids than healthy tissue, and prostate cancer patients have much higher ratios. [71,72]We therefore aimed to determine the processes by which fatty acids influence the development of prostate cancer as well as the ideal ratio of omega-6 to omega-3 fatty acids needed to take advantage of the therapeutic qualities of omega-3 fatty acids in this study.

CONCLUSION

In the prevalence of prostate cancer, American and African are more prone to the prostate cancer due to genetical variation compare to Asians with specific genetical variation such as 8Q24,10Q11,10Q12, hereditary relate mutate genes are RNASEL/HPC1, ELAC2/HPC2, MSR1(Macrophage scavenger receptor 1). Serum level of insulin can play a important role in the PC IGF1 , IGFBP3 and SRD5A2. Higjh levels of Vitamin are main in the body to induced PC carotenoid and retinol are can causes prostate cancer in the white group of people and African Caribbean. vitamin D acts as both for cure and inducing the prostate cancer because vitamin deficiency mean less amount of melanin in Tobagonian and white grouped people are more prone as well as vitamin D_3 of 4000 IU used as treatment for prostate cancer in early stage. Selenium is a trace element of vitamin it induces more in Africans -Americans and Europeans (Caucasian men).

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