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REVIEW

A comprehensive systematic review of studies on the potential of A49T and V89L polymorphism in SRD5AR2 as high susceptibility gene association with benign prostate hyperplasia and prostate cancer

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Summary ***Introduction and objectives: Being the most common disease in aged men, the etiology of Benign Prostatic Hyperplasia (BPH) is not fully defined. Recent studies have reported that the association between Benign Prostate Hyperplasia and metabolic genes is still inconsistent.***
A gene connected with BPH is SRD5AR2, whose polymorphisms, A49T and V89L, have distinct enzyme activity. This systematic review examines SRD5AR2 polymorphisms within two alleles (A49T and V89L), assessing their roles as prognostic indicators of malignancy, and response to medication.
Materials and methods: We conducted a search on six different databases, including PubMed, Scopus, Wiley, ProQuest, Cochrane Central, and Science Direct using as string of keywords (BPH) AND [(rs523349) OR (V89L)] AND [(rs9282858) OR (A49T)]. We finally selected seven articles to be extracted. Quality appraisal of clinical trials was evaluated using the Joanna Briggs Institute Approach for systematic reviews.
Results: We sorted nine clinical studies from various countries examining SRDA52 polymorphism and its association of BPH and prostate cancer. About V89L we found that the "LL" genotype, indicating reduced 5α-reductase activity, is linked to a lower BPH risk, while the "VV" genotype may slightly increase BPH risk. About A49T, compared to "AA" genotype, "AT" tends to be associated to higher risk in developing prostate cancer. A49T polymorphism does not show any effect on medical treatment while V89L showed a protective effect on the clinical progression of BPH when treated with 5a-reductase inhibitors, a-adrenergic receptor antagonists, and alpha blockers.
Conclusions: SRD5A2 polymorphisms could be a good indicator for prognostic malignancy and a potential tool for personalized medicine of BPH. The findings strongly support the recommendation for further study about SRD5AR2 to enhance its use for screening and prevention and to optimize the medical treatment of Benign Prostatic Hyperplasia.

KEY WORDS: *Benign prostatic hyperplasia; Prostate cancer; Genetic polymorphism; Prognosis; Personalized medicine.*

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INTRODUCTION

Benign prostatic hyperplasia (BPH) is the most common cause of *lower urinary tract symptoms* (LUTS) in men due to bladder outlet obstruction (1). Symptoms range from increased urinary hesitancy, urgency, and frequency to acute urinary retention. Histologic BPH is found in approximately 50% of men aged 50 years, and its prevalence increases about 10% each subsequent decade (2). Likewise, significant LUTS are documented to occur in about 10%-20% of men aged 50-59 and increase to one-third of men by ages 70-79. In parallel, prostate volume increases between age 40 and age 79, with the greatest increases appearing in the sixth and seventh decades of life (3).
Recent studies have uncovered several genes linked to both BPH and prostate cancer. For instance, *Li et al.* (4) investigated the V89L and A49T SRDA52 polymorphisms, while *Zhang et al.* expanded the search by examining genotype distributions of SRD5A2, CYP17, CYP19, and VDR genes in Chinese populations (4, 5). Additionally, *Choubey et al.* (5) focused on polymorphisms at the (TA)n locus. Together, these investigations, alongside others exploring correlations across diverse populations, significantly enhanced our understanding of the genetic factors that may impact the development of BPH and prostate cancer. Previous researchers have noted the presence of alleles with low catabolic activity including two polymorphic sites: an alanine to threonine substitution at codon 49 (A49T) and a valine to leucine substitution at codon 89 (V89L) (6). The V89L polymorphism correlates with reduced concentrations of androstanediol glucuronide, free testosterone, and testosterone (7). Individuals with the "LL" genotype exhibit a slight, nonsignificant, decrease in androstanediol glucuronide concentrations compared to those with the "VV" genotype. The L allele's moderate reduction in SRD5A2 activity results in lower *dihydrotestosterone* (DHT) levels, although the biological mechanism behind this genotype's connection with decreased DHT production remains unclear (4). However, DHT levels in the prostate are influenced by various factors, including testosterone metabolism and DHT inactivation. Testosterone, not DHT, appears to be the primary androgen promoting prostate

carcinogenesis (8). In addition to the V89L polymorphism, the SRD5A2 A49T is linked to a significantly lower concentration of androstanediol glucuronide, indicating its impact on androgen metabolism (9). The SRD5A2 polymorphism likely represents a crucial point in DHT metabolism, possibly explaining its association with prostate cancer risk. This underscores the complexity of genetic factors influencing prostate cancer susceptibility. Both polymorphisms likely contribute to variations in androgen levels, potentially influencing prostate cancer development (10).
To the best of our knowledge, there has been limited research about A49T and V89L polymorphisms of SRD5AR2 as BPH risk factor. Considering the role in benign prostatic hyperplasia and in the risk of malignancy and in their treatment, the Authors were interested in reviewing evidence about SRD5AR2 polymorphisms A49T and V89L, in order to assess their roles as prognostic indicators for malignancy and response to medication.

Materials and methods

Data sources and search strategy

The systematic review was carried out based on the *Preferred Reporting Items for Systematic Reviews and Meta Analysis* (PRISMA) guidelines by utilizing the *PubMed, Scopus, Wiley, ProQuest, Cochrane Central*, and *Science Direct*. Article search for papers in English was done using boolean operators with the following keywords: [(Benign Prostatic Hyperplasia) OR (BPH) OR (Prostate Cancer)] AND [(rs523349 OR V89L) AND (rs9282858 OR A49T)].
The inclusion criteria were: case-control or cohort study; study investigating gene polymorphisms A49T and V89L in SRD5AR2 and their association with BPH and prostate cancer; written in English. Quality appraisal of clinical trials was evaluated using the *Joanna Briggs Institute Approach* for systematic reviews.

Selection process

The authors individually evaluated findings of literature search, beginning with the titles and abstracts of papers which passed eligibility criteria screening.
Any disagreement was freely discussed with one senior author to settle them. The entire text was then examined to weed out research that were not relevant.

Data extraction

The selected articles were extracted by the Authors, who then assessed their suitability. Disagreements were discussed and ultimately settled after each author reviewed the articles on his own. Name of the author, year of publication, country, study design, number of samples, sample characteristics, intervention, comparison, length of follow-up, and desired outcomes were taken from eligible studies.

Results

Study selection

After the literature search, 116 articles were retrieved by the six databases. Several articles were excluded due to duplication of studies (n = 29). Some papers were excluded because they did not adhere to inclusion criteria (n = 36). There were 41 articles excluded due to ineligible data, such as review articles and books, and inaccessible articles due to subscriptions. Finally, nine articles were included in the systematic review to be analysed qualitatively and quantitatively.
Figure 1 shows the PRISMA flowchart.

Study design

This review consists of 9 clinical studies with varying designs: 1 cross-sectional, 3 case-control, 2 cohort studies, and 3 clinical trials. The total number of participants across all studies includes 1,226 individuals, comprising prostate cancer patients, BPH patients, and healthy controls. Methods of diagnosis and assessment included blood diagnostic criteria, *prostate-specific antigen* (PSA) testing, *digital rectal examination* (DRE), and biopsy results. The geographic distribution of the studies includes Bulgaria, China, Japan, the USA, India, and Sweden. The review emphasizes the impact of gene polymorphism and its associations with prostate diseases, explores and discusses their implications for personalized medicine.

Risk of bias summary

The risk of bias for various study designs; case-control, cohort, and cross-sectional was evaluated using the *JBI Critical Appraisal Tools*. According to the risk of bias assessment, three studies were found to have a moderate risk of bias, primarily due to ambiguous statements in areas such as the identification of confounding factors and the strategies used to address them, as well as incomplete data throughout the studies.
The remaining studies (n = 6) were classified as having a low risk of bias (see Figure 2).
Despite the varying levels of bias across the included studies, most of the data have been thoroughly examined and discussed. The reviewers concluded that, overall, the studies are sufficiently suitable for analysis.

Study result summary

Gene polymorphism

Results for V89L variant of SRD5A2 are reported in Table 1. For the A49T, men with the AT/TT genotypes were at increased risk for BPH, asymptomatic, and symptomatic BPH and prostate cancer compared to men with the AA genotype, although none of the OR reached statistical significance.

Association to malignancy

Based on the studies on V89L polymorphism that were evaluated, it was shown that "LL" allele, that confers a low activity of 5 alpha reductase, was less common in patients with prostate cancer. On the other hand, "VV" locus, which is commonly found in the Hispanic population, is associated with a higher risk of BPH.
The A49T gene consists of "AA" locus and "TT" locus producing "AA", "AT", and "TT" genotypes. All of the genotypes mentioned have no statistically significant correlation to malignancy, although "AT" and "TT" genotypes have a higher risk of developing prostate cancer. "AT"

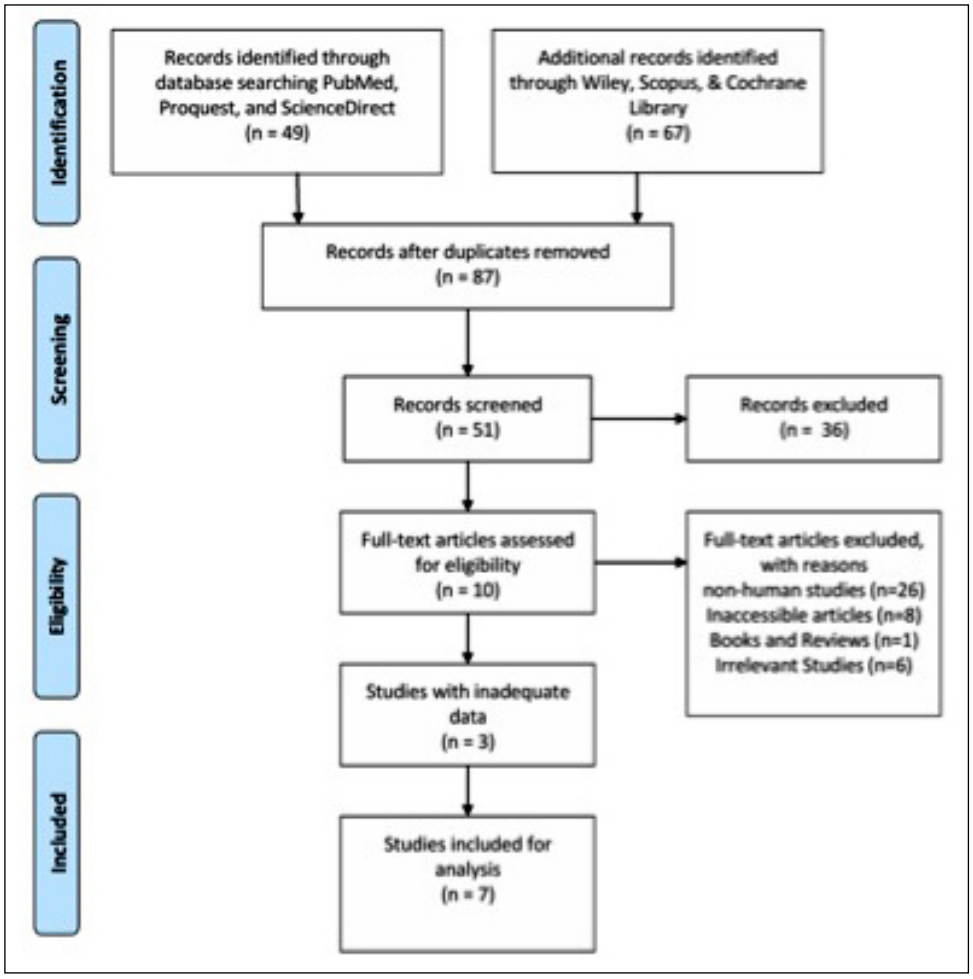

Figure 1.
PRISMA flowchart of the literature selection.

Figure 2.
Risk of bias assessment

No	Authors; year	Countries	Study Design	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Overall Risk of Bias
1	Gu X, 2013	China	Cross Sectional	Yes	Yes	Yes	Yes	Un clear	Un clear	Yes	Yes	NS	NS	NS	Low Risk of Bias (6/8)
2	Li Z, 2003	Japan	Cohort	Yes	Yes	Yes	Un clear	Yes	Yes	Yes	Yes	No	No	Yes	Low Risk of Bias (8/11)
3	Lin-lin Z, 2017	China	Cross Sectional	Yes	Yes	Yes	Un clear	No	Yes	Yes	Yes	NS	NS	NS	Low Risk of Bias (6/8)
4	Choubey, 2015	India	Case-control	Yes	Yes	Yes	Yes	Yes	Un clear	Un clear	Yes	Yes	Yes	NS	Low Risk of Bias (8/10)
5	Rajender, 2009	India	Case-control	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	NS	Low Risk of Bias (8/10)
6	Roberts, 2005	USA	Cohort	Yes	Yes	Yes	Un clear	No	Yes	Yes	Yes	Un clear	Un clear	Yes	Moderate Risk of Bias (7/11)
7	Salam, 2005	USA	Cross Sectional	Yes	Un clear	Yes	Yes	Un clear	No	Yes	Yes	NS	NS	NS	Moderate Risk of Bias (5/8)
8	Delgado-Balderas, 2020	Mexico	Case-control	Yes	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	NS	Moderate Risk of Bias (7/10)
9	Giwercman, 2005	Sweden	Cohort	Yes	Yes	Yes	Un clear	Un clear	Yes	Yes	Yes	Yes	No	Yes	Low Risk of Bias (8/11)

Table 1.
Gene polymorphism.

No	Authors, year	Country	Study design	Study periode	Diagnostic criteria	Association with BPH	
						rs9282858 (A49T)	rs523349 (V89L)
1	*Li Z, 2003*	Japan	Cohort	2001-2002	PSA > 4	"AA" genotype detected in patients with BPH	LL Genotype: significantly increased risk, VV and VL genotypes not significantly increased risk
2	*Lin-lin Z, 2017*	China	Case control	2014-2015	PSA > 4 ng/mL; PV > 30 mL; PVR > 30 mL;	No significant difference in the distribution frequency of SRD5A2 A49T	The frequency was significantly different between the control group and the BPH group
3	*Choubey, 2015*	India	Case control	NR	Age > 45 years, presence LUTS, prostate weight > 25 g on USG, AUAS score > 7, PSA < 4.0, enlarged smooth prostate on DRE	A49T locus exhibited "AA" monomorphic in all population (BPH, PC, and control)	Presence of "VV" showed a marginally significant correlation with increased BPH risk
4	*Rajender, 2009*	India	Observational study	NR	PSA Level > 4	PC, BPH, and control samples invariably had the wild-type allele (A) at this site	BPH cases possessed alleles and genotypes similar to the control samples at all the 3 polymorphic sites
5	*Roberts, 2005*	USA	Cohort	1990-2000	AUASI	There were no significant differences in AUASI, flow rates, prostate volume, or serum PSA level across genotype	There were no consistent associations between the V89L, the A49T, and TA repeat polymorphisms of the SRD5A2 gene and surrogate measures of BPH
6	*Salam, 2005*	USA	Clinical trial	1999-2002	Digital rectal examination (DRE), prostate specific antigen (PSA) testing, AUA symptom score, and prostate biopsy.	For the A49T loci, compared to men with the AA genotype, those with the AT/TT genotypes were at increased risk for BPH, asymptomatic, and symptomatic BPH and prostate cancer, but none of the OR reached statistical significance	– Compared to men with the VV genotype, those with the LL genotypes were at nonsignificant increased risk for BPH and symptomatic BPH and at significant increased risk for asymptomatic BPH. – Furthermore, among Hispanic men, there were statistically significant increasing trends with increasing number of L alleles for both BPH (Ptrend < 0.03) and asymptomatic BPH (Ptrend < 0.01), and a marginally significant increasing trend for symptomatic BPH (Ptrend < 0.07)
7	*Giwercman, 2005*	Sweden	Case control	NR	Prostate biopsy, Gleason Score, PSA levels	Not significantly associated with BPH incidence	Not significantly associated with BPH incidence

variants were more frequently found among Prostate Cancer patients while "AA" variants were least likely to be found on patients with prostate cancer and BPH.

Response to drugs
Both genes demonstrated a protective effect against the clinical progression of BPH when treated with 5α-reductase inhibitors, α-adrenergic receptor antagonists, and alpha blockers. Populations with the "LL" genotype were likely more suitable to have a standard or herbal treatment for BPH.

Discussion

The results of the present study, when contextualized with previous research (11-16), provide a deeper understanding of the role of genetic polymorphisms in the SRD5A2 gene, particularly V89L and A49T, in the development and progression of prostate pathological conditions like BPH and *prostate cancer* (PCa). The associations between these polymorphisms and disease risk highlight the genetic mechanisms that may influence prostate enlargement and malignancy, as well as the potential for personalized treatment strategies based on these genetic markers.
Our findings on the V89L polymorphism align with previous studies showing that the SRD5A2 gene encoding an enzyme responsible for converting testosterone into *dihydrotestosterone* (DHT), plays a key role in prostate growth. The activity of this enzyme also known as 5-alpha reductase type 2 is linked to the severity of BPH. The V89L polymorphism shows distinct enzyme activity variations that influence androgen levels and drive prostate growth, potentially leading to prostate cancer.
Our review found that the "LL" genotype is less common in prostate cancer patients, suggesting that this allele may have a protective effect by lowering 5-alpha reductase activity and, consequently, DHT production.

Table 2.
Prognostic to Malignancy

No	Authors; Year	Country	Study Design	Study Period	Diagnostic Criteria	Population		Association to Malignancy	
						Sample size (n)	Mean Age (years) (Mean ± S.D)	Association to malignancy A49T	Association to malignancy Val89
1	*Li Z, 2003*	Japan	Cohort	2001-2002	PSA > 4	773 subjects, including 302 patients with prostate cancer, 228 with benign prostatic hyperplasia (BPH) and 243 male controls	PC: 72 ± 8.84 years old BPH: 70 ± 9.32 years old control: 71 ± 6.68 years old	Failed to detect the T allele	V89L polymorphism may have a significant role in prostate cancer development in Japanese males
2	*Lin-lin Z, 2017*	China	Case control	2014-2015	PSA > 4 ng/mL; PV > 30 mL; PVR > 30 mL;	452 patients with BPH; 501 healthy individuals	Control 57.28 ± 7.61 BPH 58.02 ± 7.38	No significant difference was found	Reduced risk of progression to malignancy, especially "LL" genotype
3	*Choubey, 2015*	India	Case Control	NR	Age >45 years, presence LUTS, prostate weight > 25 g on USG, AUAS score > 7, PSA < 4.0, enlarged smooth prostate on DRE	580 subjects, including 192 patients with prostate cancer (PC), 217 patients with BPH, and 171 control subjects	PC: mean 66 years (age range 50- 96 years) BPH: mean 63 years (age range 45-80 yeas) controls: mean 61.88 (age range 45- 75 years)	The presence of "AA" locus showed a lower risk in prostate problem at Indian population	V89L found highly polymorphic. "LL" confers lowest 5α-reductase activity in PCa patient. This could explain reduced risk of BPH in "LL" carriers. Longer (TA)n repeats showed strong protective effect against BPH. "VV" locus may correlate with marginally increased risk of BPH
4	*Salam, 2005*	USA	Clinical trial	1999-2002	Digital rectal examination (DRE), prostate specific antigen (PSA) testing, AUA symptom score, and prostate biopsy	Control (N = 113) Any BPH (N = 393) Symptomatic BPH (N = 280) Asymptomatic BPH (N = 113) Prostate Cancer (N = 100)	60 and 86 years of age Controls: 66.6 (0.48) Any BPH: 66.9 (0.28) Symptomatic BPH: 67.4 (0.34) Asymptomatic BPH: 65.7 (0.44) Prostate Cancer: 66.5 (0.53)	Compared to men with the AA genotype, those with the AT/TT genotypes were at increased risk for prostate cancer, but none of the OR reached statistical significance	Compared to men with the VV genotype, the OR of prostate cancer associated with 1 or 2 L alleles were 1.81 and 4.47, respectively (Ptrend < 0.01). The associations were even stronger in Hispanics, in which the OR were 2.02 and 7.26, respectively (Ptrend < 0.005).
5	*Delgado-Balderas, 2020*	Mexico	Clinical trial	2018-2019	PSA levels	PCa cases (n = 101) and non-PCa subjects (n = 100) composed of males without prostate abnormalities (n = 60) BPH (BPH; n = 40)	PCa cases (n = 101; median age, 70 years; age range, 64.5-75.0 years) and non-PCa subjects (n = 100; median age, 58 years; age range, 48–67 years) composed of males without prostate abnormalities (n = 60) and subjects with benign prostatic hyperplasia (BPH; n = 40)	The present study, no association was identified between SRD5A2 gene variants and PCa. The results demonstrated that 3% of subjects were carriers of the A49T (Thr/Thr allele) variant and it was not associated with PCa development (p = 0.327)	There was no association between the SRD5A2 rs523349 genotypes and Gleason scores ≥8; however, there was a decreased tendency between patients with metastasis and rs523349 genotypes (Val/Val vs. Leu/Leu+Val/Leu; p = 0.048; OR = 0.390; CI = 0.142–1.073)

6	Giwercman, 2005	Sweden	Case Control	NR	Prostate biopsy, Gleason Score, PSA levels	134 swedish men	In men with CaP, the mean age at diagnosis was 69.3, whereas men with BPH on average were 64.5 years	The high activity AT variant was more frequent among CaP patients compared to the general population (p = 0.02)	The low activity homozygote V89L LL allele was less common in patients with CaP compared to the general population (p = 0.05)

Table 3.
Response to medical treatment.

No	Authors; Year	Country	Study Design	Study Period	Diagnostic Criteria	Population		Personalized Medicine			
						Sample size (n)	Mean Age (years) (Mean ± S.D)	Intervention (Treatment)	Outcome Measure	rs9282858 A49T result	rs523349 V89L Result
1	*Gu X, 2013*	China	Clinical Trial	2010-2012	I-PSS, TPV, Urine flow	426 patients with BPH	61.24 ± 8.96 years.	A combination of type II 5a-reductase inhibitors (5 mg once daily) and a-adrenergic receptor antagonists (4 mg once each night)	I-PSS (increased by 2 points) Urine flow rate (decrease), tPSA, fPSA, TPV	No significant difference was found	On SRD5A2 rs523349 (V89L nonsynonymous SNP) and rs612224 were significantly associated with I-PSS (decrease) in G/G, but in C/C and G/C increased, TPV, PSA change
2	*Lin-lin Z, 2017*	China	Case control	2014-2015	PSA > 4 ng/mL; PV > 30 mL; PVR > 30 mL;	452 patients with BPH; 501 healthy individuals	Control 57.28 ± 7.61 BPH 58.02 ± 7.38	One tablet of Terazosin (2 mg) and 1 tablet of Finasteride (5 mg)	- Decreased dynamic maximum urinary flow rate; - Presence of complications such as acute urinary retention, hematuria urinary tract infection, bladder stones and renal dysfunction	No significant difference was found	May be a protective factor during the clinical progression of BPH
3	*Roberts, 2005*	USA	Cohort	1990-2000	AUASI	510 samples	Median 60 years	NR	NR	No significant difference was found	Men with the LL genotype were slightly more likely to have had standard medical or herbal treatment for BPH

These results are consistent with a study by *Konwar et al.* (17), which reported that the LL genotype is associated with lower androstanediol glucuronide concentrations, thereby reducing free testosterone and DHT levels.
This may explain the reduced prostate volume and lower cancer risk in individuals with the "LL" genotype compared to those with the "VV" genotype. Furthermore, the higher risk of BPH associated with the "VV" allele was also supported by *Lunn et al.* (18) research, which indicated ethnic differences in V89L polymorphism prevalence.
In Asian populations, such as those in India and Japan, the polymorphism was found at higher rates, contribut-

ing to an increased risk of BPH. This suggests that the genetic impact of the V89L variant may vary across different ethnicities, with certain populations exhibiting a higher predisposition to prostate diseases.

Regarding the A49T polymorphism, our review found no statistically significant association with malignancy, though the "AT" and "TT" genotypes tended to be associated with a higher risk of developing prostate cancer compared to the "AA" genotype. This aligns with *Giwerchman et al.* (15), who estimated that the A49T polymorphism could be found in approximately 8% of prostate cancer patients and 6.3% of BPH patients, indicating its role in increasing the probability of developing BPH and prostate cancer. Although not as prominent in Asian populations, this polymorphism is commonly observed in Hispanic populations, as well as in certain countries like Turkey and China.

While the statistical significance of the A49T polymorphism in relation to malignancy remains inconclusive in our review, these findings emphasize its potential importance as a genetic marker for prostate cancer susceptibility. This warrants further research, especially in non-Hispanic populations, to determine whether the A49T variant can be used as a predictive tool for prostate disease risk in other ethnic groups.

The study findings on gene polymorphisms in the SRD5A2 gene also underscore the potential for personalized medicine in treating prostate-related conditions. According to *Li et al.* (14), the SRD5A2 gene regulates critical hormonal pathways, influencing prostate growth and function. This insight into the biochemical pathways driven by V89L and A49T polymorphisms supports the idea of genotype-driven therapeutic approaches.

Both V89L and A49T polymorphisms demonstrated protective effects against the clinical progression of BPH when treated with 5-alpha reductase inhibitors and α-adrenergic receptor antagonists.

These findings imply that personalized treatment strategies based on genetic markers could optimize therapeutic outcomes and reduce the likelihood of disease progression, offering a more tailored approach to managing BPH and prostate cancer.

A study by *Daryanto et al.* (19) showed that combination of dutasteride with tamsulosin could give a more significant effect in terms of lowering the contractility of prostate smooth muscle.

While the findings of this review are compelling, they also reveal the need for further research. The prevalence of V89L and A49T polymorphisms in Hispanic populations has been well-documented, but additional studies in Asian populations are necessary to understand their role in diverse genetic backgrounds. For example, as noted by *Lunn et al.* (18), the V89L polymorphism shows high prevalence in India and Japan, suggesting a population-specific effect. Expanding genetic studies to include other Asian regions may yield valuable insights into the global relevance of these polymorphisms.

Additionally, larger cohort studies and more diverse population sampling are needed to strengthen the associations between these polymorphisms and prostate cancer or BPH risk. A more detailed exploration of the mechanistic pathways involved in DHT production and androgen activity, particularly in relation to the SRD5A2 gene, will be essential for translating these genetic insights into clinical practice.

This study confirms the significant role of the SRD5A2 gene and its V89L and A49T polymorphisms, in influencing the risk of prostate disease and its progression. Both variants have distinct effects on the enzyme activity and androgen levels, impacting on prostate growth and the likelihood of developing BPH or prostate cancer. Ethnic differences in polymorphism prevalence further highlight the importance of population-specific genetic research. By integrating genetic profiling into clinical practice, personalized medicine approaches may offer more effective and targeted treatment options for prostate-related conditions, improving patient outcomes while minimizing unnecessary interventions.

Conclusions

In conclusion, this systematic review proves that SRD5A2 is a high susceptibility gene that is linked to BPH. A49T and V89L are the polymorphism of the gene involved.

ninBoth polymorphism varies in different ethnic populations. Further studies are required to evaluate different risk factors and outcomes after medical treatment in different geographical situation in order to provide a better theoretical basis to study the role of genetic in the pathogenesis of BPH and prostate cancer.

References

1. Roehrborn CG. Benign prostatic hyperplasia: an overview. Rev Urol. 2005; 7(Suppl 9):S3-S14.

2. Goodarzi D, Cyrus A, Khoddami Vishteh HR, et al. Effect of celecoxib on benign prostatic hyperplasia: Results of a preliminary study. Urological Science. 2011; 22:147-150.

3. Middleton LW, Shen Z, Varma S, et al. Genomic analysis of benign prostatic hyperplasia implicates cellular re-landscaping in disease pathogenesis. JCI Insight. 2019; 5:e129749.

4. Li Q, Zhu Y, He J, et al. Steroid 5-alpha-reductase type 2 (SRD5A2)

Declarations

Ethical approval: *Not applicable.*

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V89L and A49T polymorphisms and sporadic prostate cancer risk: a meta-analysis. Molecular biology reports 2013; 40:3597-3608.

5. Choubey VK, Sankhwar SN, Carlus SJ, et al. SRD5A2 gene polymorphisms and the risk of benign prostatic hyperplasia but not prostate cancer. Asian Pac J Cancer Prev. 2015; 16:1033-1036.

6. Salam MT, Ursin G, Skinner EC, et al. Associations between polymorphisms in the steroid 5-alpha reductase type II (SRD5A2) gene and benign prostatic hyperplasia and prostate cancer. Urol Oncol. 2005; 23:246-253.

7. Zeng XT, Su XJ, Li S, et al. Association between SRD5A2 rs523349 and rs9282858 Polymorphisms and Risk of Benign Prostatic Hyperplasia: A Meta-Analysis. Front Physiol. 2017; 8:688.

8. Price DK, Chau CH, Till C, et al. Association of androgen metabolism gene polymorphisms with prostate cancer risk and androgen concentrations: Results from the Prostate Cancer Prevention Trial. Cancer. 2016; 122:2332-2340.

9. Elzanaty S, Giwercman YL, Giwercman A. Significant impact of 5alpha-reductase type 2 polymorphisms on sperm concentration and motility. Int J Androl. 2006; 29:414-20.

10. Neslund-Dudas C, Bock CH, Monaghan K, et al. SRD5A2 and HSD3B2 polymorphisms are associated with prostate cancer risk and aggressiveness. Prostate 2007; 67:1654-1663.

11. Allen NE, Forrest MS, Key TJ. The association between polymorphisms in the CYP17 and 5α-reductase (SRD5A2) genes and serum androgen concentrations in men. Cancer Epidemiol Biomarkers Prev. 2001; 10:185-9.

12. Van Gils CH, Onland-Moret NC, Roest M, et al. The V89L Polymorphism in the 5-α-Reductase Type 2 Gene and Risk of Breast Cancer. Cancer Epidemiol Biomarkers Prev. 2003; 12:1194-9.

13. Wang C, Tao W, Chen Q, et al. SRD5A2 V89L polymorphism and prostate cancer risk: A meta-analysis. Prostate. 2010; 70:170-8.

14. Li J, Coates RJ, Gwinn M, Khoury MJ. Steroid 5-α-reductase type 2 (SRD5a2) gene polymorphisms and risk of prostate cancer: A HuGE review. Am J Epidemiol. 2010; 171:1-13.

15. Giwercman YL, Abrahamsson PA, Giwercman A, et al. The 5alpha-reductase type II A49T and V89L high-activity allelic variants are more common in men with prostate cancer compared with the general population. Eur Urol. 2005; 48:679-85.

16. Tekin Neijmann S, Kural A, Tinay I, et al. Association of missense substitution of A49T and V89L in the SRD5A2 gene with prostate cancer in Turkish patients. Turkish Journal of Biochemistry. 2017; 42:37-43

17. Konwar R, Chattopadhyay N, Bid HK. Genetic polymorphism and pathogenesis of benign prostatic hyperplasia (BPH). BJU international. 2008; 5:536-44.

18. Lunn RM, Bell DA, Mohler JL, Taylor JA. Prostate cancer risk and polymorphism in 17 hydroxylase (CYP17) and steroid reductase (SRD5A2). Carcinogenesis. 1999; 20:1727-31.

19. Daryanto B, Naim HY, Budaya TN. The Effect of Tamsulosin, Dutasteride Monotherapy and Tamsulosin-Dutasteride Combination on Prostate Smooth Muscle Contractility in BPH Model Wistar Strain Rattus Novergicus. Medical Archives. 2023; 77:13.

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