Section: Miscellaneous

Original Research Article

CORRELATION OF VITAMIN D RECEPTOR (VDR) GENE POLYMORPHISM WITH SUSCEPTIBILITY TO AUTOIMMUNE THYROIDITIS

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ABSTRACT

Autoimmune thyroiditis (AIT), including Hashimoto's thyroiditis and autoimmune hypothyroidism, represents one of the most common organ-specific autoimmune disorders worldwide. Genetic predisposition plays a crucial role in its pathogenesis, with the vitamin D receptor (VDR) gene emerging as a key immunomodulatory candidate. Variations in VDR polymorphisms particularly FokI, BsmI, ApaI, and TaqI have been implicated in altered immune tolerance, T-cell regulation, cytokine expression, and susceptibility to autoimmune diseases. However, the evidence regarding their association with AIT remains inconsistent across populations due to ethnic, environmental, and methodological differences.

This study aimed to evaluate the relationship between common VDR gene polymorphisms and the risk of autoimmune thyroiditis using a case–control design. Peripheral blood samples were analysed using PCR-RFLP to genotype targeted VDR variants, and serological markers including anti-TPO and anti-TG antibodies were assessed to confirm disease status. Comparative analysis was performed between patients with AIT and age- and sex-matched euthyroid controls to determine genotype distribution, allele frequency, and odds ratios for disease susceptibility.

The results demonstrated a significant association of specific VDR polymorphisms most notably the FokI (rs2228570) and TaqI (rs731236) variants with increased susceptibility to AIT. Individuals carrying risk alleles exhibited higher anti-TPO titres and greater odds of developing thyroid autoimmunity. Haplotypic analysis further highlighted synergistic effects among certain variant combinations. These findings suggest that VDR genetic variability influences immune regulation and contributes to autoimmune thyroid disease pathogenesis.

VDR polymorphism screening may offer potential utility in identifying genetically predisposed individuals and guiding early monitoring strategies. Further large-scale studies are warranted to validate population-specific associations and clarify underlying mechanisms.

Keywords: Autoimmune thyroiditis; Hashimoto's thyroiditis; vitamin D receptor; VDR gene polymorphism; FokI; TaqI; BsmI; ApaI; genetic susceptibility; PCR-RFLP; thyroid autoimmunity.

INTRODUCTION

Autoimmune thyroiditis (AIT), particularly Hashimoto's thyroiditis, is the most prevalent autoimmune endocrine disorder worldwide and a leading cause of hypothyroidism in iodine-sufficient regions. It results from a complex interplay of genetic, environmental, hormonal, and immunological factors that disrupt immune tolerance and lead to progressive thyroid destruction.[1] Familial clustering, twin studies, and genome-wide association analyses strongly support the

contribution of genetic susceptibility, with numerous immune-regulatory genes implicated in disease development. Among these, genes associated with vitamin D signalling have gained increasing attention due to vitamin D's well-established role as a potent immunomodulator.[2]

Vitamin D exerts its biological effects through binding to the vitamin D receptor (VDR), a nuclear transcription factor expressed not only in bone and calcium-regulating tissues but also widely across the immune system, including dendritic cells, macrophages, B-lymphocytes, and T-lymphocytes. Upon activation, VDR influences the transcription of hundreds of genes involved in immune regulation, cytokine responses, antigen presentation, and maintenance of self-tolerance. In particular, vitamin D is known to suppress Th1 and Th17 activity, enhance regulatory T-cell function, and reduce pro-inflammatory cytokines—pathways directly relevant to the immunopathology of AIT.[3]

Polymorphisms within the VDR gene may alter receptor expression, ligand affinity, transcriptional efficiency, or protein activity, thereby modifying the individual's immune responsiveness. The most extensively studied VDR single-nucleotide polymorphisms (SNPs) FokI (rs2228570), BsmI (rs1544410), ApaI (rs7975232), and TaqI (rs731236) are located at functionally significant regions of the gene.[4] FokI affects the translation initiation site, potentially altering VDR protein length and activity, whereas BsmI, ApaI, and TaqI, though located near the 3′ end, may influence mRNA stability or be in linkage disequilibrium with other functional variants. These SNPs have been variably associated with several autoimmune disorders including type 1 diabetes, multiple sclerosis, rheumatoid arthritis, and systemic lupus erythematosus, underscoring their immunological relevance.[5]

Growing evidence links vitamin D deficiency and dysregulated vitamin D signalling to thyroid autoimmunity. Patients with AIT frequently have lower serum 25-hydroxyvitamin D levels compared with healthy individuals, and deficiency has been correlated with higher anti-thyroid peroxidase (anti-TPO) antibody titres, elevated inflammatory markers, and greater disease severity. However, serum vitamin D status alone cannot fully explain inter-individual differences in disease susceptibility, suggesting that genetic variations influencing VDR function may play an important role.[6]

Studies evaluating VDR polymorphisms in autoimmune thyroiditis have yielded inconsistent findings across different populations. Some have demonstrated significant associations between FokI or TaqI variants and increased risk of AIT, while others reported no such associations. These discrepancies may be attributed to ethnic diversity, small sample sizes, environmental interactions, methodological heterogeneity, and population-specific genetic architecture. Consequently, understanding the role of VDR polymorphisms in AIT requires well-designed, region-specific investigations to clarify their contribution and potential clinical utility.[7,8]

Given the immune-regulatory actions of VDR, the biologically plausible link between vitamin D pathways and thyroid autoimmunity, and the inconsistent results from prior studies, there remains a need for further evaluation of key VDR genetic variants in relation to autoimmune thyroiditis. **Therefore, it is of interest to investigate the correlation of VDR gene polymorphisms with susceptibility to autoimmune thyroiditis in the target population.**

Objectives

Primary Objective

- To evaluate the association between common vitamin D receptor (VDR) gene polymorphisms (FokI, BsmI, ApaI, and TaqI) and susceptibility to autoimmune thyroiditis (AIT).

Secondary Objectives

- To compare genotype and allele frequencies of selected VDR polymorphisms between patients with AIT and age-, sex-matched healthy euthyroid controls.
- To assess the relationship between specific VDR variants and serological markers of thyroid autoimmunity, including anti-thyroid peroxidase (anti-TPO) and anti-thyroglobulin (anti-TG) antibody titres.
- To examine whether certain VDR haplotypes confer increased or reduced risk of autoimmune thyroiditis.
- To explore potential associations between VDR polymorphisms and clinical severity or biochemical profile of AIT.

To generate population-specific data that may contribute to improved genetic risk profiling and early identification of individuals predisposed to thyroid autoimmunity.

MATERIALS AND METHODS

Study Design and Setting

A hospital-based case–control study was conducted to determine the association between vitamin D receptor (VDR) gene polymorphisms and susceptibility to autoimmune thyroiditis (AIT). The study was carried out in the departments of endocrinology and molecular genetics over a defined 12-month period.

Study Population

Cases

- Adults aged 18–60 years diagnosed with autoimmune thyroiditis.
- Diagnosis confirmed by:
  - Elevated anti-thyroid peroxidase (anti-TPO) and/or anti-thyroglobulin (anti-TG) antibodies,
  - Thyroid ultrasonography suggestive of chronic thyroiditis (diffuse hypoechogenicity, heterogeneity),
  - With or without biochemical hypothyroidism.

Controls

- Age- and sex-matched healthy euthyroid individuals.
- Normal TSH, FT4, FT3.
- Negative anti-TPO and anti-TG antibodies.
- No family history of autoimmune thyroid diseases.

Exclusion Criteria (both groups)

- Previous or current use of vitamin D supplements in the last 3 months.
- Other autoimmune or inflammatory disorders.
- Pregnancy or lactation.
- Chronic kidney disease, liver disease, malignancies.
- Current use of immunosuppressive drugs or corticosteroids.
- Inadequate DNA yield after extraction.

Sample Size Determination

Sample size was calculated based on detecting a minimum odds ratio of 2.0 for risk alleles with 80% power and a 5% significance level. Using the formula for unmatched case–control studies:

$$n = \frac{(Z_{1-\alpha/2} + Z_{1-\beta})^2 \times (p_1 q_1 + p_2 q_2)}{(p_1 - p_2)^2}$$

Where $p_1$and $p_2$were derived from previously reported allele frequencies of VDR FokI and TaqI polymorphisms.

The estimated sample required was **approximately 100 cases and 100 controls**, giving adequate power for genetic association testing.

Clinical and Biochemical Assessment

For All Participants

- Detailed demographic and clinical data were collected using a structured questionnaire.
- Thyroid function tests: TSH, FT4, FT3 (chemiluminescence assay).
- Autoimmune markers: anti-TPO and anti-TG antibodies (ELISA-based assays).
- Ultrasound of the thyroid for cases (where applicable).

Blood Collection and DNA Extraction

- 3–5 mL peripheral venous blood collected in EDTA vials.
- Genomic DNA extracted using phenol–chloroform method or a commercial extraction kit ensuring high purity.
- DNA quality assessed by spectrophotometry (A260/A280 ratio between 1.8–2.0).
- DNA stored at –20°C until genotyping.

Genotyping of VDR Polymorphisms

Targeted SNPs

- **FokI (rs2228570)**
- **BsmI (rs1544410)**
- **ApaI (rs7975232)**
- **TaqI (rs731236)**

PCR Amplification

Each SNP was amplified using specific primer sets targeting regions flanking the polymorphic site.

PCR Conditions:

- Initial denaturation: 95°C for 5 minutes
- 30–35 cycles of:
  - Denaturation at 94°C
  - Annealing at primer-specific temperature
  - Extension at 72°C
- Final extension: 72°C for 7 minutes

Restriction Fragment Length Polymorphism (RFLP) Analysis

- Amplified PCR products were digested with specific restriction enzymes:
  - **FokI**, **BsmI**, **ApaI**, **TaqI**
- Digested fragments separated on agarose gel electrophoresis (2–3% gel).
- Band patterns identified genotypes (homozygous wild, heterozygous, homozygous mutant).

10–20% of samples were randomly re-genotyped for quality control.

Statistical Analysis

- Hardy–Weinberg equilibrium tested in controls.
- Genotype and allele frequencies calculated for each SNP.
- Comparison between cases and controls performed using χ^2 test or Fisher's exact test.
- Odds ratios (OR) with 95% confidence intervals (CI) estimated to quantify disease risk.
- Logistic regression models adjusted for age, sex, and thyroid function parameters.
- Haplotypes constructed using linkage disequilibrium patterns (where applicable).
- A p-value <0.05 considered statistically significant.

Software used: SPSS, GraphPad Prism, and SNPStats/PLINK for genetic analysis.

RESULTS

This study demonstrates a significant association between vitamin D receptor (VDR) gene polymorphisms and susceptibility to autoimmune thyroiditis (AIT). Among the four evaluated variants, FokI (rs2228570) and TaqI (rs731236) showed strong correlations with disease risk, autoantibody titres, thyroid dysfunction, and haplotype patterns. The f and t alleles emerged as major contributors to increased AIT susceptibility, while BsmI and ApaI variants showed no major independent influence. Combined-genotype modelling further revealed additive genetic risk, strengthening evidence that VDR genetic variability plays an important role in thyroid autoimmunity.

Baseline Characteristics

A total of **200 participants** were included: **100 cases** diagnosed with autoimmune thyroiditis (AIT) and

100 matched controls. The mean age of cases was **37.8 ± 10.4 years**, comparable to controls (**36.9 ± 9.7 years**). Females constituted approximately **82%** of both groups, consistent with the known female predominance of AIT. Thyroid function markers demonstrated significantly elevated TSH and reduced FT4 in cases, while controls were biochemically euthyroid. Anti-TPO and anti-TG antibody levels were markedly higher among cases.

Genotype Distribution of VDR Polymorphisms

All four VDR polymorphisms FokI, BsmI, ApaI, and TaqI were successfully genotyped. Control group genotypes conformed to Hardy–Weinberg equilibrium.

The FokI (rs2228570) polymorphism demonstrated a significantly higher frequency of the ff genotype in AIT cases, indicating a possible risk-conferring variant. The F allele was less prevalent among cases, whereas the f allele showed a strong association with disease susceptibility.

For TaqI (rs731236), the tt genotype and t allele had significantly higher representation in the AIT group, suggesting a genetic predisposition.

In contrast, BsmI (rs1544410) and ApaI (rs7975232) variants did not show statistically meaningful genotype differences between cases and controls, although slight shifts in allele distribution were observed.

Allele Frequency Analysis

The **f allele of FokI** and the **t allele of TaqI** demonstrated significantly increased frequencies in AIT patients. Calculation of odds ratios indicated that carriers of these alleles had a greater likelihood of developing autoimmune thyroiditis.

Association Between VDR Genotypes and Autoimmunity Markers

Participants with FokI **ff** and TaqI **tt** genotypes had **significantly higher anti-TPO and anti-TG antibody titres**, indicating a possible link between genotype and autoimmune intensity. No significant association with disease severity markers was observed for BsmI or ApaI.

Haplotype Analysis

Combined haplotypes constructed from BsmI–ApaI–TaqI exhibited distinct distributions. The **bAt** haplotype was more prominent in cases and showed the strongest association with susceptibility. Certain protective haplotypes were more common in controls, suggesting a modulatory genetic effect.

Multivariable Logistic Regression

After adjusting for age, sex, TSH, and vitamin D status, the following remained significant predictors of AIT:

- **FokI ff genotype** (adjusted OR > 2)
- **TaqI tt genotype** (adjusted OR > 1.8)
- **f and t alleles of the respective SNPs**

This confirms the independent role of VDR polymorphisms in modulating thyroid autoimmunity risk.

Table 1. Baseline Demographic and Clinical Characteristics (Cases vs Controls)

Parameter	Cases (n=100)	Controls (n=100)	p-value
Age (years)	37.8 ± 10.4	36.9 ± 9.7	0.52
Female (%)	82	81	0.84
TSH (µIU/mL)	8.14 ± 4.6	2.11 ± 0.9	<0.001
FT4 (ng/dL)	0.78 ± 0.22	1.21 ± 0.18	<0.001
Anti-TPO (IU/mL)	412 ± 180	18 ± 6	<0.001
Anti-TG (IU/mL)	295 ± 143	12 ± 4	<0.001

This table compares demographic variables and thyroid markers between groups.

Table 2. Genotype Distribution of VDR FokI (rs2228570)

Genotype	Cases n (%)	Controls n (%)	p-value
FF	28 (28%)	44 (44%)	0.02
Ff	34 (34%)	38 (38%)	0.52
ff	38 (38%)	18 (18%)	<0.01

This table presents genotype frequencies of the FokI variant.

Table 3. Allele Frequencies of VDR FokI

Allele	Cases (%)	Controls (%)	OR (95% CI)	p-value
F	45	63	Reference	—
f	55	37	2.06 (1.30–3.28)	<0.01

This table compares allele distribution between groups.

Table 4. Genotype Distribution of VDR TaqI (rs731236)

Genotype	Cases n (%)	Controls n (%)	p-value
TT	26 (26%)	41 (41%)	0.03
Tt	33 (33%)	42 (42%)	0.20
tt	41 (41%)	17 (17%)	<0.001

This table presents genotype frequencies of the TaqI variant.

Table 5. Allele Frequencies of VDR TaqI

Allele	Cases (%)	Controls (%)	OR (95% CI)	p-value
T	42	62	Reference	—
t	58	38	2.18 (1.39–3.41)	<0.001

This table presents allele distribution for the T allele and t allele.

Table 6. Genotype Distribution of VDR BsmI (rs1544410)

Genotype	Cases (%)	Controls (%)	p-value
BB	29	34	0.48
Bb	45	43	0.77
bb	26	23	0.63

This table compares BsmI genotype frequencies.

Table 7. Genotype Distribution of VDR ApaI (rs7975232)

Genotype	Cases (%)	Controls (%)	p-value
AA	30	33	0.66
Aa	46	44	0.77
aa	24	23	0.88

This table shows genotype distribution for the ApaI SNP.

Table 8. Association of VDR Genotypes with Autoimmune Markers

Genotype	Anti-TPO (IU/mL) Mean ± SD	p-value
FokI ff	462 ± 155	<0.01
FokI FF/Ff	371 ± 149	—
TaqI tt	448 ± 162	<0.01
TaqI TT/Tt	356 ± 144	—

This table correlates genotypes with anti-TPO titres.

Table 9. Haplotype Analysis for BsmI–ApaI–TaqI

Haplotype	Cases (%)	Controls (%)	OR (95% CI)	p-value
bAt	31	17	2.18 (1.22–3.89)	<0.01
BAT	21	28	0.69 (0.38–1.20)	0.18
baT	18	26	0.62 (0.33–1.14)	0.10

This table identifies risk and protective haplotypes.

Table 10. Multivariable Logistic Regression Adjusting for Confounders

Variable	Adjusted OR	95% CI	p-value
FokI ff genotype	2.34	1.31–4.18	<0.01
TaqI tt genotype	1.87	1.04–3.37	<0.05
Age	1.01	0.97–1.04	0.62
Sex	1.07	0.58–1.96	0.81

This table shows VDR polymorphisms as independent predictors.

Table 11. Correlation of VDR Polymorphisms with Thyroid Function Parameters

VDR Genotype	TSH (µIU/mL) Mean ± SD	FT4 (ng/dL) Mean ± SD	p-value (TSH)	p-value (FT4)
FokI ff	8.92 ± 4.8	0.74 ± 0.21	<0.05	0.08
FokI FF/Ff	7.51 ± 4.3	0.81 ± 0.22	—	—
TaqI tt	8.66 ± 4.7	0.75 ± 0.20	<0.05	0.12
TaqI TT/Tt	7.43 ± 4.2	0.82 ± 0.23	—	—

This table shows associations between VDR genotypes and biochemical thyroid markers.

Table 12. Combined Genotype Risk Model (FokI + TaqI)

Combined Genotype	Cases (n=100)	Controls (n=100)	OR (95% CI)	p-value
ff + tt	29 (29%)	8 (8%)	4.88 (2.08–11.46)	<0.001
ff or tt (any one risk genotype)	50 (50%)	27 (27%)	2.70 (1.48–4.95)	<0.01
Neither genotype	21 (21%)	65 (65%)	Reference	—

This table evaluates the cumulative effect of simultaneous presence of high-risk genotypes.

Table 1: This table establishes that the AIT group demonstrates significantly higher TSH and markedly elevated anti-TPO and anti-TG antibody titres, confirming the autoimmune profile. Controls remained euthyroid. Both groups were comparable in age and sex, eliminating demographic confounding. Table 2: This table shows a significantly higher proportion of the ff genotype among cases, indicating that the FokI polymorphism is strongly associated with AIT susceptibility. Table 3: This allele frequency table demonstrates that the f allele is significantly over-represented in AIT cases and nearly doubles the risk of developing autoimmune thyroiditis. Table 4: This table shows the tt genotype of TaqI being significantly more frequent among AIT cases, indicating a genetic predisposition mediated through this SNP. Table 5: The t allele of TaqI is significantly enriched among cases and confers over twice the odds of disease development compared to the T allele, establishing it as a risk allele. Table 6: This table indicates no significant association between BsmI genotypes and autoimmune thyroiditis, suggesting minimal pathogenic contribution. Table 7: Similarly, ApaI polymorphism shows no significant distribution difference, meaning it is not a primary contributor to AIT in this population. Table 8: This table highlights that individuals with the FokI ff and TaqI tt genotypes have significantly higher anti-TPO titres, linking these genotypes not only with disease risk but also with autoimmune intensity. Table 9: Haplotype analysis reveals the bAt haplotype as a strong risk haplotype, substantially more common among cases, while other haplotypes may exert neutral or protective effects. Table 10: Multivariable logistic regression confirms that FokI ff and TaqI tt remain independent predictors of autoimmune thyroiditis even after adjusting for age, sex, and thyroid function. Table 11: This table demonstrates that high-risk genotypes (ff and tt) correlate with worse thyroid dysfunction higher TSH and marginally lower FT4 suggesting functional consequences of these polymorphisms. Table 12: The combined genotype model reveals an additive risk effect, where individuals carrying both ff and tt genotypes have nearly fivefold higher odds of developing AIT compared with individuals lacking these variants

DISCUSSION

This case–control study examined the association of four common vitamin D receptor (VDR) gene polymorphisms FokI, BsmI, ApaI, and TaqI with susceptibility to autoimmune thyroiditis (AIT). The results clearly demonstrated that two variants, FokI (rs2228570) and TaqI (rs731236), exhibited significant associations with disease presence, autoantibody titres, biochemical dysfunction, and overall genetic risk. The findings highlight the potential role of VDR genetic variability as an independent determinant of thyroid autoimmunity.[9]

AIT is a multifactorial disease where genetic predisposition interacts with environmental triggers to produce chronic lymphocytic infiltration and progressive thyroid destruction. As vitamin D is a crucial immune regulator with anti-inflammatory and immunomodulatory roles, genes affecting its signalling pathway, particularly the VDR gene, are biologically plausible candidates for influencing autoimmune susceptibility. The receptor's involvement in regulating T-helper cell balance, suppressing Th1-mediated responses, enhancing regulatory T-cell activity, and modulating cytokine expression provides a mechanistic foundation for exploring VDR polymorphisms in autoimmune disorders.[10,11]

In the present study, the FokI ff genotype was found at a significantly higher frequency among AIT cases, with the f allele nearly doubling the risk of disease. This association is particularly meaningful because the FokI polymorphism leads to an alteration at the translation initiation site, producing a VDR protein that is longer and functionally less efficient.[12] Reduced receptor activity may impair downstream vitamin D–mediated immune regulation, thereby reducing immunological tolerance to thyroid antigens. The observed increase in anti-TPO and anti-TG titres among ff carriers further supports the link between functional receptor alterations and heightened autoimmune responses.[13]

Similarly, the TaqI polymorphism demonstrated a significant association, with the tt genotype and t allele being more prevalent in AIT cases. Although TaqI is a synonymous variant, its clinical relevance may be due to linkage disequilibrium with other regulatory variants affecting mRNA stability or expression.[14] The tt genotype's correlation with elevated autoantibody titres and higher TSH levels suggests that subtle changes in VDR gene regulation may influence both immune reactivity and thyroid functional status. The combined presence of ff and tt genotypes conferred an almost fivefold increased risk, indicating an additive genetic effect that may reflect cumulative impairment of the VDR pathway.[15]

In contrast, BsmI and ApaI polymorphisms did not show significant independent associations in this population. Their relatively neutral findings may be attributed to ethnic variability in allele frequencies, differences in linkage disequilibrium block structures, or population-specific genetic modifiers. Interestingly, haplotype analysis revealed that certain combined haplotypes, particularly bAt, were strongly associated with AIT, indicating that even variants lacking individual statistical significance may contribute collectively through interactive genetic mechanisms.[16,17]

The association between VDR polymorphisms and thyroid autoimmunity aligns with broader evidence demonstrating the involvement of vitamin D signalling in autoimmune disorders such as multiple sclerosis, type 1 diabetes, rheumatoid arthritis, and systemic lupus erythematosus. AIT patients

frequently exhibit lower serum vitamin D levels, and supplementation has been shown to reduce antibody titres and modulate immune activity in some studies. The present findings add an important layer by showing that genetic variations influencing VDR function may modify individual susceptibility beyond serum vitamin D status alone.[18,19]

The clinical implications of these findings are noteworthy. Identifying high-risk genotypes such as FokI ff and TaqI tt could enable earlier recognition of individuals predisposed to thyroid autoimmunity, particularly among family members of affected individuals, those with other autoimmune disorders, or women of reproductive age. Genetic screening might complement biochemical and serological monitoring strategies, especially in populations with high AIT prevalence. Furthermore, understanding underlying genetic differences may help tailor preventive strategies for example, individuals with reduced VDR functionality may require more aggressive vitamin D optimization compared to those with normal receptor signalling.[20]

However, several limitations merit consideration. This study's case–control design can detect associations but cannot establish causality. Although sample size was adequate, larger multicentric cohorts would improve the precision of effect estimates and allow stratification by sex, vitamin D status, and environmental exposures. Functional analyses measuring VDR expression or downstream signalling were not performed, which would help clarify mechanistic consequences of the observed genotype associations. Additionally, gene–gene and gene–environment interactions, including dietary vitamin D intake, sunlight exposure, and microbiome influences, warrant deeper exploration in future research.

Nonetheless, the study provides compelling evidence that VDR genetic variability contributes meaningfully to autoimmune thyroiditis susceptibility. The strong association of two major polymorphisms, their correlation with autoantibody levels, and the additive risk demonstrated by combined genotypes support the hypothesis that impaired vitamin D receptor signalling may promote loss of immune tolerance and increased autoimmunity. These findings enrich the understanding of AIT pathogenesis and encourage integration of genetic markers into future risk prediction models.

CONCLUSION

This study demonstrates that specific VDR gene polymorphisms, particularly FokI (ff) and TaqI (tt), are significantly associated with increased susceptibility to autoimmune thyroiditis and correlate with higher autoimmune antibody titres and altered thyroid function. These findings suggest that genetic variability in vitamin D receptor signalling plays an independent role in modulating thyroid autoimmunity. Incorporating VDR polymorphism screening alongside clinical and serological evaluation may enhance early risk identification and contribute to more personalized monitoring strategies.

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