Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(2), 1756-1769 | ISSN:2251-6727

Unveiling the Genetic Contribution to Male Infertility: FSHR, and LHCGR Polymorphisms

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(Received: 04 February 2024 Revised: 11 March 2024 Accepted: 08 April 2024)

KEYWORDS

Male infertility, Genetic factors, Single Nucleotide Polymorphisms, Sperm DNA damage

ABSTRACT:

Introduction: Male infertility is a global concern affecting many couples. Understanding genetic factors in male infertility offers valuable insights into its causes and guides treatment strategies.

Objectives: Identify nucleotide polymorphisms linked to male infertility, focusing on (-29G>A) and 680A>G variants in the FSHR gene, and the 312G>A variant in the LHCGR gene.

Methods: We enrolled 243 male infertility patients from Visakhapatnam district, Andhra Pradesh, India. Participants, aged 25 to 50, had tried to conceive for at least a year without success. Semen samples were analyzed for physical traits and DNA fragmentation using the Sperm Chromatin Dispersion (SCD) assay. Single Nucleotide Polymorphisms (SNPs) related to infertility were analyzed using ARMS-PCR. Statistical analysis used SPSS, Epi Info, and MDR software.

Results: Analysis showed high levels of sperm DNA fragmentation, with 65% of participants exhibiting significant DNA damage. ARMS-PCR identified SNPs associated with male infertility, including FSHR (-29G>A), FSHR (680A>G), and LHCGR (312 G>A). Genotype frequencies varied significantly, with Chi-square tests indicating associations between certain genotypes and infertility risk. Odds ratios suggested increased infertility likelihood with specific SNP variants. MDR analysis revealed complex gene-gene interactions contributing to infertility.

Conclusions: Our study highlights sperm DNA damage prevalence and significant genetic variants associated with male infertility in Andhra Pradesh, India. Significant associations were found with FSHR (-29G>A polymorphism, suggesting the importance of genetic factors in male infertility and potential targets for diagnostic and therapeutic interventions.

1. Introduction

Male infertility is a significant issue globally, with estimates suggesting that it contributes to around 50% of infertility cases in couples. The World Health Organization indicates that male factor infertility affects approximately 20-30% of all infertility cases, with a global prevalence ranging from 8-12% [1,2]. Various factors contribute to male infertility, including genetic mutations, lifestyle choices, medical conditions, and medications [3]. Despite efforts to understand male infertility, idiopathic sperm abnormalities still make up about 30% of cases, highlighting the complexity of the condition [4]. Research emphasizes the importance of evaluating reversible and irreversible causes of male infertility to guide appropriate treatment strategies, including assisted reproductive technology when necessary. Understanding the underlying mechanisms of male infertility is crucial for improving outcomes for affected individuals.

Male infertility is a complex issue influenced by various factors, with genetics playing a significant role [5]. Recent studies have shed light on the impact of genetic factors, particularly gene polymorphisms, on male infertility. Polymorphisms within genes like FSHR, and LHCGR have been identified as crucial in disrupting sperm production, quality, and hormonal regulation, ultimately contributing to infertility [6]. These variations in DNA sequences can affect gene expression and increase

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JCHR (2024) 14(2), 1756-1769 | ISSN:2251-6727

susceptibility to certain diseases, highlighting the importance of genetic screening in understanding and addressing male infertility [7]. The exploration of gene polymorphisms offers valuable insights into the molecular mechanisms underlying male infertility, paving the way for more targeted diagnostic and therapeutic approaches.

Follicle-stimulating hormone receptor (FSHR), primarily found in the Sertoli cells of the testes, plays a crucial role in the response to follicle-stimulating hormone (FSH) signals, which are essential for male reproductive function [8]. FSH binds to the FSH receptor (FSHR) in spermatozoa, affecting sperm function [9]. Polymorphisms in the FSHR gene can impact receptor structure and function, potentially reducing sperm count and motility, thus contributing to male infertility [10]. Studies have shown that FSHR is expressed in various segments of human spermatozoa and that FSH incubation can lead to decreased motility and mitochondrial function in both patients and controls [11]. Additionally, FSH activates the AKT473 signaling pathway, further influencing sperm function [12]. Investigating the FSHR interactions allows researchers to pinpoint specific genetic variations that may affect FSHR signaling and contribute to infertility. Such insights offer potential avenues for developing targeted interventions to manage male infertility and enhance reproductive health.

Luteinizing hormone (LH) binds to the luteinizing hormone/choriogonadotropin receptor (LHCGR) on Leydig cells, stimulating testosterone production crucial for sperm development [13]. Genetic variations in the LHCGR gene, like the rs68073206 polymorphism, can impact gonadotropin sensitivity and male infertility risk. Additionally, LH plays a role in ovarian functions and endometrial receptivity, affecting fertility outcomes in assisted reproduction [14]. Research suggests that LH addition to FSH treatment may enhance ovarian response in sub/poor responders, potentially improving ART success rates [15]. Understanding genetic polymorphisms in genes like LHCGR is vital for unraveling male infertility mechanisms, guiding personalized interventions for optimizing sperm quality and hormonal balance to address fertility issues effectively.

In summary, the investigation of genetic polymorphisms within FSHR, and LHCGR genes provides insights into their involvement in male infertility. Understanding these genetic factors and their impact on sperm production, quality, and hormonal regulation can inform targeted interventions and treatment strategies to address male infertility effectively.

2. Objectives

This study aimed to investigate various aspects of male infertility through comprehensive analysis. The objectives of this research were to analyze sperm parameters, evaluate sperm DNA fragmentation and its effects, and conduct genetic analysis to identify polymorphisms associated with male infertility. The study identified nucleotide polymorphisms in infertile men, focusing on (-29G>A) and 680A>G variants in the FSHR gene, as well as the 312G>A variant in the LHCGR gene. Additionally, the study analyzed the association between identified polymorphisms and male infertility, including their correlation with abnormal semen parameters.

3. Methods

Study Population:

The study involved 243 male infertility patients, identified using the formula proposed by [16]. Patients were recruited from infertility clinics, including Vasudha Women & Children Hospital, Medicover Hospital, and Sri Clinic, in Visakhapatnam district, Andhra Pradesh, India.

To be eligible for the study, men had to be aged between 20 and 50, with partners under 50, and actively trying to conceive for at least a year

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without success despite regular unprotected sexual intercourse. Men with various semen abnormalities, from mild to severe, were included. All participants provided informed consent. Exclusions from the study were men with azoospermia and those with specific genetic causes of infertility such as Klinefelter's syndrome, Y-chromosome microdeletion, etc. Additionally, men whose partners had conditions like salpingitis, polycystic ovarian syndrome, or endometriosis were not included. Excluded also were men with a history of cancer, cryptorchidism, mumps orchitis, or vasectomy.

Ethical clearance was obtained from the Ethical Committee of Andhra University, Visakhapatnam, Andhra Pradesh, India (Approval No. IEC 54, dated 01-04-2022), and all participants provided informed consent before enrolment.

Collection and Analysis of Seminal Fluid:

Semen samples were collected after 48 hours to 6 days of abstinence. Detailed records were kept, and collection was done in private rooms adjacent to the lab. Samples were examined for volume, pH, color, liquefaction time, and viscosity. Samples were collected via masturbation into clean containers to avoid contamination. Incomplete samples were not analyzed.

Evaluation of Spermatozoa DNA Fragmentation using Sperm Chromatin Dispersion Assay (SCD):

To assess sperm DNA damage, the Sperm Chromatin Dispersion (SCD) test was used. This test identifies DNA damage by observing "halo" structures. Agarose-coated slides were prepared, and semen samples were mixed with agarose and dispensed onto the slides. The slides were treated with denaturation solution and lysis buffer and then stained with Giemsa. Microscopic analysis was done to observe halo size, and the sperm DNA fragmentation index (sDFI) was calculated.

Analysis of Single Nucleotide Polymorphisms (SNPs) Using Probe-Based ARMS-PCR:

Genomic DNA was extracted from the semen samples obtained from participants using the NucleoSpin® Tissue kit as per the manufacturer's instructions. Following DNA extraction, ARMS-PCR (Amplification Refractory Mutation System Polymerase Chain Reaction) was utilized for the analysis of Single Nucleotide Polymorphisms (SNPs). specific primers were designed to target the SNPs of interest, as listed in Table 1.

PCR Master Mix for each reaction was prepared by adding 5 µl of 2X TB Green Premix Ex Taq, along with 1 µl of forward primer (1F or 2F at 10 Pmol), 1 µl of reverse primer (1R or 2R at 10 Pmol), and 1 µl of molecular grade water. Additionally, 2 µl of DNA sample was included in both normal and mutant reactions. The PCR amplification was performed with an initial denaturation at 95°C for 3 minutes, followed by 35 cycles of denaturation at 95°C for 10 seconds each. The annealing temperature varies: it's 66°C for FSHR-29 and LHCGR, For FSHR 680, it's 62°C for normal samples and 60°C for mutant samples. Extension occurs at 72°C for 20 seconds in each cycle for all targets. Graphs 1-3 depict the outcomes of Probe-Based ARMS PCR analysis, showcasing various scenarios of SNP genotypes. In the first graph, only the normal DNA (depicted in green) is detected, indicating a homozygous wild-type genotype. Conversely, the second graph illustrates detection of only mutant DNA (depicted in red), signifying a homozygous mutant genotype. The third graph shows both mutant (red) and normal (green) DNA, indicating heterozygosity. These visual representations are pivotal for discerning genetic variations within the studied population, providing insights into the distribution of SNP genotypes and their potential implications.

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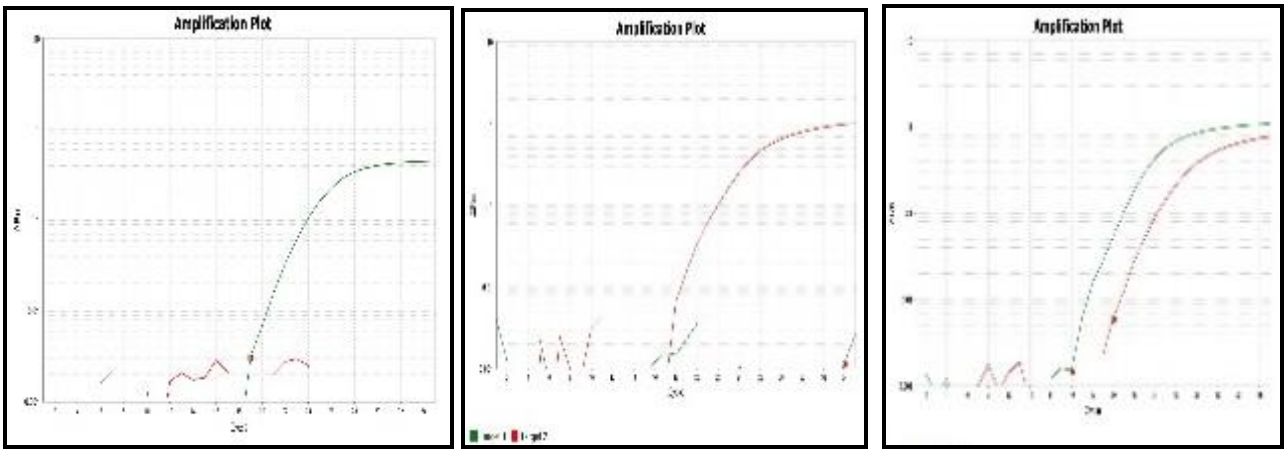
Table 1: Primer Sequences and Target Lengths for SNP Amplification

SNP	Primer Name	Primer Sequence	Target Length
FSHR (-29)	FSHR -29 1F	ATGGTTCTATTTGCTGTGTGCCTTA	260 bp
	FSHR -29 1R	TGCATCCATCCACCTGATTTCTTC	
	FSHR -29 2F	GAGGTTTTTCTCTGCAAATGCAGA	174 bp
	FSHR -29 2R	GGAATCTCTGTCACCTTGCTCTCTT	
FSHR 680	FSHR680 1F	TGTGTCCAAAGCAAAGATTC	254 bp
	FSHR 680 1R	ACAAGTATGTAAGTGGAACCAC	
	FSHR 680 2F	TTCAGCTCCCAGAGTCACCAA	122 bp
	FSHR 680 2R	AAAGGCAAGACTGAATTATC	
LHCGR 312	LHCGR 312 1F	GACAATGGTGCAGAACGAGATG	230 bp
	LHCGR 312 1R	CATGCAAATACTTACAGTGTTTTGTTAT	
	LHCGR 312 2F	TGAAAGCACAGTAAGGAAAGTGAG	147 bp
	LHCGR 312 2R	GCAACAGCTCCGTAACCAAGAC	



Graphs 1-3: ARMS-PCR Analysis of SNP Genotypes

Statistical Analysis:

The statistical analysis of the data involved the utilization of several software tools including SPSS (v.24), Epi Info (v.5), and MDR (v.3.0.2). This included the calculation of allele and genotype frequencies to understand their distribution within our study group. Chi-square tests were employed to compare differences both within and between groups, providing insights into the significance of these differences. Additionally, odds ratios and their corresponding 95% confidence intervals were calculated to quantify the strength of association between specific factors and outcomes of interest, offering a deeper understanding of the relationships observed. Moreover, we utilized Multifactor Dimensionality Reduction (MDR) software to explore interactions between genes, allowing for the identification of complex genetic patterns contributing to infertility within our study population.

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4. Results

The study aimed to explore the relationship between specific gene variants and DNA fragmentation in infertile men. Three key single nucleotide polymorphisms (SNPs) were analyzed, FSHR (-29G>A), FSHR (680A>G), and LHCGR (312 G>A). Results revealed varying degrees of association between genotypes and DNA fragmentation, summarized in Tables 2 and 3.

FSHR -29 (rs1394205, c.-29G >A) Genotypes: Analysis showed notable disparities in genotype distribution between individuals with abnormal (>30) and normal (<30) DNA fragmentation indexes. Statistically significant differences were observed between observed and expected counts in both abnormal ($\chi2$=6.4814) and normal ($\chi2$=3.7726) DNA fragmentation groups. Individuals carrying the GA genotype had a significantly increased risk of abnormal DNA fragmentation compared to those with the GG genotype. However, when considering the inter-group heterogeneity (differences between the abnormal and normal DFI groups), the chi-square value is non-significant ($\chi2$=5.1890). This indicates that the differences in allele frequencies between the abnormal and normal DFI groups are not statistically significant.

FSHR 680 (rs6166, 680A>G) Genotypes: Comparable distribution of FSHR genotypes was observed between individuals with normal and abnormal DNA fragmentation levels, with no significant intra-group or intergroup heterogeneity, indicating that the FSHR 680 genotype is not significantly associated with DNA fragmentation status and is unlikely to be a causative factor in male infertility.

LHCGR 312 (rs2293275, 312 G>A) Genotypes: A comparable distribution of LHCGR genotypes was observed between individuals with normal and abnormal DNA fragmentation levels. No significant association was found between LHCGR 312 genotypes and DNA fragmentation status.

Overall, these findings suggest that while there are some disparities in genotype distribution and potential associations with abnormal DNA fragmentation, none of the investigated polymorphisms showed consistent significant associations with male infertility parameters. Further research into other genetic factors contributing to male infertility is warranted to gain a more comprehensive understanding of the condition.

In the assessment of genetic associations with male infertility, Table 4 presents the results of tests for association, alongside odds ratios (OR) and 95% confidence intervals (CI) for FSHR (-29), FSHR 680, and LHCGR 312 genotypes/alleles. These measures provide valuable insights into the potential risk conferred by specific genotypes or alleles on infertility status. For FSHR (-29), individuals carrying the GA genotype and A allele show increased odds of abnormal spermia compared to those with the GG genotype and G allele, suggesting a potential association with male infertility. However, no significant associations were found for FSHR 680 and LHCGR 312, indicating that these SNPs may not play a substantial role in male infertility.

Additionally, Table 5 shows that among the genotypes analyzed (FSHR -29, FSHR 680, and LHCGR 312), no significant associations with male infertility were found for either abnormal spermia or normospermia groups, as indicated by non-significant p-values (>0.05) and odds ratios close to 1, suggesting no strong effect on the risk of either condition.

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Table 2: Distribution of FSHR, and LHCGR genotype frequencies in infertile men

Gene	Genotype	Abnormal DFI Group (>30)		Normal DFI Group (<30)	
		Observed	Expected	Observed	Expected
FSHR (-29)	GG	36.00	32.44	86.00	80.02
	GA	14.00	21.12	72.00	83.96
	AA	7.00	3.44	28.00	22.02
	Total	57.00	57.00	186.00	186.00
	Chi-square	χ^2=6.4814** (0.95>p>0.90)		χ^2= 3.7726* (0.90>p>0.80)	
FSHR 680	Asn/Asn (AA)	16.00	15.79	59.00	57.04
	Asn/Ser (AG)	28.00	28.42	88.00	91.92
	Ser/Ser (GG)	13.00	12.79	39.00	37.04
	Total	57.00	57.00	186.00	186.00
	Chi-square	χ^2=0.0125^{NS} (0.95>p>0.90)		χ^2= 0.3391^{NS} (0.90>p>0.10)	
LHCGR 312	Ser/Ser (GG)	22.00	20.28	82.00	79.37
	Ser/Asn (GA)	24.00	27.44	79.00	84.27
	Asn/Asn (AA)	11.00	9.28	25.00	22.37
	Total	57.00	57.00	186.00	186.00
	Chi-square	χ^2=0.8952^{NS} (0.5>p>0.10)		χ^2= 0.7264^{NS} (0.5>p>0.10)	

***p<0.05, **p<0.01, ***p<0.001, NS Non-significant** DFI – DNA Fragmentation Index

Table 3: Distribution of allele frequencies in study population

Gene	Alleles	Abnormal DFI Group (>30)	Normal DFI Group (<30)	Inter-group χ^2
FSHR (-29)	G	0.7500 ± 0.0196	0.6600 ± 0.0215	5.1890^{NS}
	A	0.2500 ± 0.0196	0.3400 ± 0.0215	
FSHR 680	A	0.5300 ± 0.0226	0.5500 ± 0.0226	0.2870^{NS}
	G	0.4700 ± 0.0226	0.4500 ± 0.0226	
LHCGR 312	G	0.5900 ± 0.0223	0.6500 ± 0.0004	1.319^{NS}
	A	0.4100 ± 0.0223	0.3500 ± 0.0004	

***p<0.05, **p<0.01, ***p<0.001, NS Non-significant** DFI – DNA Fragmentation Index

Table 4: Test of Association, Odds Ratio, and 95% Confidence Interval Estimates of FSHR, and LHCGR phenotypes in infertile men

Gene	Genotypes/ Alleles	DFI Abnormal	DFI Normal	OR	(95%CI)	p-value

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FSHR (-29)	GG	36 (63.2)	86 (46.2)	Reference		1
	GA	14 (24.6)	72 (38.7)	2.15	(1.08-4.30)	0.0200
	AA	7 (12.3)	28 (15.1)	1.67	(0.67-4.18)	0.2672
	GA+AA	21 (37.0)	100 (53.8)	1.99	(1.08-3.67)	0.0254
	G	86 (75.0)	242 (65.0)	Reference		1
	A	28 (25.0)	130 (35.0)	1.65	(1.02-2.66)	0.0384
FSHR 680	AA	16 (28.1)	59 (31.7)	Reference		1
	AG	28 (49.1)	88 (47.3)	0.85	(0.42-1.71)	0.6530
	GG	13 (22.8)	39 (21.0)	0.81	(0.35-1.88)	0.6283
	AG+GG	41 (71.9)	127 (68.3)	0.84	(0.44-1.62)	0.6017
	A	204 (55.0)	60 (53.0)	Reference		1
	G	168 (45.0)	54 (47.0)	1.09	(0.72-1.66)	0.6789
LHCGR 312	GG	22 (38.6)	82 (44.1)	Reference		1
	GA	24 (42.1)	79 (42.5)	0.88	(0.46-1.70)	0.7102
	AA	11 (19/3)	25 (13.4)	0.61	(0.26-1.43)	0.2528
	GA+AA	35 (61.4)	104 (55.9)	0.80	(0.43-1.46)	0.4637
	G	68 (59.0)	242 (65.0)	Reference		1
	A	46 (41.0)	130 (35.0)	0.79	(0.52-1.22)	0.2951

***p<0.05, **p<0.01, ***p<0.001, NS Non-significant** DFI – DNA Fragmentation Index

Table 5: Association of FSHR and LHCGR Genotypes with Diagnosis (Normospermic and Abnormospermic) in Infertile Men

Gene	Genotypes	Diagnosis N (%)		OR	(95%CI)	χ^2 value	p-value
		Ab.Spermia	Normospermia				
FSHR (-29)	GG	90 (37.0)	32 (13.2)	Reference			1
	GA+AA	91 (37.4)	30 (12.3)	0.93	(0.52-1.65)	0.066	0.797
FSHR 680	AA	57 (23.5)	10 (7.4)	Reference			1
	AG+GG	124 (51.0)	44 (18.1)	1.12	(0.60-2.11)	0.131	0.717
LHCGR 312	GG	79 (32.5)	25 (10.3)	Reference			1
	GA+AA	102 (42.0)	37 (15.2)	1.15	(0.64-2.06)	0.208	0.648

Gene-Gene Interactions:

Table 6 presents results from Multifactor Dimensionality Reduction (MDR) analysis for various combinations of genetic loci studied. FSHR -29 G>A emerged as the most effective single locus model (TBA= 0.5846, CVC=10/10, P=0.05) and FSHR -29G>A and LHCGR 312G>A combination as the best two-locus model (TBA= 0.6246, CVC=10/10, P=0.01) for predicting infertility and three loci were analyzed. These combinations, detailed in the table, highlight associations between multi-locus genotype combinations and infertility.

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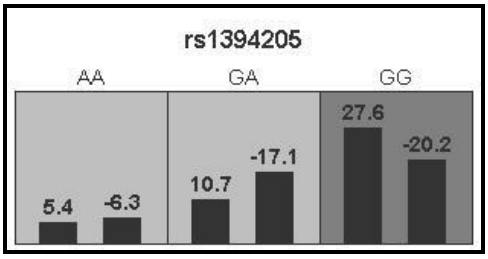
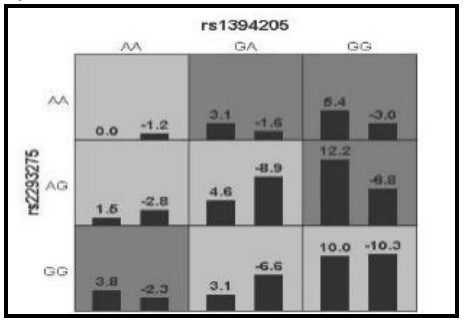
Table 6: Multi-locus interaction model by MDR method for gene polymorphisms

Locus No. & Combinations	Training Bal. Acc.	Testing Bal Acc.	CVC	Sign Test (p)
FSHR_29	0.5846	0.5860	10/10	8 (0.0547)*
FSHR_29, LHCGR_312	0.6246	0.5787	10/10	9 (0.0107)*
FSHR_29,FSHR_680,LHCGR_312	0.6534	0.4952	10/10	5 (0.6230)

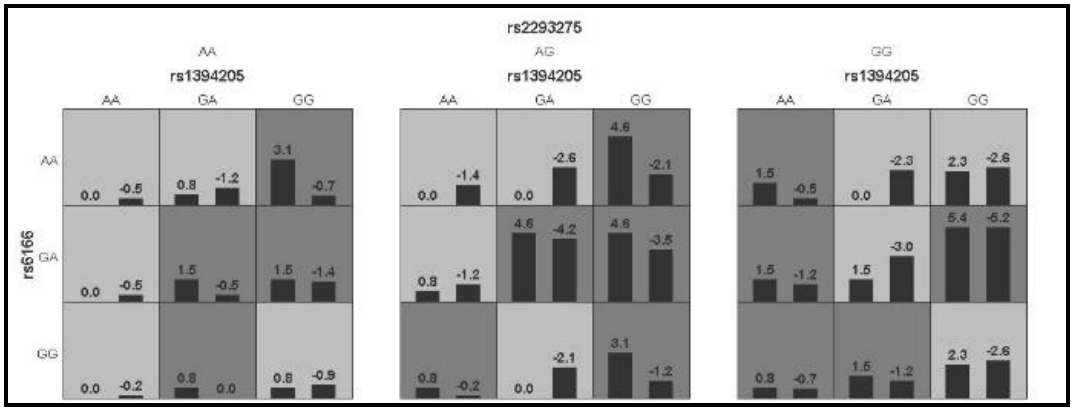
*P≤0.05 based on 1000 permutations; CVC = cross-validation consistency



Graph 4: Single-loci model



Graph 5: Single-loci and Two-locus model



Graph 6: Three-locus model

Graph 7: Interaction Dendrogram for polymorphisms studied in male infertility

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Graphs 4 to 6 depict gene combinations associated with the risk of infertility. Dark shading represents high-risk genotypes, light shading indicates low-risk and white cells signify no data. According to the single-locus model, the FSHR (-29G>A) gene is a significant predictor of male infertility, with the GG genotype carrying the highest risk. In the two and three-locus models, specific combinations of genes are correlated with varying levels of infertility risk. The dendrogram in Graph 7 illustrates the degree of dependence between genes, with weaker links shown as orange bars and stronger associations depicted by red bars. These findings provide valuable insights into the genetic factors influencing the risk of infertility.

5. Discussion

Male infertility is a multifactorial condition influenced by various genetic and environmental factors. In this study, we investigated the relationship between specific gene variants and DNA fragmentation in infertile men within the Indian population. Our findings provide valuable insights into the genetic basis of male infertility-related DNA fragmentation, shedding light on potential biomarkers for diagnostic and therapeutic interventions.

Studying the FSHR -29 gene in male infertility has provided important insights. FSH-R, found in the early male genital tract, testicular tumors, and sperm, plays a crucial role in various testicular disorders. Its positive effects on sperm motility, survival, and other factors suggest it could be useful in infertility treatments. However, the association between the FSHR (-29G>A) gene variant and male infertility is still debated. Initial investigations by Simoni et al., [17], Asatiani et al., [18], Ahda et al., [19], and Galan et al. [20] found no association between FSHR (-29G>A) genotype and male infertility. This trend continued in subsequent studies by Pengo et al., [21], Tüttelmann et al., [22], Zalata et al., [23], and others. Similarly, studies conducted by Balkan et al., [24], Lend et al., [25], Li [26], Safarinejad et al., [27], Ghirelli et al., [28] and Wu [29] also reported no association between FSHR (-29G>A) genotype and male infertility. More recent studies by Wu et al., [30] Shkelzen et al., [31], Mongioì et al., [32] Bang et al., [33], Cannarella et al., [34], Pirtea et al., [35]. In contrast, some studies including ours reported an association between FSHR (-29G>A) genotype and male infertility. Grigorova et al., [36], Lazaros et al., [37], Gharesi Fard et al., [38], Nahal et al., [39], Tsitlakidis et al., [40], Wu Q et al., [41], Zhylkova et al., [42] and Kadhum and Hassan [43] demonstrated such an association. These findings suggest a mixed picture regarding the association between FSHR (-29G>A) genotype and male infertility, indicating a need for further research to clarify its role in this condition.

The association of the FSHR 680A>G gene variant with male infertility has been investigated by various studies. Initial research by Ahda et al., [19] Wunsch et al., [44] and Pengo et al., [21] found no association between FSHR 680A>G genotype and male infertility. This lack of association was consistently reported in subsequent studies by Balkan et al., [24], Lend et al., [25], Li [26], Wu [29], Wu [30] and others. Similarly, recent studies by Mongioì et al., [32], Bang et al., [33], Cannarella et al., [34] and our own survey conducted in 2024 found no association between FSHR 680A>G genotype and male infertility. However, some studies suggest otherwise. Tamburino et al., [45] reported an association between FSHR 680A>G genotype and male infertility. On the contrary, Tsitlakidis et al., [40] found no association in their study. These findings indicate some disagreement regarding the association between FSHR 680A>G genotype and male infertility. Further research is needed to clarify the role of this gene variant in male infertility.

The luteinizing hormone/chorionic gonadotropin receptor gene (LHCGR) plays a pivotal role in male reproductive physiology, influencing crucial aspects such as testicular development, steroidogenesis, and spermatogenesis. Given its

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significance, genetic variations within the LHCGR gene have been the subject of considerable investigation, particularly regarding their potential association with male infertility. Among these variations, the LHCGR 312 polymorphism (rs2293275) has garnered substantial interest due to its plausible involvement in the pathophysiology of male infertility. In our study, no significant association was found between this polymorphism and infertility. This finding aligns with the results from other studies, such as the study by Simoni et al., [46] which found that the S312N SNP in exon 10 of the LHCGR was not significantly associated with maldescended testes, a condition often linked to male infertility. Moreover, the study by Ali et al., [47] investigated the association of LHCGR gene rs68073206 SNPs with non-obstructive azoospermia (NOA) in Iraqi infertile men. Although no significant difference in genotypic prevalence was observed between infertile men with NOA and fertile men, variable gonadotropin sensitivity was revealed, suggesting a potential impact on hormonal treatment outcomes for male infertility. Lastly, Pirtea et al., [35] conducted a study to assess the consequences of specific genotype profiles of FSHR and LHCGR on assisted reproductive technology outcomes. They found no significant association between gonadotropin receptor polymorphisms, including LHCGR N312S, and assisted reproductive technology outcomes, indicating that these variants should not be considered predictive factors for reproductive outcomes. Together, these findings highlight the complexity of genetic influences on fertility outcomes and emphasize the importance of further research to elucidate the role of LHCGR polymorphisms in both male and female infertility.

Conclusion

In conclusion, our study aimed to investigate the association between FSHR (-29G>A), FSHR 680A>G, and LHCGR 312G>A gene variants and male infertility. Our analysis revealed a significant association between FSHR (-29G>A) genotype and male infertility, aligning with previous studies indicating a potential role of this variant in infertility. However, no significant associations were found between FSHR 680A>G, LHCGR 312G>A variant, and male infertility in our study population. These findings contribute to the growing body of evidence regarding genetic factors influencing male infertility. The association of FSHR (-29G>A) genotype with male infertility suggests its potential as a genetic marker for infertility risk assessment. However, further research with larger and more diverse populations is needed to validate these findings and elucidate the underlying mechanisms. In conclusion, our study underscores the importance of genetic variations, particularly FSHR (-29G>A), in male infertility. Understanding the genetic basis of infertility can aid in better diagnosis, prognosis, and personalized treatment strategies for affected individuals.

Acknowledgments

The authors thank the patients, who willingly participated in the study.

Funding: No funding sources

Conflict of interest: None declared

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