RESEARCH PAPER

"Integrative Assessment of Genetic Variants and Ayurvedic *Prakriti* in Endometriosis Using Whole Exome Sequencing"

Whole Exome Sequencing-Based Genetic Profiling of Endometriosis and Its Association with Ayurvedic *Prakriti*

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Abstract

Background: Endometriosis is defined by the presence of endometrial-like tissue outside of its usual location, which is the lining of the uterus. This Endometriosis is a complex gynaecological disorder with heterogeneous clinical presentations and poorly understood genetic underpinnings. Whole exome sequencing (WES) has enabled the discovery of novel variants associated with disease susceptibility and progression. *Ayurveda*, the traditional system of Indian medicine, classifies individuals into constitutional types or *prakriti* (*Vata, Pitta, Kapha*), which are hypothesized to influence disease predisposition and phenotypic variability. *Prakriti* is influenced by culture, inherited characteristics, and geographical origin.

Objective: This study aimed to integrate WES-based genetic profiling with *prakriti* analysis in diagnosed cases of endometriosis to explore potential associations between constitutional types and genetic variants.Materials and **Methods :**This study was conducted on 50 clinically diagnosed cases of endometriosis at Sir Sunderlal Hospital, Institute of Medical Sciences, Banaras Hindu University (BHU), in collaboration with the Centre for Genetic Disorders, Institute of Science, BHU. Exome Analysis –The exome sequencing will be done illumine HiseqR NGS platform either through outsourcing or on the platform available in Centre for Genetic Disorders, BHU.

Prakriti

Assessment: Constitutional typing (*prakriti*) was performed using a validated questionnaire-based proforma, followed by expert clinical evaluation, classifying patients into *Vata, Pitta*, or *Kapha* predominance.

Genetic Analysis: Peripheral blood samples were collected from all participants. Genomic DNA was extracted using the salting-out method. Next-generation sequencing (NGS) was performed to identify genetic variants, with subsequent bioinformatics analysis to annotate and prioritize genes associated with endometriosis.

Clinical Correlates: In addition to genomic analysis, patient demographics and clinical profiles, including age, chief complaints, menstrual history, and endocrine parameters, were recorded and analyzed.

Statistical Analysis: Correlation between *prakriti t*ypes and genetic variations was assessed, along with associations with clinical parameters. Statistical significance was evaluated using chi-square.

Results: Among the 50 endometriosis patients, *prakriti* distribution revealed a predominance of *Vataja prakriti*, followed by *Pittaja* prakriti, with minimal representation of *Kaphaja* type. NGS analysis demonstrated a higher burden of gene variations in *Vataja prakriti* individuals compared to other groups. Variants in genes implicated in endometriosis pathogenesis were particularly enriched in the *Vataja* subgroup, whereas *Pitta*-dominant patients exhibited moderate associations, and *Kapha*-dominant individuals showed minimal variations.

Correlational analysis suggested a possible association between *Vataja prakriti* and genetic susceptibility to endometriosis. Additionally, clinical parameters such as menstrual irregularities and endocrine profile alterations were more frequent in *Vataja* patients, supporting a *prakriti*-linked predisposition.

Conclusion: The integration of WES with *prakriti* analysis provides novel insights into the molecular and constitutional basis of endometriosis. This interdisciplinary approach may facilitate a more personalized framework for understanding disease heterogeneity and pave the way toward individualized management strategies combining genomic and Ayurvedic perspectives.

Keywords: Endometriosis, Whole Exome Sequencing, *Ayurveda*, *Prakriti*, Genomics, Personalized Medicine

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1.Introduction

Endometriosis is a long-lasting condition characterized by inflammation that is dependent on estrogen. It causes severe discomfort in the pelvic area and can also lead to difficulties in conceiving or becoming pregnant. It impacts approximately 10% to 15% of women of reproductive age, which amounts to around 176 million women[1,2] and

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teenagers globally. Endometriosis is defined by the presence of endometrial-like tissue outside of its usual location, which is the lining of the uterus. This tissue is normally seen on pelvic structures; however it can also be found in locations far from the pelvis.[3] *Prakriti* refers to the combination of three *doshas* that every individual possesses from birth (Wallace, 2020). Every individual possesses a distinct proportion of *Tridosha*, which is influenced not just by genetic factors but also by the environment during fetal development. The features of an individual are determined by their primary *Dosha Prakriti*, and the dominance of *Dosha* regulates their physiology. By identifying the *Dosha* dominance and using it as a basis, preventive measures and treatments may be created. This approach can assist find the most effective lifestyle interventions and medications. The genetic makeup of an individual determines the proportions of *Tridoshas*, with *Shukra* being a determining factor. However, the environment, including the maternal nutrition and lifestyle, can also have an influence on these proportions during development. Nevertheless, *Prakriti* is influenced by culture, inherited characteristics, and geographical origin. *Doshik* diseases manifest when the levels of *Vata, Pitta*, and *Kapha* exceed an individual's tolerance. *Prakriti* refers to the *dosha* balance at conception. The integration of *Ayurvedic Prakriti* categorization methods with current genomics has led to the identification of the molecular and genomic foundation of the *Dosha Prakriti* hypothesis. Individuals with different *Prakriti* types, as identified by Ayurveda, exhibit notable variations in their biochemical and haematological markers. The genomic studies revealed notable variations in gene expression levels among the primary *Prakriti* types, particularly in genes related to immunity, cell division, blood coagulation, and other relevant functions (Chatterjee and Pancholi, 2011). Ayurveda and genomics can mutually enhance each other, particularly through the implementation of preventive care measures. Specifically, it is highly pertinent to the field of P4 medicine, which encompasses the principles of prediction, prevention, personalization, and participation. These principles are derived from certain core concepts in Ayurveda (Flores et al., 2013; Lemonnier et al., 2017). Access to well-established tailored preventative and lifestyle control recommendations would facilitate individuals' ability to engage in self-care. The integration of *Ayurvedic Prakriti* differentiation methods with sophisticated genomics has allowed for the discovery of the molecular genetic foundation of the *Dosha Prakriti* idea (Hawkins *et al*., 2010; Chatterjee and Pancholi, 2011; Prasher et al., 2016). Ayurgenomics is founded on similar ideas as pharmacogenomics/pharmacogenetics and can serve as a framework for implementing the concept of individualized medicinal treatment. Several attempts have been implemented to integrate *Ayurveda* with pharmacogenetics, including the integration of epigenetics with *Ayurveda*, Ayurnutrigenomics, and other related approaches. Ayurgenomics is currently attracting significant study interest in the field of tailored treatment. (4-14)

2. Material and Method:

1. Statement of Ethics

Each participant provided written informed consent to participate in the study and have their blood samples collected for research purposes. The study adhered to the Helsinki Declaration, and the Ethics Committee of the Institute of Medical Science at Banaras Hindu University in Varanasi, India, granted its clearance.

2. Participant recruitment and clinical evaluation

Nine adult women with confirmed clinical diagnoses of Endometriosis were recruited from the Department of Obstetrics and Gynaecology at the Institute of Medical Science, Banaras Hindu University.

Each patient underwent a comprehensive clinical assessment upon enrolment. More specifically, detailed information on demographics (including age and anthropometric measurements), medical history (both personal and family), and gynaecological history (including age of first menstruation, diagnosis of endometriosis, number of pregnancies, and diagnosis of infertility) was collected. Prior to commencing medical treatment or surgery, every patient underwent a comprehensive evaluation of the most common symptoms associated with electromagnetic hypersensitivity, including ovulation, premenstrual and postmenstrual discomfort, painful menstruation, painful sexual intercourse, difficulty with bowel movements, and painful urination.

3. Extraction and Assessment of DNA

A sample of peripheral whole blood was collected in order to extract genomic DNA from each patient.

4. Whole-Exome Sequencing (WES)[15,16,17,18]

WES is a genomic technique that involves sequencing the protein-coding regions of the genome.

The Whole Exome Sequencing (WES) procedure was performed using an Illumina Next Seq 550 device.

Preparation of the library

The construction of the Whole Exome libraries was carried out utilizing the MGIEasy Exome FS Library Prep Kit. 200 ng of genomic DNA underwent fragmentation and purification using MGIEasy DNA Clean beads. The DNA fragments that had been purified underwent end repair and dA-tailing. Additionally, adapter ligation was conducted to connect sequencing technology-specific adapters that include an index. The DNA ligated with the adapter was purified using MGIEasy DNA clean beads. The adaptor and indexed DNA were amplified using PCR for 8 cycles and then purified using MGIEasy DNA clean beads. The library underwent a quality check using the Qubit Fluorimeter from Thermofisher Tech. and the Agilent Bio analyzer 2200. Additionally, the libraries were combined in equal amounts and subjected to a hybridization process for target capture using MGIEasy Exome Capture V5 Probes for a duration of 24 hours. The process of capturing the target was carried out using Streptavidin beads, followed by amplification of the library on the beads using PCR for a total of 12 cycles. An assessment of the intended library's quality was conducted.

Genomic sequencing

The double-stranded DNA libraries underwent single-stranded DNA circularization and production of DNA

nanoballs according to the specified loading criteria. The libraries were sequenced using the G400 MGI sequencer according to the company's methodology.

5. Statistical analysis

Genomic variant detection and assessment of data integrity

Variant calling was performed following the alignment of the sample reads and subsequent quality check. Concisely, each sample's NovaSeq WES reads were aligned to the hg38 reference genome using BWA MEM. We utilized the We Call tool to identify the different versions. The gVCFs were merged with GLnexus to create a joint-genotyped, multi-sample project-level VCF (pVCF). SNV genotypes with a read depth (DP) of less than 7 and indel genotypes with a read depth of less than 10 were classified as no-call genotypes. After applying the DP genotype filter, a variant-level allele-balance filter was utilized. The variations meeting either of the following criteria were retained: (i) presence of at least one homozygous variant carrier; or (ii) presence of at least one heterozygous variant carrier with an allele balance (AB) exceeding the specified thresholds (AB $\geq$ 0.15 for SNVs and AB $\geq$ 0.20 for indels). Samples exhibiting discrepancies between reported sex and genetically determined sex were excluded. A pVCF was generated for subsequent analysis, utilizing the GLnexus joint genotyping program.

Creation of analysis-ready files

A Plink2 file set that is ready for analysis was created using the following steps. Initially, the exome data was divided into separate categories based on the samples. Secondly, we eliminate the variants that have a missingness rate greater than 0.1 and are monomorphic. Following the use of these filters, the data was utilized for association studies.

Utilizing machine learning to detect low-quality variations in exome sequencing

The filtering process was conducted based on the following criteria: (i) identifying Mendelian inconsistencies in the exome sequencing data, (ii) detecting changes in allele MAF frequencies between different exome sequencing batches, (iii) analyzing principal components derived from variants with a MAF of less than 1%, and (iv) considering transmitted singletons. The model was subjected to a maximum of thirty WeCall/GLnexus quality measures, including allelic balance and coverage depth.

The data was partitioned into two groups: 80% for training and 20% for testing. A grid search was performed using a 5-fold cross-validation on the training set to determine the hyperparameters that yield the maximum accuracy in cross-validation. This was employed on the test group to verify the accuracy.

Annotation of genetic variants

The variations discovered by WES were annotated using SnpEff. The genic areas were found using Ensembl release 85. The variants were annotated with frameshift, start loss, stop gain, splice acceptor, and splice donor. Annotation resources such as SIFT, PolyPhen2 HDIV, PolyPhen2 HVAR, LRT, and Mutation Taster were used to identify highly harmful pathogenic missense variants. Missense variations were classified as 'likely harmful' if all five algorithms expected them to be deleterious, 'potentially deleterious' if at least one algorithm predicted them to be deleterious, and 'likely benign' if none of the algorithms predicted them to be deleterious.

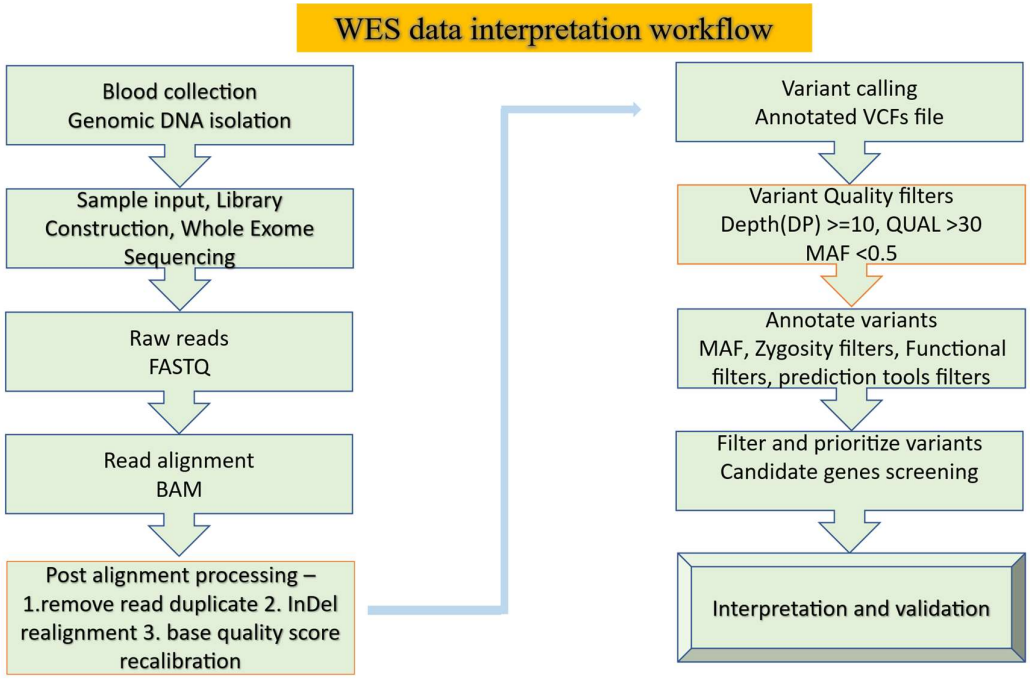
Filtering of genetic variants

Several filters were employed to eliminate variations that were not clinically significant. Additional criteria, such as depth quality and allele frequency, were considered when modifying the variant. All synonymous variations were excluded from the analysis. The following filters were used for the analysis:

The depth (DP) must be equal to or greater than 10.

The value of QUAL is greater than 30.

Minor Allele Frequency is less than 0.05.



Creation of Gene Burden Masks

The rare variants were classified based on the gene areas, while ensuring precise genotyping of homozygous normal, heterozygous, and homozygous mutants (minor alleles). Genotypes were not phased in order to accurately count compound heterozygotes during burden testing. Two categories of masks were employed for each gene: one for rare protein-truncating variants (pLOFs) with tight criteria (M1), and another for rare pLOFs and potentially harmful missense variants with more lenient criteria (M3). Each of the indicated organizations utilized five distinct burden masks per gene, depending on the minor alleles of the variations. Concisely, 10 load tests were performed for each gene.

Comparison with Other Extensive Resources

The variant statistics obtained from whole exome sequencing were compared to the publically available resources gnomAD v.3.1 and TOPMed Freeze 8. Only PASS variations and annotated datasets were kept

3. Results

Table 1: List of 122 Genes associated with endometriosis enlisted from various database.

- AR
- ABCA13
- BCL6
- BDNF
- C3
- CA125
- CARD-9
- CCL17
- CCNB1
- CCR1
- CCR10
- CCDC170
- CCRL2
- CDC42
- CDKN2A-AS1
- CEP112
- CIITA
- COX-2
- CSMD1
- CUBN
- CYP17
- GREB
- GREB-1
- GSTM1
- GSTP1
- GSTT1
- HIF-1α
- HLA-G
- HOX-9
- OXA-10
- OXA-13
- HOXC10
- HSD17B1
- HSD17B7
- ICAM
- IL1
- IL1R1
- IL2RB
- IL1A
- IL-4
- IL-6
- IL-10
- MUC-1
- MUC-2
- MUC-4
- MUC-17
- MUC5AC
- NALCN
- NAV-2
- NEB
- NFE2L3
- NFKB1
- NGF
- NLRP3
- PARP4
- PDHA1
- PLGF
- PR
- PTPRD
- RBM43
- RHOA
- RHOJ
- RND3

- CYP17A1
- CYP19
- CYP19A1
- CYP1A
- CYP1B1
- CYP2C19
- DYSF
- EGFR
- ER
- ERAP-1
- ERBB-3
- ESR1
- FAS
- FCRL3
- FGFR4
- FN1
- FOS
- FSHB
- FUT-2
- GDF15
- IL-15
- IL12B
- IL-16
- IL-17A
- IL-18
- IL-1B
- INK4
- KAZN
- KDR
- KRAS
- LAMA5
- LILRB1
- LILRB2
- MAP3K4
- MCP1
- MMP2
- MMP3
- MMP7
- MMP9
- MST-1
- SETBP1
- SIRT1
- SKAP1
- SYNE1
- SYNE2
- TNFRSF1A
- TP53
- TNF
- TYK2
- UGT2B28
- USP17L2
- VEGF
- VEGFA
- VEZT
- VTI1A
- VWF
- WNT4
- WT1
- ZNF366

Table 2: List of 34 genes association in 09 diagnosed cases of endometriosis during WES.

	Gene	Pt.
	ABCA13	2,3,4,5,9
	BCL6	6
	CSMD1	2,3,4,6
	CUBN	2,5,6,9
	CYP2C19	1
	DYSF	2
	EARP4	7
	ERAP1	4
	ERBB3	2
	GREB1	1
	IL1R1	6
	KAZN	5
	KDR	8
	LAMA5	8
	LILRB1	7,9,10
	LILRB2	2
	MAP3K4	1,2,3,4,6,8
	MST1	1,3,6,10
	MUC17	3,7,8
	MUC4	2,4,5,6,8,9,10
	MUC5AC	3,4,6
	MUC6	10
	NEB	1,3,6
	NFKB1	8
	NGF	3
	NLRP3	8
	PARP4	2,4,5,6,8,9
	SETBP1	8
	SYNE1	2,3,5
	SYNE1	2,3,5
	SYNE2	1,7
	TYK2	1
	USP17L2	4
	VWF	2,8

List of Abbreviation

NA stands for "not available.
D: Detrimental.
T: Endured without resistance or objection.
GENE: The gene symbol or name.
FEATURE-ID: Identifier for the specific feature or variant within the gene.
HGVS_CODON: The Human Genome Variation Society (HGVS) notation for the nucleotide change at the DNA level (c.3706G>A means a change from Guanine to Adenine at position 3706).
HGVS_Protien: The HGVS notation for the resulting change in the protein sequence due to the DNA variation (p.Ala1236Thr indicates an amino acid change from Alanine to Threonine at position 1236).
QUAL: Quality score associated with the variant, often indicating the reliability of the variant call.
DP: Depth of coverage or the number of reads supporting the variant.
MAF: Minor allele frequency, representing how often the variant allele appears in a population.
SIFT prediction : Prediction of the variant's effect on protein function using the SIFT algorithm, often categorized as "T" (tolerated) or "D" (deleterious).
Chr..: Chromosome where the gene is located.
SNP_ID: Identifier for the Single Nucleotide Polymorphism (SNP) associated with the variant.
REF/ALT: The reference and alternate alleles for the variant.
ANN[0].EFFECT: The effect of the variant on the gene, such as missense_variant (an amino acid change), disruptive_inframe_deletion (a deletion affecting the reading frame but in-frame), etc.
IMPACT: Impact assessment of the variant on the gene function, often categorized as MODERATE in this table.

Table 3.1: PT. 1 *(Kaphaj Prakriti*)

GENE	FEATURE-ID	HGVS_CODON	HGVS_Protien	QUAL	DP	MAF	SIFT Prediction	Chr…	SNP_ID	REF	ALT	ANN[0].EFFECT	IMPACT
GREB1	NM_014668.4	c.3706G>A	p.Ala1236Thr	545.64	39	0.001198	T	chr2	rs202215699	G	A	missense_variant	MODERATE
NEB	NM_001164507.2	c.20722C>T	p.His6908Tyr	2868.64	180	0.000419	T	chr2	rs1344594980	G	A	missense_variant	MODERATE
MAP3K4	NM_005922.4	c.3596_3598delCTG	p.Ala1199del	1176.03	47	2.03E-03	T	chr6	.	CCTG	C	disruptive_inframe_deletion	MODERATE
CYP2C19	NM_000769.4	c.518C>T	p.Ala173Val	2754.64	215	0.008586	T	chr10	rs61311738	C	T	missense_variant	MODERATE
SYNE2	NM_182914.3	c.4912T>C	p.Tyr1638His	1845.64	114	3.99E-04	T	chr14	rs146801942	T	C	missense_variant	MODERATE
TYK2	NM_003331.5	c.1702C>T	p.Arg568Trp	685.64	48	5.99E-04	D	chr19	rs569896082	G	A	missense_variant	MODERATE
MST1	NM_020998.4	c.55C>T	p.Pro19Ser	262.64	54	0.000247	T	chr3	rs62262686	G	A	missense_variant	MODERATE

This table appears to contain information related to genetic variations Out of 132 screened genes for endometriosis we found 34 genes total in 9 patients and 7 gene variation in Pt 1.

Table 3.2: PT. 2 (*Vataja Prakriti*)

Gene	**FEATURE-ID**	**HGVS_CODON**	**HGVS_Protien**	**QUAL**	**DP**	**MAF**	**SIFT prediction**	**Chr…**	**SNP_ID**	**REF**	**ALT**	**ANN[0].EFFECT**	**IMPACT**
DYSF	NM_001130987.2	c.1465G>A	p.Glu489Lys	1944.6	128	0.008187	D	chr2	rs61740288	G	A	missense_variant	MODERATE
MUC4	NM_018406.7	c.11176G>A	p.Val3726Ile	1293.64	46	4.32E-04	T	chr3	rs775439938	C	T	missense_variant	MODERATE
MUC4	NM_018406.7	c.6256G>A	p.Ala2086Thr	2158.64	36	0.004193	T	chr3	rs71617308	C	T	missense_variant	MODERATE
MUC4	NM_018406.7	c.338_339insTGTTACGCAGGAGAC	p.Thr113_Ala114ins	374.6	204	0.000821	NA	chr3	rs711810965	T	TGTC	disruptive_	MODERATE

			ValThrGlnGluThr								TCCTGCGTAACA	inframe_insertion	
SYNE1	NM_182961.4	c.24952C>T	p.Leu8318Phe	2353.6	38	0.002196	D	chr6	rs141716975	G	A	missense_variant	MODERATE
SYNE1	NM_182961.4	c.18326C>T	p.Ala6109Val	791.6	54	2.00E-04	T	chr6	rs549373990	G	A	missense_variant	MODERATE
SYNE1	NM_182961.4	c.9349G>A	p.Gly3117Arg	929.6	133	7.99E-04	D	chr6	rs566953005	C	T	missense_variant	MODERATE
MAP3K4	NM_005922.4	c.3596_3598delCTG	p.Ala1199del	452.64	46	0.002458	NA	chr6	.	CCTG	C	disruptive_inframe_deletion	MODERATE
ABCA13	NM_152701.5	c.5605G>A	p.Glu1869Lys	220.64	184	3.41E-04	D	chr7	rs745787119	G	A	missense_variant	MODERATE
ABCA13	NM_152701.5	c.11732C>T	p.Ser3911Leu	341.64	144	9.98E-04	D	chr7	rs371682152	C	T	missense_variant	MODERATE
CSMD1	NM_033225.6	c.6059C>G	p.Ser2020Cys	68.64	110	0.000214	D	chr8	.	G	C	missense_variant	MODERATE
CUBN	NM_001081.4	c.8635C>A	p.Leu2879Ile	437.64	130	0.01398	D	chr10	rs1801238	G	T	missense_variant	MODERATE
VWF	NM_000552.5	c.6187C>T	p.Pro2063Ser	248.6	209	0.01118	D	chr12	rs61750615	G	A	missense_variant	MODERATE
VWF	NM_000552.5	c.3797C>A	p.Pro1266Gln	334.64	57	0.001797	D	chr12	rs61749370	G	T	missense_variant	MODERATE
VWF	NM_000552.5	c.3692A>C	p.Asn1231Thr	3335.6	45	0.004992	T	chr12	rs61749368	T	G	missense_variant	MODERATE
VWF	NM_000552.5	c.3686T>G	p.Val1229Gly	77.64	38	0.008986	T	chr12	rs61749367	A	C	missense_variant	MODERATE
ERBB3	NM_001982.4	c.1253T>C	p.Ile418Thr	1008.6	84	0.002496	D	chr12	rs141230043	T	C	missense_variant	MODERATE
PARP4	NM_006437.4	c.2248G>A	p.Ala750Thr	958.64	109	0.004792	D	chr13	rs199572791	C	T	missense_variant	MODERATE
LILRB2	NM_001080978.4	c.721delC	p.Leu241fs	1332.03	133	0.001284	D	chr19	.	AG	A	frameshift_variant	HIGH
LILRB2	NM_001080978.4	c.716_717insG	p.Ser240fs	54.64	140	0.004937	NA	chr19	.	T	TC	frameshift_variant	HIGH
LILRB1	NM_001081637.3	c.154G>A	p.Gly52Ser	124.64	153	0.001198	NA	chr19	rs554096090	G	A	missense_variant	MODERATE
LILRB1	NM_001081637.3	c.158A>T	p.Gln53Leu	301.6	158	0.001198	T	chr19	rs199588814	A	T	missense_variant	MODERATE
LILRB1	NM_001081637.3	c.176G>A	p.Arg59His	1157.64	169	4.01E-04	T	chr19	rs774715846	G	A	missense_variant	MODERATE
LILRB1	NM_001081637.3	c.257C>T	p.Pro86Leu	1048.64	190	7.99E-04	T	chr19	rs200880414	C	T	missense_variant	MODERATE

LILRB1	NM_001081637.3	c.289C>T	p.Arg97Cys	1034.64	174	0.000543	D	chr19	rs766498638	C	T	missense_variant	MODERATE
LILRB1	NM_001081637.3	c.295T>A	p.Tyr99Asn	1569.64	170	2.00E-04	D	chr19	rs570016342	T	A	missense_variant	MODERATE
LILRB1	NM_001081637.3	c.296A>T	p.Tyr99Phe	772.6	168	2.00E-04	T	chr19	rs535742370	A	T	missense_variant	MODERATE
LILRB1	NM_001081637.3	c.320G>T	p.Arg107Leu	262.6	153	3.99E-04	D	chr19	rs142396802	G	T	missense_variant	MODERATE
LILRB1	NM_001081637.3	c.368T>G	p.Ile123Ser	30.6	133	2.00E-04	T	chr19	rs370374304	T	G	missense_variant	MODERATE
LILRB1	NM_001081637.3	c.1051T>G	p.Trp351Gly	689.64	85	0.001254	T	chr19	rs765206177	T	G	missense_variant	MODERATE
LILRB1	NM_001081637.3	c.1059A>C	p.Gln353His	635.64	83	2.35E-04	T	chr19	rs764221410	A	C	missense_variant	MODERATE

This table appears to contain information related to genetic variations Out of 132 screened genes for endometriosis we found 34 genes total in 9 patients and 11 gene variation in Pt 2.

Table 3.3: PT. 3 (*Pittaj Prakriti*)

GENE	**FEATURE-ID**	**HGVS_CODON**	**HGVS_Protien**	**QUAL**	**DP**	**MAF**	**SIFT prediction**	**Chr…**	**SNP_ID**	**REF**	**ALT**	**ANN[0].EFFECT**	**IMPACT**
NGF	NM_002506.3	c.173C>T	p.Ala58Val	191.64	12	0.000195	T	chr1	rs201861727	G	A	missense_variant	MODERATE
NEB	NM_001164507.2	c.10086C>G	p.Cys3362Trp	2748.64	200	0.000891	D	chr2	.	G	C	missense_variant	MODERATE
MST1	NM_020998.4	c.55C>T	p.Pro19Ser	63.64	12	0.004571	T	chr3	rs62262686	G	A	missense_variant	MODERATE
SYNE1	NM_182961.4	c.2395G>A	p.Val799Ile	1072.64	97	0.003195	T	chr6	rs199670962	C	T	missense_variant&splice_region_variant	MODERATE
MAP3K4	NM_005922.4	c.3593_3598delCTGCTG	p.Ala1198_Ala1199del	760.02	33	0.010245	T	chr6	.	CCTGCTG	C,CCTG	disruptive_inframe_deletion	MODERATE
ABCA13	NM_152701.5	c.5740G>A	p.Val1914Met	2003.64	165	5.99E-04	D	chr7	rs549805217	G	A	missense_variant	MODERATE
MUC17	NM_001040105.2	c.2732G>A	p.Gly911Asp	570.64	223	0.005846	T	chr7	rs118141287	G	A	missense_variant	MODERATE
MUC17	NM_001040105.2	c.2875A>G	p.Thr959Ala	2131.64	498	0.000214	T	chr7	rs609400057	A	G	missense_variant	MODERATE
MUC17	NM_001040105.2	c.3476C>T	p.Thr1159Ile	1553.64	236	0.004265	D	chr7	rs77274379	C	T	missense_variant	MODERATE
MUC17	NM_001040105.2	c.3767C>T	p.Thr1256Ile	3120.64	332	0.002389	T	chr7	rs748999795	C	T	missense_variant	MODERATE
CSMD1	NM_033225.6	c.8638G>A	p.Val2880Ile	494.64	54	0.002995	T	chr8	rs199997360	C	T	missense_variant	MODERATE

MUC5AC	NM_001304359.2	c.6873A>C	p.Arg2291Ser	1315.64	132	0.004923	NA	chr11	rs1172543694	A	C	missense_variant	MODERATE
MUC5AC	NM_001304359.2	c.6884C>T	p.Ala2295Val	851.64	124	0.005284	T	chr11	rs1246985448	C	T	missense_variant	MODERATE
MUC5AC	NM_001304359.2	c.6886T>C	p.Ser2296Pro	767.64	122	0.000015	T	chr11	rs1278678680	T	C	missense_variant	MODERATE
MUC5AC	NM_001304359.2	c.6889C>A	p.Pro2297Thr	726.64	125	0.001007	T	chr11	rs1342770529	C	A	missense_variant	MODERATE
MUC5AC	NM_001304359.2	c.6892G>A	p.Ala2298Thr	700.64	139	0.004390	D	chr11	rs1228787889	G	A	missense_variant	MODERATE
MUC5AC	NM_001304359.2	c.6902C>T	p.Thr2301Ile	283.64	129	2.31E-04	D	chr11	rs1454752258	C	T	missense_variant	MODERATE
MUC5AC	NM_001304359.2	c.16673G>A	p.Arg5558Gln	116.64	19	7.99E-04	T	chr11	rs568269309	G	A	missense_variant	MODERATE

This table appears to contain information related to genetic variations Out of 132 screened genes for endometriosis we found 34 genes total in 9 patients and 9 gene variation in Pt 3.

Table 3.4: PT. 4 (*Kaphaj Prakriti*)

GENE	**FEATURE-ID**	**HGVS_CODON**	**HGVS_Protien**	**QUAL**	**DP**	**MAF**	**SIFT Prediction**	**Chr…**	**SNP_ID**	**REF**	**ALT**	**ANN[0].EFFECT**	**IMPACT**
MUC4	NM_018406.7	c.8429C>T	p.Ser2810Phe	10227.64	833	0.000098	D	chr3	rs20109261 0	G	A	missense_variant	MODERATE
MUC4	NM_018406.7	c.7720G>A	p.Ala2574Thr	6139.64	465	0.002117	T	chr3	rs20132685 3	C	T	missense_variant	MODERATE
MUC4	NM_018406.7	c.4696A>T	p.Thr1566Ser	4274.64	562	0.003725	T	chr3	rs576 14388	T	A	missense_variant	MODERATE
MUC4	NM_018406.7	c.3358C>A	p.Pro1120Thr	11907.64	1139	0.000857	D	chr3	rs119 16899	G	T	missense_variant	MODERATE
MUC4	NM_018406.7	c.3002T>C	p.Val1001Ala	7744.64	1136	0.002456	T	chr3	rs200 672669	A	G	missense_variant	MODERATE
MUC4	NM_018406.7	c.338_339ins TGTTACGCAGGAGAC	p.Thr113_Ala114ins ValThrGlnGluThr	7255.6	421	0.000157	T	chr3	rs711 80965	T	TGTCTCCTGCGTAACA	disruptive_inframe_insertion	MODERATE
ERAP1	NM_001040458.3	c.2744T>C	p.Ile915Thr	2051.64	118	0.002196	D	chr5	rs139 576768	A	G	missense_variant	MODERATE
MAP3K4	NM_005922.4	c.3596_3598delCTG	p.Ala1199del	3058.17	145	0.000759	T	chr6	.	CCTG	C	disruptive_inframe_deletion	MODERATE

ABCA13	NM_152701.5	c.4888C>G	p.Leu1630Val	4150.64	295	2.51E-04	D	chr7	rs14239148 7	C	G	missense_variant	MODERATE
CSMD1	NM_033225.6	c.10405C>G	p.Pro3469Ala	1227.64	96	0.000039	T	chr8	rs37552457 7	G	C	missense_variant&splice_region_variant	MODERATE
USP17L2	NM_201402.3	c.209T>G	p.Leu70Arg	1427.64	141	4.28E-04	D	chr8	rs10353187 20	A	C	missense_variant	MODERATE
MUC5AC	NM_001304359.2	c.1490C>T	p.Ala497Val	1362.64	92	3.01E-04	T	chr11	rs28403537	C	T	missense_variant	MODERATE
MUC5AC	NM_001304359.2	c.16057G>A	p.Ala5353Thr	238.64	26	0.000256	NA	chr11	rs34474233	G	A	missense_variant	MODERATE
MUC5AC	NM_001304359.2	c.16058C>A	p.Ala5353Glu	238.64	26	0.000197	T	chr11	rs34815853	C	A	missense_variant	MODERATE
PARP4	NM_006437.4	c.2317T>C	p.Cys773Arg	2083.64	163	2.01E-04	T	chr13	.	A	G	missense_variant	MODERATE

This table appears to contain information related to genetic variations Out of 132 screened genes for endometriosis we found 34 genes total in 9 patients and 8 genes variation in Pt 4.

Table 3.5: PT. 5 (*Kaphaj Prakriti*)

GENE	FEATURE-ID	HGVS_CODON	HGVS_Protien	QUAL	DP	MAF	SIFT Prediction	Chr…	SNP_ID	REF	ALT	ANN[0].EFFECT	IMPACT
KAZN	NM_201628.3	c.2006G>A	p.Arg669Lys	541.64	32	2.25E-04	D	chr1	rs756024690	G	A	missense_variant	MODERATE
MUC4	NM_018406.7	c.12496G>A	p.Ala4166Thr	125.64	29	0.005791	T	chr3	rs55789594	C	T	missense_variant	MODERATE
MUC4	NM_018406.7	c.11272G>A	p.Ala3758Thr	904.64	97	3.31E-04	T	chr3	rs1331388963	C	T	missense_variant	MODERATE
MUC4	NM_018406.7	c.10442C>T	p.Ala3481Val	180.64	65	2.00E-04	T	chr3	rs201765368	G	A	missense_variant	MODERATE
MUC4	NM_018406.7	c.10441G>T	p.Ala3481Ser	138.64	64	0.000542	D	chr3	rs61388923	C	A	missense_variant	MODERATE
MUC4	NM_018406.7	c.8477T>C	p.Phe2826Ser	1344.64	108	0.001254	T	chr3	rs139925940	A	G	missense_variant	MODERATE
MUC4	NM_018406.7	c.6671C>T	p.Pro2224Leu	1041.64	463	4.21E-04	D	chr3	rs391928	G	A	missense_variant	MODERATE
MUC4	NM_018406.7	c.6574C>T	p.Pro2192Ser	938.64	179	0.006013	T	chr3	rs55824312	G	A	missense_variant	MODERATE
MUC4	NM_018406.7	c.6239C>A	p.Pro2080His	3022.64	320	2.06E-04	D	chr3	rs75588776	G	T	missense_variant	MODERATE
MUC4	NM_018406.7	c.6164C>T	p.Ser2055Phe	2853.64	357	5.21E-04	D	chr3	rs113602668	G	A	missense_variant	MODERATE
MUC4	NM_018406.7	c.4672G>A	p.Ala1558Thr	1509.64	155	0.000015	T	chr3	rs3103959	C	T	missense_variant	MODERATE
MUC4	NM_018406.7	c.3002T>A	p.Val1001Glu	240.64	115	0.000061	D	chr3	rs200672669	A	T	missense_variant	MODERATE

SYNE1	NM_182961.4	c.15847G>C	p.Ala5283Pro	65.64	29	6.34E-04	T	chr6	.	C	G	missense_variant	MODERATE
ABCA13	NM_152701.5	c.68C>T	p.Pro23Leu	321.64	20	0.000132	D	chr7	rs377369715;2477845	C	T	missense_variant&splice_region_variant	MODERATE
CUBN	NM_001081.4	c.8635C>A	p.Leu2879Ile	357.64	36	0.013981	NA	chr10	rs1801238;299399	G	T	missense_variant	MODERATE
PARP4	NM_006437.4	c.3176A>G	p.Gln1059Arg	53.64	30	4.98E-04	D	chr13	rs77269056	T	C	missense_variant	MODERATE

This table appears to contain information related to genetic variations Out of 132 screened genes for endometriosis we found 34 genes total in 9 patients and 6 genes variation in Pt 5.

Table 3.6: PT. 6 (*Vataja Prakriti*)

GENE	**FEATURE-ID**	**HGVS_CODON**	**HGVS_Protien**	**QUAL**	**DP**	**MAF**	**SIFT prediction**	**Chr…**	**SNP_ID**	**REF**	**ALT**	**ANN[0].EFFECT**	**IMPACT**
IL1R1	NM_000877.4	c.1677delA	p.Lys559fs	3627.6	269	0.000001	NA	chr2	rs376163784	GA	G	frameshift_variant	HIGH
NEB	NM_001164507.2	c.16907T>C	p.Ile5636Thr	953.64	67	0.000243	T	chr2	rs753681154	A	G	missense_variant&splice_region_variant	MODERATE
MST1	NM_020998.4	c.55C>T	p.Pro19Ser	67.64	16	5.14E-04	T	chr3	rs62262686	G	A	missense_variant	MODERATE
BCL6	NM_001706.5	c.734C>T	p.Pro245Leu	705.64	59	2.00E-04	D	chr3	rs560916500	G	A	missense_variant	MODERATE
MUC4	NM_018406.7	c.11072C>G	p.Thr3691Arg	2098.64	231	6.11E-04	D	chr3	rs967465234	G	C	missense_variant	MODERATE
MUC4	NM_018406.7	c.9784_9785insGG	p.Thr3262fs	538.6	95	0.000051	NA	chr3	rs753854746	G	GCC	frameshift_variant	HIGH
MUC4	NM_018406.7	c.9781_9782delGA	p.Asp3261fs	444.6	92	0.001002	NA	chr3	rs757413270	GTC	G	frameshift_variant	HIGH
MUC4	NM_018406.7	c.8148_8152delTGACA	p.Asp2717fs	3094.05	143	0.000041	NA	chr3	rs774832856	GTGTCA	G	frameshift_variant	HIGH
MUC4	NM_018406.7	c.7744A>C	p.Thr2582Pro	1448.64	289	0.007788	T	chr3	rs142559357	T	G	missense_variant	MODERATE
MUC4	NM_018406.7	c.7733C>A	p.Pro2578His	1102.64	298	5.51E-04	D	chr3	rs80005560	G	T	missense_variant	MODERATE
MAP3K4	NM_005922.4	c.3593_3598delCTGCTG	p.Ala1198_Ala1199del	2530.02	119	2.64E-04	D	chr6	.	CCTGCTG	C,CCTG	disruptive_inframe_deletion	MODERATE
CSMD1	NM_033225.6	c.9526G>A	p.Glu3176Lys	1715.64	145	4.63E-04	T	chr8	rs184090049	C	T	missense_variant	MODERATE
CUBN	NM_001081.4	c.10265C>T	p.Thr3422Ile	2949.64	229	0.008187	T	chr10	rs1801230	G	A	missense_variant	MODERATE
MUC5AC	NM_001304359.2	c.191_193dupGGA	p.Arg64dup	1305.6	67	3.51E-04	T	chr11	rs531636684	T	TGAG	disruptive_inframe_insertion	MODERATE
MUC5AC	NM_001304359.2	c.6913_6914delGG	p.Gly2305fs	1471.6	280	6.51E-04	NA	chr11	rs1590145211	TGG	T	frameshift_variant	HIGH

MUC5AC	NM_001304359.2	c.6917_6918insAC	p.Asn2306fs	1307.6	290	0.000051	NA	chr11	.	A	AAC	frameshift_variant	HIGH
PARP4	NM_006437.4	c.3176A>G	p.Gln1059Arg	92.64	41	0.000428	D	chr13	rs77269056	T	C	missense_variant	MODERATE
PARP4	NM_006437.4	c.3116T>C	p.Ile1039Thr	97.64	39	0.000043	D	chr13	rs73172125	A	G	missense_variant&splice_region_variant	MODERATE

This table appears to contain information related to genetic variations Out of 132 screened genes for endometriosis we found 34 genes total in 9 patients and 10 gene variation in Pt 6.

Table 3.7: PT. 7 (*Pittaj Prakriti*)

GENE	**FEATURE-ID**	**HGVS_CODON**	**HGVS_Protien**	**QUAL**	**DP**	**MAF**	**SIFT prediction**	**Chr…**	**SNP_ID**	**REF**	**ALT**	**ANN[0].EFFECT**	**IMPACT**
ERAP1	NM_001040458.3	c.1939G>A	p.Val647Ile	2593.64	139	0.001597	D	chr5	rs111363347	C	T	missense_variant	MODERATE
MUC17	NM_001040105.2	c.2875A>G	p.Thr959Ala	4577.64	842	0.000452	T	chr7	rs60940057	A	G	missense_variant	MODERATE
MUC17	NM_001040105.2	c.3476C>T	p.Thr1159Ile	5848.64	607	0.000042	D	chr7	rs77274379	C	T	missense_variant	MODERATE
MUC17	NM_001040105.2	c.3767C>T	p.Thr1256Ile	5105.64	552	0.001054	T	chr7	rs74899795	C	T	missense_variant	MODERATE
MUC17	NM_001040105.2	c.9235A>G	p.Thr3079Ala	3961.64	357	0.001997	T	chr7	rs200081080	A	G	missense_variant	MODERATE
SYNE2	NM_182914.3	c.20339G>A	p.Arg6780Gln	680.64	52	0.001398	NA	chr14	rs202240664	G	A	missense_variant	MODERATE
LILRB2	NM_001080978.4	c.968G>C	p.Gly323Ala	136.64	42	4.35E-04	T	chr19	rs971610407	C	G	missense_variant	MODERATE
LILRB2	NM_001080978.4	c.737T>G	p.Val246Gly	282.64	84	5.61E-04	T	chr19	rs780392944	A	C	missense_variant	MODERATE
LILRB2	NM_001080978.4	c.727C>T	p.Leu243Phe	330.64	83	0.000114	D	chr19	rs1473278082	G	A	missense_variant	MODERATE
LILRB1	NM_001081637.3	c.154G>A	p.Gly52Ser	788.64	62	0.001198	T	chr19	rs554096090	G	A	missense_variant	MODERATE
LILRB1	NM_001081637.3	c.158A>T	p.Gln53Leu	851.64	68	0.001198	NA	chr19	rs199588814	A	T	missense_variant	MODERATE
LILRB1	NM_001081637.3	c.176G>A	p.Arg59His	984.64	77	3.51E-04	T	chr19	rs774715846	G	A	missense_variant	MODERATE
LILRB1	NM_001081637.3	c.257C>T	p.Pro86Leu	476.64	76	7.99E-04	T	chr19	rs200880414	C	T	missense_variant	MODERATE
LILRB1	NM_001081637.3	c.289C>T	p.Arg97Cys	647.64	54	0.000042	D	chr19	rs766498638	C	T	missense_variant	MODERATE
LILRB1	NM_001081637.3	c.295T>A	p.Tyr99Asn	696.64	50	2.00E-04	D	chr19	rs570016342	T	A	missense_variant	MODERATE
LILRB1	NM_001081637.3	c.296A>T	p.Tyr99Phe	693.64	51	2.00E-04	T	chr19	rs535742370	A	T	missense_variant	MODERATE
LILRB1	NM_001081637.3	c.320G>T	p.Arg107Leu	389.64	48	3.99E-04	D	chr19	rs142396802	G	T	missense_variant	MODERATE
LILRB1	NM_001081637.3	c.368T>G	p.Ile123Ser	209.64	86	2.00E-04	T	chr19	rs370374304	T	G	missense_variant	MODERATE
LILRB1	NM_001081637.3	c.389A>T	p.Gln130Leu	240.64	82	2.65e-04	T	chr19	rs767704704	A	T	missense_variant	MODERATE

LILRB1	NM_001081637.3	c.407A>C	p.Asn136Thr	474.64	94	0.001291	T	chr19	rs758173207	A	C	missense_variant	MODERATE
LILRB1	NM_001081637.3	c.427C>A	p.Leu143Ile	972.64	111	2.00E-04	D	chr19	rs539532545	C	A	missense_variant	MODERATE
LILRB1	NM_001081637.3	c.1051T>G	p.Trp351Gly	948.64	74	3.54E-04	T	chr19	rs765206177	T	G	missense_variant	MODERATE
LILRB1	NM_001081637.3	c.1059A>C	p.Gln353His	978.64	78	5.66E-04	NA	chr19	rs764221410	A	C	missense_variant	MODERATE
LILRB1	NM_001081637.3	c.1093G>T	p.Asp365Tyr	489.64	87	6.22-04	T	chr19	rs1260040283	G	T	missense_variant	MODERATE
LILRB1	NM_001081637.3	c.1094A>C	p.Asp365Ala	489.64	87	3.01E-04	T	chr19	rs12985933	A	C	missense_variant	MODERATE
LILRB1	NM_001081637.3	c.1109G>A	p.Arg370Lys	279.64	71	0.000541	T	chr19	rs1401913528	G	A	missense_variant	MODERATE
LILRB1	NM_001081637.3	c.1128A>T	p.Gln376His	180.64	75	0.000114	T	chr19	rs1240220003	A	T	missense_variant	MODERATE

This table appears to contain information related to genetic variations Out of 132 screened genes for endometriosis we found 34 genes total in 9 patients and 4 gene variation in Pt 7.

Table 3.8: PT. 8 (*Pittaj Prakriti*)

GENE	**FEATURE-ID**	**HGVS_CODON**	**HGVS_Protien**	**QUAL**	**DP**	**MAF**	**SIFT prediction**	**Chr …**	**SNP_ID**	**REF**	**ALT**	**ANN[0].EFFECT**	**IMPACT**
NLRP3	NM_001243133.2	c.2200G>C	p.Val734Leu	3135.64	249	5.77E-04	T	chr1	.	G	C	missense_variant	MODERATE
MUC4	NM_018406.7	c.11072C>G	p.Thr3691Arg	133.64	45	6.24E-04	T	chr3	rs967465234	G	C	missense_variant	MODERATE
MUC4	NM_018406.7	c.10697C>T	p.Ala3566Val	1623.64	131	0.000124	D	chr3	rs1456561393	G	A	missense_variant	MODERATE
MUC4	NM_018406.7	c.10695G>C	p.Gln3565His	1623.64	135	0.000001	T	chr3	rs1196280021	C	G	missense_variant	MODERATE
MUC4	NM_018406.7	c.8477T>C	p.Phe2826Ser	598.64	211	0.000054	T	chr3	rs139925940	A	G	missense_variant	MODERATE
MUC4	NM_018406.7	c.6926_6927insG	p.Asp2309fs	304.6	72	0.000591	NA	chr3	rs775530889	G	GC	frameshift_variant	HIGH
MUC4	NM_018406.7	c.6239C>A	p.Pro2080His	889.64	226	6.34E-04	D	chr3	rs75588776	G	T	missense_variant	MODERATE
MUC4	NM_018406.7	c.6164C>T	p.Ser2055Phe	1050.64	194	5.55E-04	D	chr3	rs113602668	G	A	missense_variant	MODERATE
MUC4	NM_018406.7	c.6075_6077dupATC	p.Ser2026dup	1995.6	270	0.000146	NA	chr3	rs63118461	G	GGAT	disruptive_inframe_insertion	MODERATE
MUC4	NM_018406.7	c.5936C>A	p.Thr1979Lys	1367.64	326	0.001543	D	chr3	rs779935183	G	T	missense_variant	MODERATE
MUC4	NM_018406.7	c.5306T>C	p.Val1769Ala	1720.64	239	4.63E-04	T	chr3	rs879139073	A	G	missense_variant	MODERATE
MUC4	NM_018406.7	c.4672G>A	p.Ala1558Thr	527.64	126	7.91E-04	T	chr3	rs3103959	C	T	missense_variant	MODERATE

MUC4	NM_018406.7	c.338_339insTGTTACGCAGGAGAC	p.Thr113_Ala114insValThrGlnGluThr	4088.6	245	0.00421	NA	chr3	rs71180965	T	TGTCTCCTGCGTAACA	disruptive_inframe_insertion	MODERATE
KDR	NM_002253.4	c.1444T>C	p.Cys482Arg	1748.64	188	0.008986	D	chr4	rs34231037	A	G	missense_variant	MODERATE
NFKB1	NM_003998.4	c.1736G>A	p.Arg579Lys	3660.64	274	0.001597	T	chr4	rs4648086	G	A	missense_variant	MODERATE
MAP3K4	NM_005922.4	c.93_95dupGCC	p.Pro32dup	540.6	60	5.97E-04	T	chr6	.	A	ACCG	disruptive_inframe_insertion	MODERATE
MAP3K4	NM_005922.4	c.2717A>C	p.His906Pro	3297.64	227	0.011381	D	chr6	rs35533223	A	C	missense_variant	MODERATE
MAP3K4	NM_005922.4	c.3596_3598delCTG	p.Ala1199del	1738.03	74	0.002458	T	chr6	.	CCTG	C	disruptive_inframe_deletion	MODERATE
MUC17	NM_001040105.2	c.7268A>C	p.Asp2423Ala	405.64	35	0.005991	D	chr7	rs138402996	A	C	missense_variant	MODERATE
VWF	NM_000552.5	c.5285A>G	p.Gln1762Arg	2721.64	220	0.000587	T	chr12	rs199729586	T	C	missense_variant	MODERATE
VWF	NM_000552.5	c.3692A>G	p.Asn1231Ser	1386.64	98	0.004992	T	chr12	rs61749368	T	C	missense_variant	MODERATE
PARP4	NM_006437.4	c.2248G>A	p.Ala750Thr	2794.64	242	0.004792	D	chr13	rs199572791	C	T	missense_variant	MODERATE
SETBP1	NM_015559.3	c.1277C>A	p.Ala426Glu	3162.64	281	3.99E-04	D	chr18	rs187433533	C	A	missense_variant	MODERATE
LAMA5	NM_005560.6	c.8479C>A	p.Gln2827Lys	1962.64	145	0.012108	T	chr20	rs117480847	G	T	missense_variant	MODERATE

This table appears to contain information related to genetic variations Out of 132 screened genes for endometriosis we found 34 genes total in 9 patients and 10 gene variation in Pt 8.

Table 3.9: PT. 9 (*Vataja Prakriti*)

GENE	**FEATURE-ID**	**HGVS_CODON**	**HGVS_Protien**	**QUAL**	**DP**	**MAF**	**SIFT prediction**	**Chr…**	**SNP_ID**	**REF**	**ALT**	**ANN[0].EFFECT**	**IMPACT**
ABCA13	NM_152701.5	c.3149C>T	p.Thr1050Ile	1592.64	107	5.44E-04	D	chr7	rs770822658	C	T	missense_variant	MODERATE
CUBN	NM_001081.4	c.910G>A	p.Glu304Lys	1603.64	110	0.009185	T	chr10	rs78201384	C	T	missense_variant	MODERATE
CUBN	NM_001081.4	c.664G>T	p.Val222Leu	1117.64	143	0.000149	T	chr10	rs750128625	C	A	missense_variant	MODERATE
LILRB2	NM_001080978.4	c.721delC	p.Leu241fs	924.6	128	0.000043	NA	chr19	.	AG	A	frameshift_variant	HIGH
LILRB2	NM_001080978.4	c.716_717insG	p.Ser240fs	959.6	131	6.47E-04	NA	chr19	.	T	TC	frameshift_variant	HIGH

LILRB1	NM_001081637.3	c.154G>A	p.Gly52Ser	824.64	100	0.001198	T	chr19	rs554096090	G	A	missense_variant	MODERATE
LILRB1	NM_001081637.3	c.158A>T	p.Gln53Leu	914.64	99	0.001198	T	chr19	rs199588814	A	T	missense_variant	MODERATE
LILRB1	NM_001081637.3	c.176G>A	p.Arg59His	1092.64	99	0.000056	T	chr19	rs774715846	G	A	missense_variant	MODERATE
LILRB1	NM_001081637.3	c.257C>T	p.Pro86Leu	805.64	131	7.99E-04	T	chr19	rs200880414	C	T	missense_variant	MODERATE
LILRB1	NM_001081637.3	c.289C>T	p.Arg97Cys	1354.64	146	6.99E-04	D	chr19	rs766498638	C	T	missense_variant	MODERATE
LILRB1	NM_001081637.3	c.295T>A	p.Tyr99Asn	1482.64	148	2.00E-04	D	chr19	rs570016342	T	A	missense_variant	MODERATE
LILRB1	NM_001081637.3	c.296A>T	p.Tyr99Phe	1488.64	147	2.00E-04	T	chr19	rs535742370	A	T	missense_variant	MODERATE
LILRB1	NM_001081637.3	c.320G>T	p.Arg107Leu	1021.64	154	3.99E-04	D	chr19	rs142396802	G	T	missense_variant	MODERATE
LILRB1	NM_001081637.3	c.368T>G	p.Ile123Ser	355.64	135	2.00E-04	T	chr19	rs374374304	T	G	missense_variant	MODERATE
LILRB1	NM_001081637.3	c.513G>T	p.Gln171His	335.64	98	0.001543	T	chr19	rs749158954	G	T	missense_variant	MODERATE
LILRB1	NM_001081637.3	c.514C>T	p.Pro172Ser	365.64	102	0.001542	T	chr19	rs768734027	C	T	missense_variant	MODERATE
LILRB1	NM_001081637.3	c.1094A>C	p.Asp365Ala	456.64	77	0.000014	T	chr19	rs12985933	A	C	missense_variant	MODERATE
LILRB1	NM_001081637.3	c.1098_1099delAT	p.Trp367fs	438.6	79	0.000011	NA	chr19	.	CAT	C	frameshift_variant	HIGH
LILRB1	NM_001081637.3	c.1100_1101insCT	p.Trp367fs	396.6	78	6.47E-04	NA	chr19	.	G	GCT	frameshift_variant	HIGH
LILRB1	NM_001081637.3	c.1109G>A	p.Arg370Lys	336.64	84	3.91E-04	T	chr19	rs1401913528	G	A	missense_variant	MODERATE
LILRB1	NM_001081637.3	c.1114_1115insAG	p.Thr372fs	336.6	84	0.001542	NA	chr19	.	A	AAG	frameshift_variant	HIGH
LILRB1	NM_001081637.3	c.1117_1118delTA	p.Tyr373fs	324.6	89	0.000054	NA	chr19	.	GTA	G	frameshift_variant	HIGH
LILRB1	NM_001081637.3	c.1128A>T	p.Gln376His	165.64	83	5.63E-04	T	chr19	rs1240220003	A	T	missense_variant	MODERATE
MUC4	NM_018406.7	c.7193C>T	p.Thr2398Ile	344.64	116	7.11E-04	D	chr3	rs750581781	G	A	missense_variant	MODERATE
MUC4	NM_018406.7	c.6671C>T	p.Pro2224Leu	607.64	136	0.001542	D	chr3	rs391928	G	A	missense_variant	MODERATE
MUC4	NM_018406.7	c.6239C>A	p.Pro2080His	543.64	136	0.000019	D	chr3	rs75588776	G	T	missense_variant	MODERATE
MUC4	NM_018406.7	c.6164C>T	p.Ser2055Phe	464.64	105	0.000542	D	chr3	rs113602668	G	A	missense_variant	MODERATE

PARP4	NM_006437.4	c.1470C>A	p.His490Gln	250.64	126	6.45E-04	T	chr13	rs79107024	G	T	missense_variant	MODERATE

This table appears to contain information related to genetic variations Out of 132 screened genes for endometriosis we found 34 genes total in 9 patients and 5 gene variation in Pt 9.
Note: V = *Vataj Prakriti*; P = *Pittaj Prakriti*; K= *Kaphaj Prakriti*

1(K)

CYP2C19
GREB1
MAP3K4
MST1
NEB
SYNE2
TYK2

2(V)

ABCA13
CSMD1
CUBN
DYSF
ERBB3
LILRB2
MAP3K4
MUC4
PARP4
SYNE1
VWF

3(P)

ABCA13
CSMD1
MAP3K4
MST1
MUC17
MUC5AC
NEB
NGF
SYNE1

4(K)

ABCA13
CSMD1
ERAP1
MAP3K4
MUC4
MUC5AC
PARP4
USP17L2

5(K)

ABCA13
CUBN
KAZN
MUC4
PARP4
SYNE1

6(V)

BCL6
CSMD1
CUBN
IL1R1
MAP3K4
MST1
MUC4
MUC5AC
NEB
PARP4

7(P)

EARP4
LILRB1
MUC17
SYNE2

8(V)

KDR
LAMA5
MAP3K4
MUC17
MUC4
NFKB1
NLRP3
PARP4
SETBP1
VWF

9(P)

ABCA13
CUBN
LILRB1
MUC4
PARP4

4. Discussion

Among the nine clinically diagnosed endometriosis patients included in the study, *Prakriti* assessment revealed that patients 1, 4, and 5 exhibited *Kaphaja Prakriti*; patients 2, 6, and 9 were classified as *Vataja Prakriti*; and patients 3, 7, and 8 demonstrated *Pittaja Prakriti*.

A total of approximately 134 genes previously associated with endometriosis were screened across all patients using whole exome sequencing. Of these, single nucleotide polymorphisms (SNPs) were identified in 34 genes across the cohort.

In patient 1, the majority of detected variants were missense mutations with a moderate predicted functional impact. Patient 2 exhibited predominantly moderate-impact variants; however, a high-impact frameshift mutation was observed in the LILRB2 gene. In patients 3, 4, 5, and 7, most identified variants were classified as having moderate impact on gene or protein function.

Analysis of patient-wise variant distribution indicated that in patient 6, high-impact variants were identified in IL1R1, MUC4, and MUC5AC, while the remaining variants demonstrated moderate impact. Similarly, in patient 8, most variants were of moderate impact, except for high-impact alterations observed in MUC4. In patient 9, although the majority of variants were moderate in effect, high-impact mutations were detected in LILRB2 and LILRB1.

Both shared and patient-specific gene variations were observed. Certain variants were unique to individual patients, such as GREB1, CYP2C19, and TYK2 in patient 1; IL1R1 in patient 6; DYSF, ERBB3, and LILRB2 in patient 2; NGF in patient 3; ERAP1 and USP17L2 in patient 4; KAZN in patient 5; EARP4 in patient 7; and KDR, LAMA5, NFKB1, NLRP3, and SETBP1 in patient 8.

Conversely, several genes showed recurrent variations across multiple patients. MAP3K4 variants were detected in patients 1, 2, 3, 4, 6, and 8, while ABCA13 variants were observed in patients 2, 3, 4, 5, and 9. Variations in CSMD1 occurred in patients 2, 3, 4, and 6; CUBN in patients 2, 5, and 6; MUC4 in patients 2, 4, 5, 6, 8, and 9;

and PARP4 in patients 4, 5, 6, 8, and 9. Additionally, SYNE1, VWF, MST1, MUC17, MUC5AC, and LILRB1 showed repeated occurrence across different patients.

Notably, patients classified under *Vataja Prakriti* demonstrated a higher frequency of high-impact genetic variants compared to *Pittaja* and *Kaphaja Prakriti* groups. *Pittaja* patients exhibited a moderate burden of impactful variants, whereas *Kaphaja* patients predominantly showed moderate-impact variations.

These findings suggest a potential association between *Vataja Prakriti* and increased genetic susceptibility to endometriosis, supporting the hypothesis that Ayurvedic constitutional types may reflect underlying molecular and genetic heterogeneity in the disease.

5. Conclusion

This study adopts a multidisciplinary approach by integrating modern clinical evaluation with whole exome–based genetic analysis and Ayurvedic constitutional *(Prakriti)* assessment to investigate endometriosis. The findings demonstrate that genetic predisposition to endometriosis varies across *Prakriti* types, with specific gene polymorphisms showing differential distribution among *Vataja, Pittaja,* and *Kaphaja* constitutions.

The observed association between genetic variants and *Prakriti* suggests that constitutional phenotyping may reflect underlying molecular heterogeneity in endometriosis. This genetic–*Prakriti* correlation provides a rational basis for developing personalized risk stratification and targeted therapeutic strategies.

Overall, the study highlights the relevance of integrating Ayurvedic diagnostic frameworks with contemporary genomic research, particularly in the domain of women's reproductive health. Such an integrative approach supports the advancement of personalized and holistic medical models, offering potential pathways for improved understanding, prevention, and management of endometriosis.

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