AYUSHDHARA
ISSN: 2393-9583 (P)/ 2393-9591 (O)
An International Journal of Research in AYUSH and Allied Systems

Research Article

STUDY OF INDIVIDUAL'S *PRAKRITI* AND GENE POLYMORPHISM CORRELATION OF P2Y12 GENE

Shekhar Gopalrao Uike
Assistant Professor, Dept. of Kriyasharir, Shri K.R. Pandav Ayurved College, Nagpur, India.

KEYWORDS: *Prakruti, Raktadhatu,* Gene Polymorphism, P2Y12.

***Address for correspondence**
Dr Shekhar Gopalrao Uike
Assistant Professor,
Dept. of Kriyasharir, Shri K.R. Pandav Ayurved College, Nagpur, India.
Email: sgu141@gmail.com

ABSTRACT

Ayurveda is a science of self understanding. It is understood by its own unique nature or constitution i.e. *Prakruti*. Ayurveda believes that the individual's constitution (*Prakruti*) is framed at the time of conception as a genetic code or predominant *Panchamahabhautic dosha*. Ayurveda classifies human beings into three distinct types: *Vata, Pitta* and *Kapha* with multiple subtypes. *Rakta* is said to be the 4th *Dosha*, i.e. it has the importance as that of *Tridosha*. All *Dhatus* are dependent for their nourishment on *Raktadhatu*. Chakrapani explains different shades of *Raktadhatu* according to different *Prakriti*. So there is close relation between *Raktadhatu* and *Prakriti*. *Doshas* which are responsible for *Prakriti* remain constant and they do not change until death. Genetic constitution is identical and unique for every person, the same as *Prakriti*. Every gene performs a specific function. So *Prakriti* can be correlated with genetics whether there is any particular genetic pattern for the particular *Prakriti* with the help of a tool like Single Nucleotide Polymorphism. P2Y12, the receptor present on the platelet surface, initiates platelet aggregation. To analyse polymorphism in the P2Y12 gene, in exhibiting platelet aggregative response, in correlation with *Prakriti*.

INTRODUCTION

Ayurveda is an ancient science based on the studies and keen observations of intellectual seers. *Prakruti* is one of the fundamental concept and specialty of Ayurveda. Therefore, the Ayurvedic approach is very individualized, since the path to optimal health is different for each person depending upon their unique constitution or *Prakruti*. Ayurveda believes that the individual's constitution (*Prakruti*) is framed at the time of conception as a genetic code or predominant *Panchamahabhautic dosha* that can be expressed physically and mentally as disease proneness and emotional response.[1] They govern the individual's response to changes and they promote the disease process when unbalanced. Thus the constitution of an individual is a dynamic force and *Vata*, *Pitta* and *Kapha* are dynamic energies. Ayurveda classifies human beings into three distinct types: *Vata*, *Pitta* and *Kapha* with multiple subtypes. The individuals of these categories exhibit biological variations in terms of structure, functions and behaviour of an individual. *Rakta* is said to be the 4th *Dosha*, i.e., it has the importance as that of *Tridosha*. All Ayurvedic compendia realize importance of *Raktadhatu*. Sushruta tried to emphasize control of this *Dhatu* on other body entities. All *Dhatus* are dependent for their nourishment on *Raktadhatu*. [2]

Body has the special ability to control the flow of blood following vascular injury. The process of blood clotting and then the subsequent dissolution of the clot, following repair of the injured tissue. Chakrapani explains different shades of *Raktadhatu* according to different *Prakriti*. [3] So there is close relation between *Raktadhatu* and *Prakriti*. Since *Raktadhatu*, in normal condition, is in liquid (*Dravata*) state, it can reach out to all *Dhatus* to deliver its '*Jeevan' karm*. So, *Jeevan Karm* of *Raktdhatu* will also differ according to the *Dosha* involved in the *Prakriti*. It keeps flowing uninterrupted though the blood vessels. But whenever there is breach in the continuity of the vessel wall, blood oozes out of the vessel internally

or externally. So body has the special mechanism to protect this *Raktdhatu*, called as 'Hemostasis'. *Doshas* which are responsible for *Prakriti* remain constant and they do not change until death. Genetic constitution is identical and unique for every person, the same as *Prakriti*. So *Prakriti* can be correlated with Genetics whether there is any particular genetic pattern for the particular *Prakriti* with the help of a tool like Single Nucleotide Polymorphism. For this gene P2Y12 is chosen.

It is well known that platelet aggregation plays an important role in formation of platelet plug and also atherosclerotic plaque. P2Y12, the receptor present on the platelet surface, initiates platelet aggregation. So, aim of this study is to analyse polymorphism in the P2Y12 gene, in exhibiting platelet aggregative response, in correlation with *Prakriti*, in normal healthy individuals. We can identify which *Prakriti* is more prone to Atherosclerosis or bleeding disorders and advise them to prevent further consequences with the help of *Aahar, Vihar*, profession and drugs to avoid bleeding or clotting disorders. Also useful in explaining the variable outcome of antiplatelet drug therapy.

AIMS AND OBJECTIVES

1. To study correlation between *Prakriti* and Genetics with special reference to single nucleotide polymorphism of P2Y12 gene in different *Prakriti.*
2. To study the polymorphism of P2Y12, a gene responsible for ADP induced platelet aggregation in normal healthy volunteers.
3. To study the aggregative response of platelets in different *Prakriti*.

MATERIALS AND METHODS

Type of Study: This will be an open, prospective study based on Ayurvedic texts and genetic code correction.

Inclusion and Exclusion criteria

Aspirin-containing compounds should be excluded for at least 10 days prior to testing, studies should not be carried out shortly after a fatty meal, because chylomicrons can interfere with the measurement of platelet aggregation. The volunteers for whom the values for haematological and biochemical investigations will not be in the normal range. Pregnant and lactating women, person suffering from major illness or taking any kind of medication. Person of age <16years and >40 years are in exclusion criteria.

In Inclusion criteria normal and healthy individual from the age group of 16 to 40 years and having no history of major illness and should not be taking any kind of medications. Male and Female both sexes inclusive.

Study Procedure

Appropriate number of volunteers will be screened so as to recruit 30 volunteers of each *Ekdoshpradhan prakriti* type.

Group A- *Vatapradhan Prakriti* – 30 Volunteers

Group B- *Pitapradhan Prakriti* - 30 Volunteers

Group C- *Kaphapradhan Prakriti* - 30 Volunteers

By simple random method, *Prakriti* can be assessed; it is done with help of questionnaire according to MUHS, Nashik university format. Prakriti will be assessed as follows:

Prakriti	***Lakshanas***
Vatapradhan	>60% of *Vataprakriti* characters
Pittapradhan	>60% of *Pittaprakriti* characters
Kaphapradhan	>60% of *Kaphaprakriti* characters

Platelet Aggregation Tests: In citrate bulb blood sample for platelet aggregation can be collected and Platelet aggregation is studied using Chronolog platelet aggregometer, which works on the principle of Born GVR turbid metric method. Direct measurement of ATP secretion during platelet aggregation provides unequivocal evidence of normal dense granule release. Simultaneous measurement of Aggregation and dense granule release provides a better insight into the mechanism of platelet response. Aim is to study the response of platelets to Adenosine diphosphate (ADP). The method was standardised with two concentrations of ADP i.e. 5µMol/L and 10µMol/L.

Polymorphism of P2Y12: will be assessed as follows

Prakriti	H1 Haplotype			H2 Haplotype		
	No. of subjects	Platelet aggregation		No. of subjects	Platelet aggregation	
		5µM	10 µM		5µM	10µM
Vatapradhan						
Pittapradhan						
Kaphapradhan						

Literature Review

Prakruti is enumeration of body features internal as well as external. In short, *Prakruti* means nature of an individual. It is specific for an individual and idiosyncratic that is expression of one's own characteristics. [4] Knowledge of *Prakruti* is essential for a physician as well as a patient. *Prakruti* is important for maintaining health with the help of appropriate diet and daily routine. [5] *Rakta Dhatu* is very important *Dhatu* for sustenance of life. It is primal tissue of the body.

Genetics

Genetics deals with the molecular structure and function of genes. DNA naturally occurs in a double stranded form, with nucleotides on each strand complementary to each other. The sequence of nucleotides in a gene is the genetic information organisms inherit. Nucleic acids are linear polymers of nucleotides. Each nucleotide consists of three components: a purine or pyrimidine nucleobase, a pentose sugar, and a phosphate group. Nucleic acid types differ in the structure of the sugar in their nucleotides. Also, the bases found in the two nucleic acid types are different: adenine, cytosine, and guanine are found in both RNA and DNA, while thymine occurs in DNA and uracil occurs in RNA.

Nucleotide= Nucleoside (Sugar + Base) + Phosphate group

Sugar- Deoxyribose (5C, 4O) or ribose (5C, 5O)

Base– Purines are 2 ringed structures

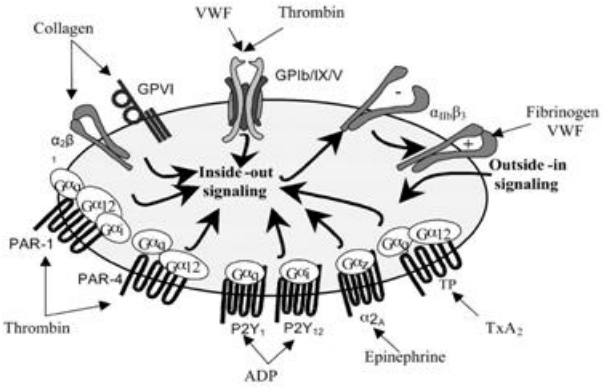
Adenine and Guanine

- Pyrimidines are 1 ringed structure Cytocine, Thymine, Uridine

Phosphate Group – Negatively charged.

A polymorphism is a DNA sequence variation that is common in the population. In this case no single allele is regarded as the standard sequence. Genetic polymorphism constitutes the genetic basis for the uniqueness of each individual. At least one in 100 base pairs (bp) of human DNA differs among individuals. Single Nucleotide Polymorphism may exist at several levels:

- ✓ Variant in DNA sequence
- ✓ Amino acid sequence
- ✓ Chromosome structure



Phenotypic trait. SNPs(Single-Nucleotide Polymorphism) are 1 base pair in length. There are two alleles in human population. The two alleles may be any two from {A, G, C, T}. Variations in the DNA sequences of humans can affect how humans develop diseases and respond to pathogens, chemicals, drugs, vaccines, and other agents. SNPs are also thought to be key enablers in realizing the concept of personalized medicine.P2Y12 is a receptor found on the platelet surface.[6] It is a Purinergic receptor which takes part in ADP induced platelet aggregation. [7]

Viscosity mainly depends on number of blood corpuscles or the amount of proteins. Platelet has got such three P2 receptors. The P2Y1 receptor, which is coupled to Gq and phospholipase C-beta, is responsible for mobilization of ionized calcium from internal stores and mediates the ADP-induced platelet shape change and initial wave of rapidly reversible aggregation.

Receptors on Platelets			
P2Y1	**P2Y12**	**P2X1**	
Receptor for ADP		Receptor for ADP	Receptor for ATP
Mobilization of Ca++ from internal source			Rapid influx of Ca++
Platelet shape change		Platelet shape does not change	
Weak aggregatory response		Maximum aggregatory response	
Gq protein coupled receptor		Gi protein coupled receptor	Ligand gated cation channel

The combined action of P2Y1 and P2Y12 is necessary for the full platelet aggregation response to ADP.

P2Y12 Receptor

Name: Purinergic receptor P2Y, G protein coupled, 12

Synonym: ADP Glucose receptor, HORK 3

Location: 3q24-q25

(Third chromosome, long arm, second region, 4th and 5th band)

Length:342 amino acids

Family:G protein coupled receptor 1 family

Variants: 2 – 'C' allele, 'T' allele

Sites: Highly expressed in the platelets, lower levels in the brain. Lowest levels in the lung, appendix, pituitary and adrenal gland. Expressed in the spinal cord and in the fetal brain.

Haplotype: Sequence of alleles along a chromosome. The two haplotypes are ABC and aBc. A haplotype is a group of genes within an organism that was inherited together from a single parent. This group of genes was inherited together because of genetic linkage**.** the term "haplotype" can also refer to the inheritance of a cluster of single nucleotide polymorphisms (SNPs), The gene P2Y12 have one SNP; so two haplotypes H1 and H2,

Blood: Blood is a specialized connective tissue which circulates in a closed system of blood vessels. Blood is a denser, viscous and feels slightly sticky. Specific Gravity is the ratio of weight of certain volume of substance to the weight of an equal volume of water. Viscosity mainly depends on number of blood corpuscles or the amount of proteins. It is five times as great as water. Platelets are produced in the bone marrow from megakaryocytes as membrane enclosed fragments of the megakaryocyte without genomic DNA. This renders them incapable of transcription of nuclear material. Platelets can respond to physiological stimuli using biosynthetic processes that are regulated at the level of protein translation. Platelets contain a large number of mitochondria, each of which contains several copies of its own 16-kb circular genome that may be actively transcribed in platelets. Adenosine diphosphate (ADP) brings about the aggregation of blood platelets in plasma. Platelet aggregation is stimulated by ADP, thromboxane, and α2 receptor-activation

Observations and Results

***Prakriti* wise Platelet Count**

Sr. No.	*Prakriti*	Platelet count
1.	*Vata Pradhan*	2.76 ± 0.59
2.	*Pitta Pradhan*	2.67 ± 0.64
3.	*Kapha Pradhan*	2.78 ± 0.70

Alkaline Phosphatase Distribution

Sr. No.	*Prakriti*	Alkaline Phosphatase conc.
1.	*Vatapradhan*	77.73 ± 24.75
2.	*Pittapradhan*	74.39 ± 22.61
3.	*Kaphapradhan*	74.66 ± 21.38

Haplotype wise Platelet Aggregation in Different *Prakriti*

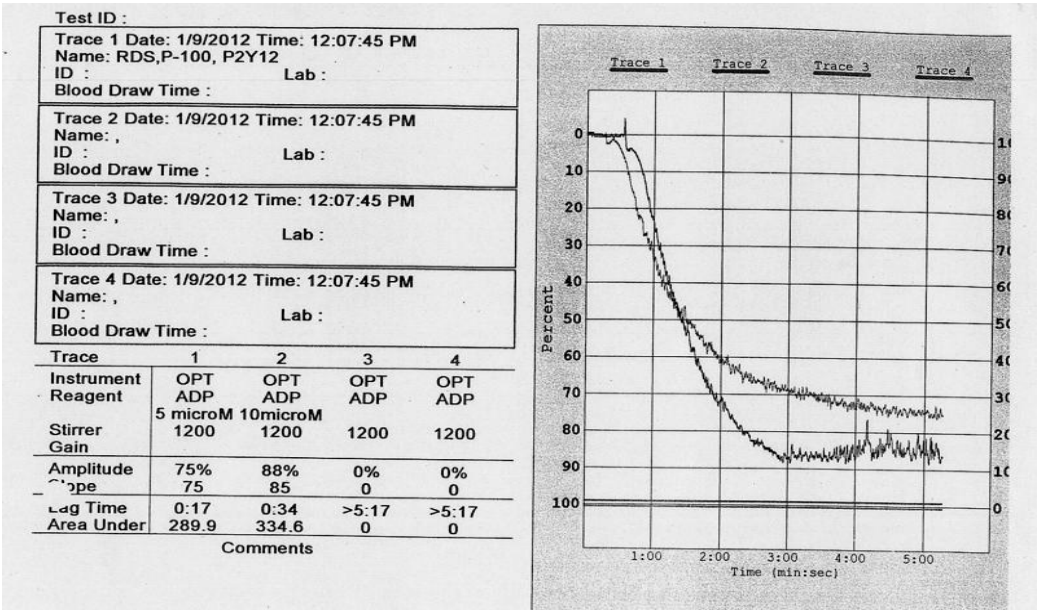
Prakriti	H1 Haplotype			H2 Haplotype		
	No. of subjects and % age	Platelet aggregation		No. of subjects and % age	Platelet aggregation	
		5µM ± S.D.	10 µM ± S.D.		5µM ± S.D.	10µM ± S.D.
Vatapradhan	26 (86.66%)	61.2% ± 15	74% ± 10.42	4 (13.33%)	74.8% ± 6.7	82% ± 4.12
Pittapradhan	28 (93.33%)	52.6% ± 18	70% ±12.80	2 (6.66%)	47% ± 14	64% ± 8.48
Kaphapradhan	26 (86.66%)	71.5% ± 6.6	81% ±7.85	4 (13.33%)	79% ± 3.8	85% ± 2

***Prakriti* wise platelet aggregation**

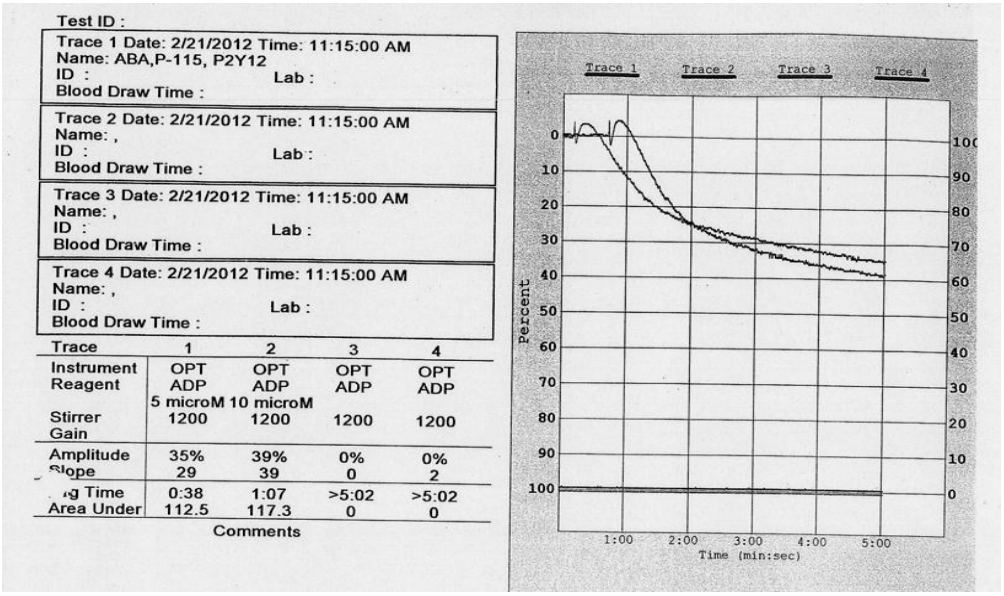
Prakriti	Platelet aggregation ± S. D.	
	5µm	10µm
Vatapradhan	63 ± 14	75 ± 10
Pittapradhan	52 ± 18	70 ± 13
Kaphapradhan	72 ± 6.8	81 ± 7.5

Total 30 *Vatapradhan* subjects have average Platelet aggregation of 63% at 5 µm and 75% at 10µm ADP concentration. Total 30 *Pittapradhan* subjects have average Platelet aggregation of 52% at 5 µm and 70% at 10µm ADP concentration. Total 30 *Kaphapradhan* subjects have average Platelet aggregation of 72% at 5 µm and 81% at 10µm ADP concentration.

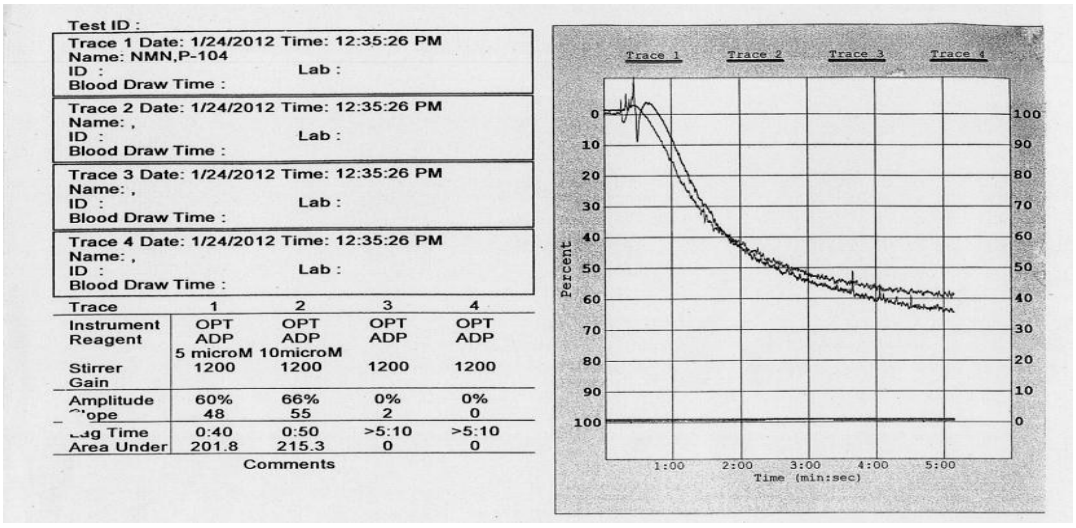
Graph: Platelet aggregation of *Kaphaprakriti* individual



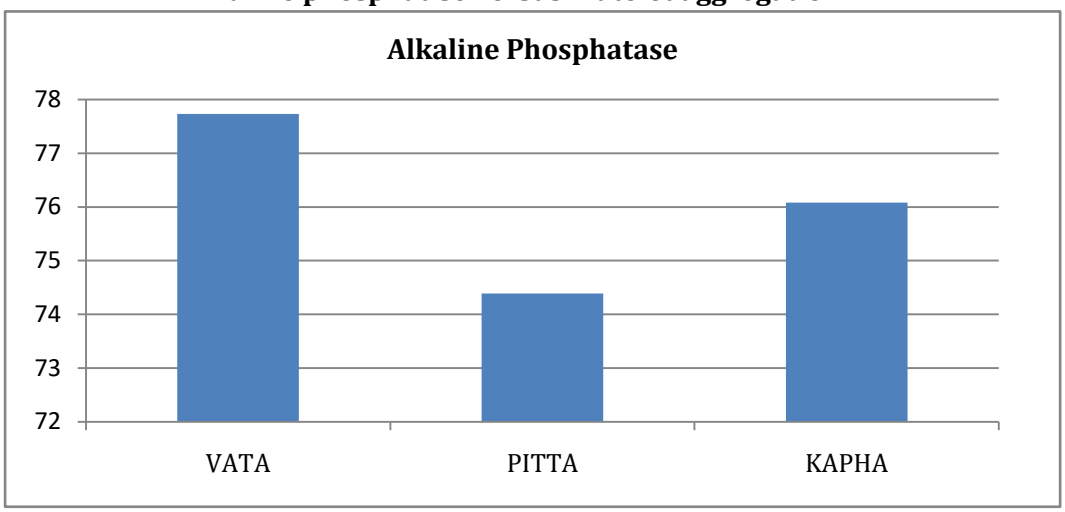
Graph: Platelet aggregation of *Pittaprakriti* individual



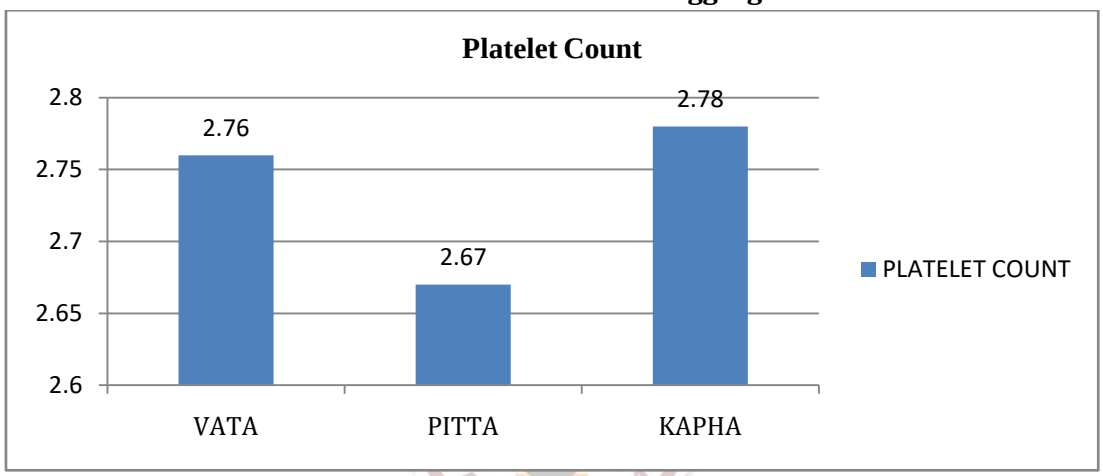
Graph: Platelet aggregation of *Vataprakriti* individual



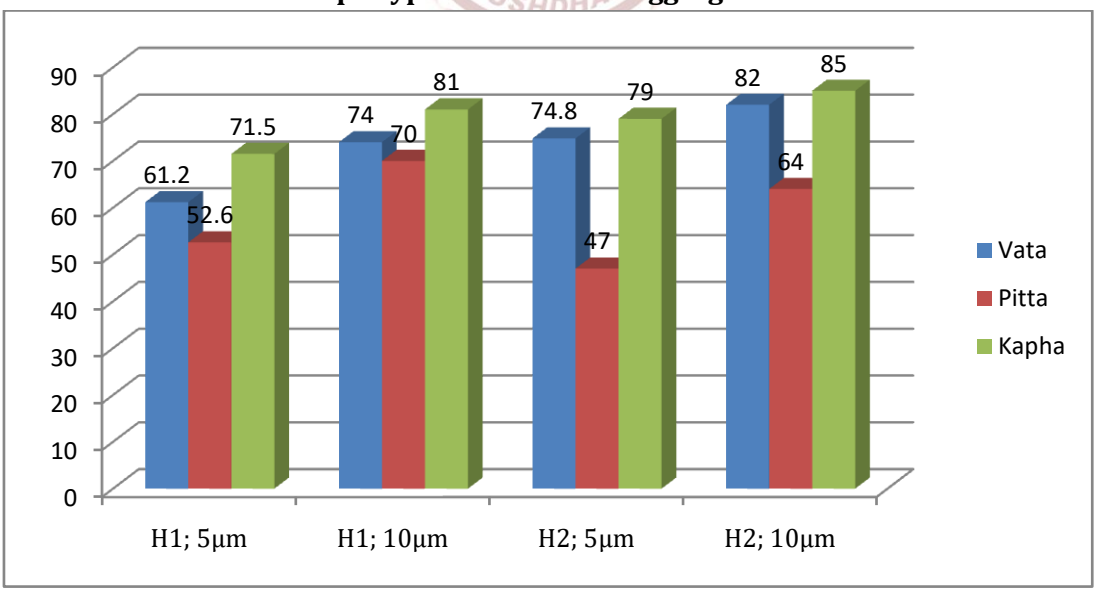
Alkaline phosphatise versus Platelet aggregation



Platelet count versus Platelet aggregation



***Prakriti* and Haplotype Wise Platelet Aggregation Distribution**



DISCUSSION

Vatapradhan subjects have more concentration of Alkaline phosphatase (77.73 ± 24.75) than *Pitta* and *Kapha* Total 30 *Vatapradhan* subjects have average concentration of Alkaline phosphatise 77.73 ± 24.75. Total 30 *Pittapradhan* subjects have average concentration of Alkaline phosphatise 74.39 ± 22.61. Total 30 *Kaphapradhan* subjects have average concentration of Alkaline phosphatise 74.66 ± 21.38.

Subjects having H1 haplotype had Average platelet aggregation 61.5% at 5µm of ADP concentration; 75.06% at 10µm of ADP

concentration. Subjects having H2 haplotype had Average platelet aggregation 71% at 5µm of ADP concentration; 79% at 10µm of ADP concentration.

CONCLUSION

Platelet aggregation in the two haplotypes of P2Y12 gene in different *Prakriti* can be statistically analysed in H1 haplotypes only; as there is very less population of H2 haplotype. In H1 haplotype, difference between the platelet aggregations of three *Prakriti* is extremely significant at 5 µM ADP concentration than at 10 µM. Platelet aggregation varies between 18% to 93% in the population included in this study. From this study we can conclude that, *Kapha prakriti* subjects have maximum platelet aggregation. *Vataprakriti* subjects are correlated with H2 haplotype having less platelet aggregation. And *Pitta prakriti* subjects have the least platelet aggregation in both H1 and H2 haplotype. So we can say that normal healthy individual has wide range of platelet aggregation. So, *Prakriti* can be used as an objective tool for prognosis of Atherosclerotic changes.

REFERENCES

1. Saarth Sushrut Samhita, Edited by Vaidhraj Datto Borkar, Rajesh Prakashan, Sharir sthan, 4/78-79, page no.337.
2. Saarth Sushrut Samhita, Edited by Vaidhraj Datto Borkar, Rajesh Prakashan, Sutrasthan, 14/21, page no.51.
3. Charak Samhita, Edited by Aacharya vidyadhar Shukla, Chaukamba rakashan, Sutrastana, 24/22, page no.324, 125.
4. Charak Samhita, Edited by Vd. Jadavji Trikamji Acharya, Chaukamba prakashan, Vimanstana, 8/95, page no 277.
5. Saarth Sushrut Samhita, Edited by Vaidhraj Datto Borkar, Rajesh Prakashan, Sharir sthan, 4/98, page no.338.
6. Pierre Fontana, Annabelle Dupont, Sophie Gandrille, Christilla Bachelot-Loza, Jean-Luc Reny, Martine Aiach, Pascale Gaussem. Adenosine Diphospate Induced Platelet Aggregation is associated with P2Y12 gene sequence variations in healthy subjects. Circulation August 26, 2003, 989-995.
7. Ugo Cavallari, Elisabetta Trabetti, Giovanni Malerba, Michele Biscuola, Domenico Girelli, Oliviero Olivieri, Nicola Martinelli, Dominick J Angiolillo, Roberto Corrocher, Pier Franco Pignatti. Gene sequence variations of the platelet P2Y12 receptor are associated with coronary artery disease. BMC Medical Genetics 2007, 8:59.

Cite this article as:
Shekhar Gopalrao Uike. Study of Individual's Prakriti and Gene Polymorphism Correlation of P2Y12 Gene. AYUSHDHARA, 2018;5(5):1862-1868.
Source of support: Nil, Conflict of interest: None Declared