ANALOGICAL COMPARISON OF URATHA PITHA VATHAM WITH HYPERTENSION AND RATHA PITHAM WITH PURPURA - AN IN-DEPTH RE-ANALYSIS OF SIDDHA LITERATURE

Usha Ayyasamy*[1], Sathiyarajeswaran Parameswaran[2], Susila Rathinam[3] Kavitha Tamilarasan[4] and Esaivani Selvarajan[5]

[1,3,4,5]Research Officer (Siddha), Department of Clinical Research, Siddha Central Research Institute, Central Council for Research in Siddha, Arumbakkam, Chennai

[2]Director, I/C Siddha Central Research Institute, Central Council for Research in Siddha, Arumbakkam, Chennai

*[1]usha.arunmay22@gmail.com

ABSTRACT

Siddha is one of the primordial medical systems of southeast Asia and twined with in Tamil Culture. According to Siddha Science and as emphasized later by Saint Tiruvalluvar, the diseases of humankind can be classified based on the tri humoral concept of Vali, Azhal and Aiyam. Siddha medical science treasures were hidden in Tamil poetic forms in palm leaf manuscript making its interpretation difficult for a layman. Recent efforts on Development of Morbidity codes - NAMASTE for Traditional medicine by Ministry of Ayush by its experts exposed the subtle features of the disease classification described in an unique style of Siddhar's would evince an analogical correlation of the Siddha Diagnostic term with contemporary medical terminology. Morbidity codes in Namaste portal is very much useful to pick up a disease from traditional Indian medicine and to match with international classification of diseases (Dual coding) add more value to Global health data base. However, there exists periodical and dynamic revision on this based on Research and further expansion in Medical science and their reflection in Traditional Indian medicine. This review is focused on making an exact match from Siddha literature for the commonest morbidity hypertension and to replace the current match from Rathapitham to Urathapithavatham. The present analysis would pave way for the diagnosis and treatment options of Hypertension as the Siddha literature has an enormous medicinal formulation in store for each of its described diseases. The study would also inculcate the interest of scholars for more such research and provide resources for further clinical study in this aspect.

Keywords: Uratta pitta vātam, Hypertension, Siddha, High Blood pressure, Traditional medicine,

DOI Number: 10.14704/nq.2022.20.7.NQ33004 **Neuro Quantology 2022; 20(7):43-49**

INTRODUCTION

The Siddha system of medicine originated in the Southern part of India is one of the twin traditional medicine systems on par with Ayurveda. Being holistic in nature treats not only the body but also the mind and the soul. According to Siddha the elements of human body are Earth, Fire, Water, Air and Space. These five elements are the components of *Vali, azhal and aiyam* which is coined as *Mukkuṟṟam* or Three humors of the body. Three humors co-exist in all the cells of the body. Three humors involved in regulating all the functions of the body, and maintain the balance in the physical, emotional and mental spheres. The equilibrium of humors ensures optimum health while any disturbance in these results in disease. According to Siddha Faulty food and Misdeeds Remove cause disturbances in three humors resulting in diseases.

The prevalence of Hypertension in India is 2 - 15 % in Urban and 2 - 8 % in rural adult population[1]. The ancient Siddha literature *Yugi Vaithiya Chinthamani 800* has indicated the term *Uratta pitta vātam* and has described its signs and symptoms that are outward manifestation of the underlying Hypertensive disorder. However the

Siddha physicians presently use the term *Iratta pittam* for Hypertension which is far away from the aim of NAMASTE PORTAL to find an exact match for dual coding to go parallel with of International standards.. This review would therefore scrutinize both the terminologies *Uratta pitta vātam* and *Iratta pittam* and their analogy with that of most appropriate modern medical terminologies.

URATHA PITHA VATHAM

In Siddha system of medicine, saint Yugi has mentioned about 42 types of *Pitha* diseases among which *Uratta pitta vātam* can be compared and correlated with Essential hypertension on the basis of signs and symptoms [2]

Mūrkkamāṅ kōpamatu mikavuṇṭākum

muṉaiyāka vaṭikkaṭik kuccaṇṭaikoḷḷum

ārkkamāyk kūviyēviraiccalākum

ātāṉapātāḷampētiyākum

nārkkamāy naṉmait iṉmaitōṉṟāmaṟṟāṉ

nalakkamākkaṇcivakkuntūkkamillai

ūrkkamāyuṭamputūlikkumuppum

murattapittavātattiluṇmaitāṉē

YugiVaithiya Chintamani-800, pg no: 251[7]

INTERPRETATION OF YUGI'S LINES OF URATHA PITHA VATHAM

Uratta pitta vātam **Symptoms**	**Symptoms of Hypertension**
Mūrkkamāṅkōpamatu mikavuṇṭākum *muṉaiyākavaṭikkaṭikkuccaṇṭaikoḷḷum* *ārkkamāyk kūviyēviraiccalākum*	Verbal expressions of anger such as yelling, shouting, arguing
ātāṉa pātāḷam pētiyākum	Abnormal bowel movements
nārkkamāynaṉmaitiṉ maitōṉṟāmaṟṟāṉ	Behavioural symptoms /cognitive impairment
nalakkamākkaṇcivakk untūkkamillai	Insomnia, Redness of Eyes (Subconjuctival haemorrhage)
ūrkkamāyuṭamputūlikkumuppum	Edema of body

Line by Line scientific analysis of symptoms of *Uratta pitta vātam* with Systemic Arterial Hypertension

Line-1-3: *Mūrkkamāṅkōpamatumikavuṇṭākum*

Several studies have examined the influence of suppressed anger ("anger-in") on BP and found that particularly under conditions of stress, anger-in was positively related to resting BP and/or prevalent hypertension.[3] Other studies, including early psychodynamic research, have found that hypertensives, including those with borderline hypertension, reported greater intensity of anger.[4] The emotion anger is said to increase the cortisol level. Chronic elevation of cortisol level have been associated with hypertension, brain atrophy and cognitive impairments.[5] Cortisol is a glucocorticoid hormone secreted by Adrenal gland, regulates metabolism, blood glucose levels, immune responses, anti-inflammatory actions, blood pressure, and emotion regulation.[6] The above facts contribute to verbal expressions of anger such as yelling, shouting, arguing that has been mentioned in the Lines 1 and 2 of the poetic lines of *Uratta pitta vātam*.

Moreover, stress can also cause hypertension through repeated blood pressure elevations as well as by stimulation of the nervous system to produce large amounts of vasoconstricting hormones that increase blood pressure.[7]

Line-4*: Ātāṉapātāḷampētiyākum*

The Line-2 of Siddha text *Ātāṉapātāḷampētiyākum* indicate the increased intestinal motility causing diarrhoea in hypertensive subjects. It is speculated that IBS may be a potential risk factor for MS. Metabolic syndrome (MS) is a well-recognized constellation of risk factors for cardiovascular disease (CVD). However, few epidemiological studies have assessed the relationship between IBS status and MS and its components in an adult population.[8] On the other hand, gut microbiota alterations could also be considered a potential link between IBS and MS and its components. The accumulated evidence has indicated that IBS is related to quantitative and qualitative changes in

gut microbiota. [9] Another study found out that IBS was reliably related to higher BP compared to healthy controls. Longer disease duration (chronicity) of IBS was related to systolic BP increase. Recent scientific reports have explored the association between diarrhoea in childhood and BP later in life.[10][11][12]

Line-5: Nārkkamāynaṉmaitiṉmaitōṉṟāmaṟṟāṉ

The Line-5 of the poetic text *Nārkkamāynaṉmaitiṉmaitōṉṟāmaṟṟāṉ* indicates behavioural symptoms /cognitive impairment. Numerous studies have demonstrated that hypertension increases the risk for cognitive impairment, vascular dementia, and Alzheimer's disease [13]. Hypertension is the main risk factor for the development of ischemic white matter lesions in the brain which is associated with impaired cognitive function [14] Arterial hypertension is considered the main modifiable vascular risk factor that causes silent damage to brain vessels. This vascular brain injury could be the common nucleus that justifies the cognitive and behavioural symptoms (late-life depression) of target organ damage mediated-hypertension.[15][16][17]

Line-6: *Nalakkamāk kaṇcivakkun tūkkamillai*

The Term *Kancivakkum* of the poetic line means the inflammatory changes/reddening of eye. The eye is the only organ in the body where the vascular changes due to systemic hypertension can be observed in vivo. The most common ocular presentation of hypertension is hypertensive retinopathy. Hypertensive retinopathy can be the presenting sign of hypertensive emergency, an acute, life-threatening condition resulting from markedly increased blood pressure that leads to acute end-organ damage. Elevated blood pressure with evidence of moderate hypertensive retinopathy has been referred to as "accelerated hypertension," while elevated blood pressure with evidence of severe hypertensive retinopathy, including optic disc swelling, has been referred to as "malignant hypertension." Early findings include generalized narrowing of the retinal arteriolar vessels due to vasospasm and increased vascular tone. Chronic hypertension leads to structural changes in the vessel wall such as intimal thickening and hyaline degeneration. These manifest as focal or diffuse areas of vessel wall opacification.[18][19] According to a report of the National Commission on Sleep Disorder Research, 30 million adults and teenagers in the United States are chronically sleep deprived.[20]

The term *tūkkamillai* indicates insomnia which is a prevalent sleep disorder that is associated with a multitude of health consequences. Particularly, insomnia has been associated with cardiovascular disease and its precursors, such as hypertension and blood pressure (BP) non-dipping.[21] Another study by National Health and Nutrition Examination Survey of 4,810 middle-aged (32-59 years) Americans in fully adjusted models, showed that short sleep duration (≤ 5 h/night) was associated with a 60% higher risk of self-reported incident hypertension over an 8- to 10-year follow-up period. Bonnet 2009, reported the fact that activation of the hypothalmic-pituitary-adrenal axis and the sympathetic nervous system as in insomnia may predispose to hypertension development. [22]

Line-7: *Ūrkkamā yuṭamputūlikkum uppum*

The final lines of the tamil traditional poetic text indicates the edema of the body. Systemic arterial hypertension is an important risk factor for cardiovascular disease that is frequently observed in populations with declining renal function. Hypervolemia due to water retention predisposes patients to hypertension and can clinically manifest in several forms, including peripheral edema. [23] Chronic venous insufficiency which refers to edema, skin trophic changes, and discomfort. Its pathophysiology is either due to reflux (backward flow) or obstruction of venous blood flow. Chronic venous insufficiency can develop from the protracted valvular incompetence of superficial veins, deep veins or perforating veins that connect them. In all cases, the result is venous hypertension of the lower extremities.[24]

INTERPRETATION OF YUGI'S LINES OF RATHA PITHAM

Iratta pittam

uṇmaiyāyirumaṟṟāṉmikavumuṇṭāy

utaṭṭiyāykkuṟṟiyērattamvīḻntu

aṇmaiyāmcarīramatumikavumvaṟṟi

aṭivayiṟucuruṅkiyēvaṟṟikkāṇum

vaṇmaiyāyvāynīriṟkaviccaṭikkum

maṟukiyēvalluṭampuvāṭṭamākum

iṇmaiyāyiṭupputāṉkuṭaiccalākum

iṭumirattapittattiṇiyaṟkaitāṉē

S.No	Ratha pitham Symptoms	Interpretation
1.	*yirumaṟṟāṉ mikavumuṇṭāy utaṭiyāykkuṟṟiyē rattamvīḻntu*	Cough with hemoptysis
2.	*Carīramatumikavum vaṟṟi aṭivayiṟucuruṅkiyē vaṟṟikkāṇum*	Emasciation of body and abdomen
3.	*Vāynīriṟkaviccaṭikkum*	Halotosis
4.	*Valluṭampuvāṭṭamākum*	Extreme Fatigue
5.	*Yiṭupputāṉkuṭaiccalākum*	Low back pain

Idiopathic Thrombocytopenic Purpura (ITP)

Thrombocytopenia can be caused by decreased production or increased destruction of platelets. Historically, Idiopathic thrombocytopenic purpura (ITP) was believed to be caused by increased platelet destruction at a rate that exceeded production by a compensating bone marrow.[25] In people with ITP, an unknown cause leads antibodies produced by the immune system to attach themselves to the platelets, marking the platelets for destruction. The spleen, which helps the body fight infection, recognizes the antibodies and removes the platelets from your system. The result of this case of mistaken identity is a lower number of circulating platelets than is normal. A normal platelet count is generally between 150,000 and 450,000 platelets per microliter of circulating blood. People with ITP often have platelet counts below 20,000 that increases the risk of bleeding.[26]

Scientific Analysis of Ratta Pittam with Idiopathic Thrombocytopenic Purpura (ITP)

Line 1 and 2: Yirumaṟṟāṉmikavumuṇṭāyutaṭṭiyāykkuṟṟiyērattamvīḻntu

A review of the literature has shown that pulmonary hemorrhage can be the first manifestation of Henoch-SchönleinPurpura (HSP) in 88% of cases with pulmonary involvement. Pulmonary hemorrhage is commonly seen with the first episode of HSP, although it can occur with recurrent episodes. Studies have shown that clinical manifestations of pulmonary hemorrhage in HSP vary greatly, ranging from mild cough to acute severe dyspnea and respiratory failure. Most patients present with dyspnea, and only about one-third of patients present with hemoptysis. The pathophysiology of HSP involves the deposition of antigen-antibody complexes (especially IgA) in small vessels activating the alternative complement pathway, resulting in neutrophil accumulation that causes inflammation and vasculitis. Clinical manifestations usually include nonthrombocytopenicpurpura, arthralgia, gastrointestinal manifestations, and renal involvement.[27]

Intraoral examination can reveal bleeding from gingiva in lower anterior region, which was inflamed, reddish, tender on palpation, soft in consistency. Petechial spots on dorsum of tongue, petechial spot on left side hard palate and left maxillary tuberosity region. [26]

Line 2: Carīramatu mikavum vaṟṟiaṭivayiṟucuruṅkiyē vaṟṟikkāṇum

Hypertension has been reported to be as a complication of Henoch-Schönlein purpura (HSP) with evidence of renal involvement, either decreased renal function or urinary abnormalities. The recent understanding of cachexia physiopathology during Chronic kidney disease progression suggests that Protein energy wasting and cachexia are closely related and that Protein energy wasting corresponds the initial state of a continuous process that leads to cachexia, implicating the same metabolic pathways as in other chronic diseases. [28] Moreover Hypertension as a complication of HS Purpura can also lead to Pulmonary hypertension-Left heart disease (PH-LHD), accounting for 65-80% of all PH patients. This can be identified as a severe marker of PH with significantly higher morbidity and mortality. [29] At these terminal stages of chronic

heart failure (CHF), Cardiac cachexia is caused. Studies show that inflammatory cytokines such as tumor necrosis factor-a trigger muscle protein degradation. Also other studies found that elevated adipokine adiponectin in patients with CHF may be correlated with muscle mass, muscle strength in the arms, or with trunk fat mass.

Another study showed that the expression of myostatin (a negative regulator of muscle growth) in skeletal muscle is decreased in spontaneously hypertensive rats with heart failure compared with control animals. This is also true for follistatin, a powerful antagonist, and its potential as a biomarker of muscle wasting. The pathways of muscle wasting in cardiac cachexia include overexpression of MuRF-1, an E3-ubiquitin ligase that facilitates myofibril degradation via the ubiquitin–proteasome pathway. The over-activity of inflammatory mediators fuels the activity of the ubiquitin–proteasome pathway.[30]

Line 3: *Vāynīriṟkaviccaṭikkum*

The appearance in the mouth of haemorrhagic petechiae, ecchymoses or blood blisters with spontaneous bleeding is suggestive of a haemorrhagic disorder that may be caused either by functional impairment of platelets or of blood vessel walls, by an abnormal decrease in the number of circulating platelets (thrombocytopaenia), or by defects in the blood clotting mechanism.[31]

In a study, bleeding from mouth, gums and tongue was found in 68 (15.9%) of 427 children.[32] For a patient with poor or inadequate oral hygiene, bleeding of the gingiva is frequent.[33]

Line 4: *Valluṭampuvāṭṭamākum, yiṭupputāṉkuṭaiccalākum*(Extreme fatigue)

The association of fatigue with thrombocytopenia was comparable to patients' responses that they had less energy when their platelet counts were low.[34] Several studies documented the presence of multiple symptoms, including 'physical fatigue', which improved when the platelet count increased. These observations suggest that fatigue is an important symptom for patients with ITP, that it may be related to the severity of thrombocytopenia, and that it is potentially treatable.[35]

Line 5: *Yiṭupputāṉkuṭaiccalākum* (Low back pain)

Low back pain (LBP) is now regarded as the first cause of disability worldwide and should be a priority for future research on prevention and therapy. Intervertebral disc (IVD) degeneration is an important pathogenesis of LBP. Although the exact mechanism of IVD degeneration remains unknown, the biochemical changes typical of the degenerative IVD are known to include progressive decreases in proteoglycan and collagen type II contents with subsequent dehydration and increased content of collagen type I leading to tissue fibrosis.[36] PRP (Platelet-rich Plasma) has been widely used in the clinical setting for tissue regeneration and repair, as the main function of platelets is to contribute to hemostasis through adhesion, activation, and the aggregation process. In response to vessel injury, platelets are activated and their granules release coagulation factors that generate a fibrin clot. In addition to the factors that coagulate blood, activated platelets release growth factors. These growth factors increase inflammation and revascularization and accelerate epithelial regeneration in the inflammatory and proliferative stages of wound healing.

Once platelets are activated, these bioactive proteins are generated and released to the damaged tissues, synergistically regulating multiple pathways, including cell proliferation, cellular chemotaxis, angiogenesis, cell differentiation, and ECM synthesis.[37]

CONCLUSION

This review provides a keen analysis of the two Siddha diagnostic terminologies term *Uratta pitta vātam* and *Iratta pittam*. The signs and symptoms of these conditions have been interpreted and efforts have been taken to correlate it with the most equivalent symptoms of modern medical terminologies. The results reveal the controversial features of *Iratta pittam* and Hypertension, but found to be interestingly correlated with the symtoms of Idiopathic thrombocytopenic purpura. [expansion] The study findings provides the scientific evidence that the characteristic features of *Uratta pitta vātam* most probably fall in line with Hypertensive disorder and its outward manifestation.

REFERENCES:

1. Taposhsarkar, Singh NP. Epidemiology and genetics of hypertension japi. 2015; 63:61 - 68.
2. Ramachandran SP. YugiVaithiyaChinthamani 800 moolamumuraium. Thaamarainoolagam. pithanoigal. 2nd edition; 2013.p.138.
3. Harburg E, Blakclock EH, Roeper PJ. Resentful and reflective coping with arbitrary authority and blood pressure: Detroit. Psychosom Med. 1979; 41:189-202.
4. Johnson EH, Spielberger CD. Assessment of the experience, expression, and control of anger in hypertension research. In Johnson EH, Gentry WD, Julius S (eds) Personality, Elevated Blood Pressure, and Essential Hypertension. Washington DC. Hemisphere Publishing; 1992. p3-24.
5. Gold SM, Dziobek I, Rogers K, Bayoumy A, Pauline F, McHugh, Antonio Convit. Hypertension and Hypothalamo-Pituitary-Adrenal Axis Hyperactivity Affect Frontal Lobe Integrity. The Journal of Clinical Endocrinology & Metabolism. 2005; 90(6):3262–3267.
6. Sroykham W, Wongsawat Y. Effects of brain activity, morning salivary cortisol, and emotion regulation on cognitive impairment in elderly people. Medicine (Baltimore). 2019; 98(26):e16114.
7. Kulkarni S, O'Farrell I, Erasi M, Kochar MS. Stress and hypertension. WMJ. 1998 Dec; 97(11):34-8.
8. Guo Y, Niu K, Momma H, et al. Irritable bowel syndrome is positively related to metabolic syndrome: a population-based cross-sectional study. PLoS One. 2014; 9(11):e112289.
9. Ghoshal UC, Shukla R, Ghoshal U, Gwee KA, Ng SC, et al. The gut microbiota and irritable bowel syndrome: friend or foe? Int J Inflam 2012; 2012: 151085.
10. Batty GD, Smith GD, Fall CHD, Sayer AA, Dennison E, Cooper C, et al. Association of diarrhoea in childhood with blood pressure and coronary heart disease in older age: analyses of two UK cohort studies. Int J Epidemiol. 2007; 36:1349–1355.
11. Pearce MS, Relton CL, Unwin NC, Adamson AJ, Davey Smith G. The relation between diarrhoeal episodes in infancy and both blood pressure and sodium intake in later life: the Newcastle Thousand Families Study. J Hum Hypertens. 2008; 22:582–584.
12. Ma W, Li Y, Heianza Y,et al. Associations of Bowel Movement Frequency with Risk of Cardiovascular Disease and Mortality among US Women. Sci Rep. 2016; 6: 33005.
13. Aronow WS. Hypertension and cognitive impairment. Ann Transl Med. 2017;5(12):259.
14. Skoog I. A review on blood pressure and ischaemic white matter lesions. Dement Geriatr Cogn Disord 1998; 9(l1):13-9.
15. Vicario A, Cerezo GH. El impactocognitivo-conductual de la hipertensión [The cognitive-behavioural impact of hypertension].HipertensRiesgoVasc. 2020; 37(3):125-132.
16. Nolan RP, Feldman R, Dawes M , Kaczorowski J, et al. Randomized Controlled Trial of E-Counseling for Hypertension: Reach. Circ Cardiovasc Qual Outcomes. 2018;11(7):e004420.
17. Reitz C, Ming-Xin Tang, Manly J, et al. Hypertension and the Risk of Mild Cognitive Impairment. Arch Neurol. 2007; 64(12):1734-1740.
18. Wong TY, Mitchell P. The eye in hypertension. Lancet. 2007; 369:425–435.
19. Tarlan B, Kiratli H. Subconjunctival hemorrhage: risk factors and potential indicators. Clin Ophthalmol. 2013;7:1163–1170.
20. Lusardi P, Zoppi A, Preti P,et al. Effects of insufficient sleep on blood pressure in hypertensive patients: A 24-h study. American Journal of Hypertension.1999; 12(1):63–68.
21. Jarrin DC, Alvaro PK, Bouchard MA, Jarrin SD, Drake CL, Morin CM. Insomnia and hypertension: A systematic review. Sleep Med Rev. 2018;41:3-38.
22. Bonnet MH. Evidence for the pathophysiology of insomnia. Sleep. 2009; 32(4):441–442.
23. Ferreira-Filho SR, Machado GR, Ferreira VC, Rodrigues CFMA, Proença de Moraes T,

Divino-Filho JC, et al. Back to Basics: Pitting Edema and the Optimization of Hypertension Treatment in Incident Peritoneal Dialysis Patients (brazpd). PLoS ONE.2012; 7(5): e36758.

24. Patel SK, Surowiec SM. Venous Insufficiency. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: **Error! Hyperlink reference not valid.**.
25. Neunert C, Lim W, Cohen A, Solberg L, Crowther M. The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia. Blood. 2011; 117(16): 4190-4207
26. Kayal L, Jayachandran S, Singh K. Idiopathic thrombocytopenic purpura. Contemp Clin Dent [serial online] 2014;5:410-4. Available from: **Error! Hyperlink reference not valid.**
27. Ngobia A, TarekAlsaied, Ndidi I. Unaka, Henoch-SchönleinPurpura With Hemoptysis: Is It Pneumonia or Something, Else?, Hospital Pediatrics 2014;4:316.
28. Koppe L, Fouque D, Kalantar-Zadeh K. Kidney cachexia or protein-energy wasting in chronic kidney disease: facts and numbers. J Cachexia Sarcopenia Muscle. 2019;10(3):479-484.
29. Guazzi M, Borlaug B. Pulmonary hypertension due to left heart disease. Circulation 2012; 126:975–90.
30. Kung T, Szabó T, Springer J, Doehner W, Anker SD, von Haehling S. Cachexia in heart disease: highlights from the ESC. J Cachexia Sarcopenia Muscle. 2011; 2(1):63-69.
31. Khammissa RAG, Fourie J, Masilana A, Lawrence S, Lemmer J, Feller L. Oral manifestations of thrombocytopaenia,The Saudi Dental Journal. 2018; 30(1): 19-25. ISSN 1013-9052.
32. Bolton-Maggs PH, Moon I. Assessment of UK practice for management of acute childhood idiopathic thrombocytopenic purpura against published guidelines. Lancet 1997; 350: 620–623.
33. Stamps JT. The role of oral hygiene in a patient with idiopathic aplastic anemia. J Am Dent Assoc 1974; 88: 1025–1027.
34. Newton JL, Reese JA, Watson SI, Vesely SK, Bolton-Maggs PH, George JN, Terrell DR. Fatigue in adult patients with primary immune thrombocytopenia. Eur J Haematol. 2011; 86(5):420-9.
35. George JN, Mathias SD, Go RS, et al. Improved quality of life for romiplostim-treated patients with chronic immune thrombocytopenic purpura: results from two randomized, placebo-controlled trials. Br J Haematol 2008;144:409–15.
36. Vo NV, Hartman RA, Patil PR, Risbud MV, Kletsas D, Iatridis JC, Hoyland JA, Le Maitre CL, Sowa GA, Kang JD. Molecular mechanisms of biological aging in intervertebral discs. J Orthop Res. 2016; 34(8):1289-306.
37. Anitua E, Andia I, Ardanza B, Nurden P, Nurden AT. Autologous platelets as a source of proteins for healing and tissue regeneration. Thromb Haemost. 2004; 91(1):4-15.