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Effect of One Bout Submaximal Endurance Exercise on Blood Coagulation and Fibrinolytic Factors in Patients with Hypertension

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Abstract

Introduction: Hypertension is considered as a major risk factor for thrombotic events. The aim of this study was to investigate the effect of one bout submaximal endurance exercise on blood coagulation and fibrinolytic factors in patients with hypertension.

Methods: 20 subjects were randomly selected out of 70 adult males with hypertension (Mean ± SD; age: 60.25±4.59 yr, body mass index (BMI): 29.57± 3.68 kg/m^2, body fat percentage (BFP): 20.25± 5.31%, maximal oxygen uptake34.83±2.11ml/kg/min, systolic blood pressure(SBP): 147.20± 6.43 mm Hg,diastolic blood pressure(DBP): 94.40±3.70 mm Hg). The participants carried out one bout submaximal endurance running for 30 minutes within 60 to 65% of maximal heart rate reserve (MHRR). Blood samples were immediately taken before and after exercise. Dependent variables were categorized into three groups including 1.Coagulation: fibrinogen (FIB), factor VIII (FVIII), prothrombin time (PT), prothrombin time activity (PTA), international normalized ratio (INR), activated partial thromboplastin time(aPTT), platelet (PLT), mean platelet volume (MPV) 2. Anticoagulation: protein C (PC), antithrombinIII (ATIII) 3. Fibrinolytic: d-dimer (D-D), tissue plasminogen activator (tPA), plasminogen activator inhibitor1 (PAI-I), tPA/PAI-1. For normalizing research data Shapiro- Wilk test was used. Data analysis was done by paired samples t-test at a significant level of (P≤0.05). Testing of the considered assumptions was carried out by SPSS software version 19.

Results: Paired sample t-test showed a significant reduction in aPTT (P=0.001), tPA (P=0.001), tPA/PAI-1(P=0.014), PV (P=0.001) and a significant increase in FIB (P=0.001), FVIII (P=0.001), PLT (P==0.001), MPV (P=0.001), PC (P=0.001) and ATIII (P=0.001) levels. There was no significant change in PT (P=0.068), PTA (P=0.156), INR (P=0.060) and D-D (P=0.436)levels. Considering the volume of plasma, no significant changes in FIB were observed (P=0.814).

Conclusion: It seems that submaximal endurance exercise activates the anticoagulation system which can overcome thrombotic conditions.

Keywords: Exercise, Coagulation, Fibrinolysis, Hypertension

Introduction

Hypertension is regarded as the highest cardiovascular risk factor in adults. It reduces life expectancy by seven years (1). This disease is considered as the foremost risk factor regarding various heart attacks (2). It has also been considered as the most dangerous factor regarding thrombotic events including myocardial infarction and heart attack (3). Strong indications show that hypertension is related to pro-thrombotic condition caused by endothelial dysfunction, reduction of fibrinolytic potential and also platelet over activity (3). It has also been shown that thrombotic conditioncan be agitated by angiotensin system which rises during high blood pressure (3). Changes in endothelium due to hypertension have been

widely confirmed. Endothelium activation causes increase in pre-coagulation and inflammatory factors (4). It accompanies changes in endothelium vasodilation, pre-inflammatory and prothrombotic conditions. Being constantly exposed to hypertension, and due to inflammatory mediators plus effects of neutrophils and platelets which stick endothelium, process of endothelium dysfunction begins (4). Following this dysfunction, damaging or activation of endothelium starts a vicious cycle process which can lead to more damage and dysfunction. Under these conditions, due to changes in nitric oxide (NO) and endothelin bioavailability hypertension has a tendency to remain high. This activation of endothelium will cause a chain reaction including: reduction of NO activity, endothelin increase, increase in tissue plasminogen activator (tPA) levels and plasminogen activator inhibitor-1 (PAI-1), and increased levels of angiotensin-converting enzyme (ACE)(4). Endothelial dysfunction at presence of atherosclerosis has also been observed. It has been shown that a combination of risk factors lead to endothelial dependent vasodilation damages. Changes in NO also have especially importance. They effect platelet aggregation, smooth muscle proliferation and migration, as well as monocyte adhesion and adhesion molecule expression which play an important role in the genesis of thrombosis and atherosclerotic (4). Therefore, endothelial dysfunction is now considered as a relevant mechanism that promotes atherosclerosis and thrombosis. It has been shown that there is a negative correlation between resting blood pressure and the level of physical activity in both males and females (2). Regular exercise results in the reduction of resting blood pressure in young and adult people with normal, prehypertension or hypertension(2). Swati *et al.* showed that although aerobic and resistance training both bring systolic and diastolic blood pressure down as well as reduce heart rate, aerobic training regarding lowering blood pressure is more effective(5). Research shows that one bout aerobic exercise causes a significant reduction in systolic and diastolic blood pressure, peripheral vascular resistance, vascular resistance and norepinephrine(NE) in hypertensive individuals(6). While in healthy people's blood pressure and NE no significant changes have been observed. It appears that peripheral vascular resistance reduction due to exercise is the main factor in blood pressure reduction in hypertensive patients (6, 7).Therefore, considering the positive effects of exercise on hypertension, it is predicted that one bout submaximal endurance exercise, while reducing high blood pressure in hypertension patients, is likely to also reduce the damaging process in endothelium function caused by hypertension and in this way could change pre-inflammatory and endothelium protherombic conditions to a hemostasis condition. Therefore, this research aims to investigate the effect of one bout submaximal endurance exercise on fibrinogen (FIB), factor VIII (FVIII), prothrombin time (PT), prothrombin time activity(PTA), international normalized ratio (INR), activated partial thromboplastin time(aPTT), platelet (PLT), mean platelet volume (MPV),protein C(PC), antithrombin III(ATIII), d-dimer(D-D), tPA, PAI-I, tPA/PAI-1 and plasma volume(PV) in hypertensive patients.

Methods

The present research was carried out as a practical project based on semi-experimental method and pretest-posttest research design. In this study, the effect of one bout submaximal endurance exercise on coagulation and fibrinolytic factor in hypertensive cardiovascular patients was undertaken. The study protocols and procedures had previously been approved by the Research Ethics Committee of Sport Sciences Research Institute of Iran with the code IR.SSRI.REC.1397.203. The statistical sample was 20 male employees in National Iranian South Oil Company (NISOC).They were

selected out of 70 males with age range of 55 to 65yrs. The selection was based on determined inclusion/exclusion criteria for this research. The inclusion criteria were: participation consent, age range 55 to 65 yrs, VO_{2max}> 7.5 METs, ejection fraction of 50 to 70%, systolic blood pressure ≥ 140 mm Hg or diastolic blood pressure ≥ 90 mm Hg (8, 9). Exclusion criteria included: lack of willingness for continuation, ages below 50 or above 65yrs, VO_{2max}< 7.5 METs, ejection fraction below 50%, systolic blood pressure < 140mm Hg or diastolic blood pressure < 90 mm Hg, smoking, presence of other diseases such as coronary artery disease or diabetes. In order to investigate the cardiovascular endurance, the modified bruce protocol stress test was used. Ejection fraction was carried out by echocardiography Eco Color Doppler M-Mode (Esaote MyLab Model). The systolic and diastolic resting blood pressures were measured by digital manometer. Also; anthropometric characteristics were determined by VIVENTE body composition analyzer (494-34.Banahwa-dona.aanaseo-au.seoul.korea). Once selected, following one week, the samples adhering to 8 hours night fasting protocol underwent one bout submaximal endurance running exercise for 30 minutes within 60 to 65% of maximal heart rate reserve (MHRR) (10). To prevent the effect of other activities on the coagulation, anticoagulation and fibrinolytic factors, all participants were requested not to enter any exercise 48 hours before the intervention (10, 11). Blood samples were taken just before and after the intervention. The tests included: coagulation (FIB, FVIII, PT, PTA, INR, aPTT, PLT, MVP), anticoagulation (PC, ATIII) and fibrinolytic (D-D, tPA, PAI-1, tPA/PAI-1) factors. PV was also tested. For surveying complete blood count (CBC), two milliliters of venous arm blood in tubes containing EDTA with density of 1.5 to 2 mg/ml were collected. Also, 5 ml of blood was placed in tubes containing sodium citrate with density of 0.2 ml in 1.8 ml of blood. For the purpose of plasma separation the tubes were centrifuged at 2500 revs/minute for 30 minutes. Plasma volume reduction due to undertaken activity affects the density factors, and in particular FIB. Therefore for calculating plasma volume changes and normalization factors Dill and Costill formula was used (12, 13). For normalizing research data Shapiro- Wilk test was used. In order to investigate the effect of exercise on blood coagulation, anticoagulation and fibrinolytic factors in hypertensive cardiovascular patients, one bout submaximal endurance running was carried out. Paired samples t-test at a significant level of ($P \leq 0.05$) was used. Testing of the considered assumptions was carried out by SPSS software version 19.

Results

Table 1 shows descriptive data on the anthropometric and physiological characteristics of the subjects. Since calculations of plasma volume changes by Dill and Costill formula requires data such as blood volume (BV), red cell volume (RCV), hematocrit (HCT), number of hemoglobin (HB), therefore Table2 presents the related data regarding these indexes just before and after the exercise. Table 3 presents data related to paired samples t-test of research variables. The results showed that regardless of plasma volume changes, submaximal endurance exercise gives significant rise in the level of FIB (P=0.001). Considering the level of plasma volume changes and FIB levels adjustment, sub-maximal endurance exercise has not changed FIB (P=0.814). Submaximal endurance exercise has also caused a significant reduction in aPTT, tPA, PV (P=0.001) andtPA/PTI-1 (P=0.014). There was also a significant increase in FVIII, PLT, MPV, PC, and ATIII (P=0.001). In the meantime, significant changes in PT (P=0.068), PTA (P=0.156), INR (P=0.060) and D-D (P=0.436) were not observed.

Table 1. Descriptive data on the anthropometric and physiological characteristics of the subjects

Variable	Mean±SD
Age(yrs)	60.25±4.59
Height(cm)	6.34±171.10
Weight(kg)	12.33±86.70
Body Mass Index(BMI) (kg/m^2)	3.68±29.57
Waist to Hip Raito(WHR) (kg)	0.96±0.08
Fat Free Mass(FFM) (kg)	66.45±3.70
Body Fat Mass(BFM) (kg)	3.18±23.00
Protein (kg)	1.45±13.12
Body Fat Percentage (BFP) (%)	3.18±23.00
Minerals (kg)	0.50±4.28
Vo_{2max}(ml/kg/min)	2.11 ±34.83
Systolic Blood Pressure(SBP) (mm Hg)	6.43±147.20
Diastolic Blood Pressure(DBP) (mm Hg)	3.70±94.40
Resting Heart Rate(RHR) (beat/min)	3.61±76.25
Ejection Fraction (EF) (%)	1.83±55.75

Table 2. Mean and standard deviation of some hematologic indexes before and after the exercise

Variable	Pre- exercise Mean ± SD	Post-exercise Mean ± SD	Changes (%)
HB(g/dl)	15.01±1.50	15.62±1.54	4.06
HCT (%)	42.64±2.81	44.34±2.81	3.98
BV (%)	100.00±0.00	96.08±2.91	-3.92
RCV (%)	42.64±2.81	42.60±2.83	-0.09
PV (%)	57.36±2.81	53.48±3.29	-6.76

Discussion

Current results showed that one bout submaximal endurance exercise within the 60 to 65% of MHRR caused a significant reduction of 6.76% in plasma volume in hypertension patients. Karampour *et al.* showed one bout high intensity interval exercise at 85 to 95% of MHRR caused a 12% reduction in plasma volume, and one bout high intensity resistance exercise at 85 to 95% 1RM caused a 4.24% plasma reduction in elite athletes (14). As was presented there was a large difference in plasma volume after submaximal endurance exercise presented in this research and other exercises. The reason for this could be due to the type and intensity of the exercise. Plasma volume reduction can be due to a number of causes including: increase in capillary hydrostatic pressure due to increase in blood pressure, reduction of body water by sweating, some hormonal activity such as aldosterone, antidiuretic hormone (ADH), atrial natriuretic peptide (ANP) and accumulation of some metabolic products such as lactate ions, ammonium and potassium in working muscles (15). Therefore, it can be stated that intensity and type of exercise can produce different effects on blood pressure, body water reduction, hormonal function and accumulation of metabolic products. Results of the present study showed that submaximal endurance exercise without

Table3. Paired sample t-test results

Variable	Number	Pretest Mean ± SD	Posttest Mean ± SD	Changes (%)	t	df	Sig
FIB (mg/dl) *	20	306.80±41.22	328.15±49.85*	+ 4.06	-4.024	19	0.001•
FIB (mg/dl) **	20	306.80±41.22	305.38±44.50**	-0.46	0.239	19	0.814✪
FVIII (%)	20	94.65±22.70	110.75±24.64	+ 17.01	-4.729	19	0.001•
PT(s)	20	12.57±0.59	12.41±0.61	-1.27	1.939	19	0.068✪
PTA (%)	20	93.90±5.78	95.13±5.86	+ 1.30	1.478	19	0.156✪
INR (%)	20	1.02±0.06	1.00±0.06	- 1.96	1.997	19	0.060✪
aPTT(s)	20	28.60±1.75	27.60±1.65	- 3.49	6.149	19	0.001•
PLT(10^3/mm^3)	20	228.50±42.12	266.30±47.93	+ 16.54	-7.423	19	0.001•
MPV(fL)	20	11.23±0.81	11.39±0.89	+ 1.42	-2.427	19	0.001•
D-D(ng/ml)	20	264.82±81.66	285.43±95.42	+ 7.78	-0.795	19	0.436✪
tPA(IU/mL)	20	21.22±6.01	15.15±4.91	- 28.60	4.644	19	0.001•
PAI-1(AU/mL)	20	38.83±19.95	33.88±20.13	- 12.74	1.80	19	0.081✪
tPA/PAI-1	20	0.72±0.31	0.58±0.31	- 19.44	2.712	19	0.014•
PC (%)	20	99.60±16.97	106.80±16.38	+ 7.22	-8.461	19	0.001•
ATIII (%)	20	112.29±6.98	118.49±7.34	+ 5.52	-9.710	19	0.001•
PV (%)	20	57.36±2.81	53.48±3.29	- 6.76	5.602	19	0.001•

FIB: fibrinogen, FVIII: factor VIII, PT: prothrombin time, PTA: prothrombin time activity, INR: international normalized ratio, aPTT: activated partial thromboplastin time, PLT: platelet, MPV: mean platelet volume, D-D: d-dimer, tPA: tissue plasminogen activator, PAI-1: plasminogen activator inhibitor1, PC: protein C, ATIII: antithrombin III, PV: plasma volume,*without considering plasma volume changes, **with consideration of plasma volume changes, • significant changes, ✪ no significant changes.

considering plasma volume changes resulted in a significant increase in the levels of FIB in hypertensive cardiovascular patients. FIB is an acute phase reactant which has been identified as the main independent risk factor regarding coronary arteries (16). It is a 340 kDa plasma glycoprotein that plays a key role in coagulation (17). Researches indicate that there is a positive correlation between FIB and both cardiovascular disease and hypertension (16, 18). Ghaediyan *et al.* (19) showed a bout submaximal endurance jugging at 70 to 75% maximal heart rate did not cause significant changes of FIB in young girls (19).While the present study shows a significant FIB increase in the middle aged male hypertensive patients following a bout submaximal endurance exercise. Maple Brown *et al.* indicated that FIB levels increase by age (20). Hence it is apparent that age, gender, physical fitness and physiological conditions are amongst factors influencing FIB levels. On the other hand the research results considering the plasma volume show that one bout submaximal endurance exercise resulted insignificant reduction in FIB in the middle aged male hypertensive patients. While Nascimento *et al.* (21) and Ahmadizad *et al.* (22) have indicated a significant increase in FIB levels following one bout exercise. The reason for this difference can be due to the differences between the type and intensity of exercise regardless of plasma volume changes. Hence, calculation of plasma volume changes for determining exact effect of exercise on FIB response is one of the cases to be taken seriously. Regarding the results of study, it is apparent that participating in one bout

submaximal endurance exercise not only does not present cardiovascular risk of increased FIB in hypertensive patients, but by stabilizing and decreasing FIB, can have positive cardiovascular effects in these patients. The research showed that one bout submaximal endurance exercise results in a significant increase in FVIII, aPTT, PLT and MPV which agrees with many previous studies. (14, 23). FVIII is an essential cofactor for IXa coagulation factor within intrinsic coagulation cascade (24). Intrinsic pathway is measured by aPTT (25). FVIII level is increased in coronary heart patients. It has been shown that FVIII reduction is associated with a reduction of cardiovascular risk factors and its increase is accompanied with high risk of vascular events (26). Also, it has been shown that PLT and MPV increase after exercise. Moreover, the results indicated one bout submaximal endurance exercise increased PC and ATIII.These two proteins are plasma soluble that can neutralize coagulation factors and also inhibit and control the coagulation system (27). Thus, it appears that there is a certain balance between the coagulation and anti coagulation systems in hypertensive patients after one bout submaximal endurance exercise. In fact, it can be stated that during submaximal endurance exercise anticoagulation system is responsible for protective role for cardiovascular patients against coagulation effects. As seen above, after one bout submaximal endurance exercise, changes in PT, PTA and INR were not significant. PT is the main factor for coagulation extrinsic pathway function. It appears that submaximal endurance exercise mostly via coagulation of intrinsic pathway and damaging endothelial cells causes increase in the formation of clot. It has also been shown that one bout submaximal endurance exercise causes a significant reduction in tPA, tPA/PAI-1 and an insignificant reduction in PAI-1. On the other hand, no significant change in D-D was observed. It appears that in hypertensive cardiovascular patients instead of coagulation and fibrinolysis balance, coagulation and anticoagulation balance is under attention. Significant increase in fibrinolysis has also been reported following high intensity exercise (28). Thus, it appears that exercise intensity is a determining factor in dynamics and functioning of coagulation, anticoagulation and fibrinolysis system. Therefore, to benefit from the effects of high intensity exercise and also to prevent the weakening effects of submaximal endurance exercise on fibrinolysis system, application of high intensity exercise in rehabilitation program of hypertensive cardiovascular patients is of special importance. Tinkham *et al.* recommended carrying out high intensity interval exercise at 80 to 95% of MHRR for the cardiovascular patients (29). It has been shown that high intensity exercise increases NO bioavailability. NO is decreased during endothelium dysfunction which could be caused by aging, BMI increase, smoking, hypertension and metabolic diseases (30). NO decrease is accompanied by decrease in vasodilation and increase in platelet adherence. Hence, high intensity interval exercise by increase in NO and reduction of platelets aggregation can bring improvements in vascular functions (30).

Conclusion

Taking part in submaximal endurance exercise resulted in improving the coagulation and anticoagulation systems in hypertensive cardiovascular patients. This occurred where dynamics of fibrinolysis system was reduced. It appears that during carrying out submaximal endurance exercise anticoagulation system neutralizes thrombotic effects of coagulation and the role of fibrinolysis is reduced. This is true while previous research findings indicate greater fibrinolysis system activity after a bout submaximal endurance exercise. Therefore, it can be concluded that the intensity of exercise is the determining factor in dynamics of hemostasis system. In general, it can be concluded that light, medium and high intensity endurance exercises are

recommended for dynamics of coagulation, anticoagulation and fibrinolysis systems in cardiovascular hypertensive patients. It appears that each of these exercise intensities will improve a part of the hemostasis system.

Ethical issues

The study was approved by the Research Ethics Committee of Sport Sciences Research Institute of Iran with the code IR.SSRI.REC.1397.203 and all participants signed a written informed consent regarding participation in the research project.

Authors' contributions

Authors equally contributed to the writing and revision of this paper.

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References

1. Joshi MD, Ayah R, Njau EK, Wanjiru R, Kayima JK, Njeru EK, et al. Prevalence of hypertension and associated cardiovascular risk factors in an urban slum in Nairobi, Kenya: a population-based survey. BMC public health. 2014; 14 (1): 1- 10.
2. Heyward VH, Gibson AL. Advanced fitness assessment and exercise prescription. (7th Ed). New Mexico, United Statesof America: Human Kinetics. 2014.
3. Galea V, Triantafyllidi H, Theodoridis T, Koutroumbi M, Christopoulou- Cokkinou V, Kremastinos D, et al. Long-term treatment with ramiprilfavourably modifies the haemostatic response to acute submaximal exercise in hypertensives. JRAAS. 2012; 14 (4): 322- 329.
4. Nadar S, Lip G. Hypertension. (2th Ed).Hampshire, United Kingdom: Oxford University Press. 2015.
5. Swati S, Pawaria S, Sheetal k. Effects of aerobic versus resistance training on blood pressure in hypertensive patients. J Anesth Crit Care. 2015; 3 (3): 1- 6.
6. Cardoso JRCG, Gomides RS, Queiroz ACC, Pinto LG, Lobo FS, Tinucci T, et al. Acute and chronic effects of aerobic and resistance exercise on ambulatory blood pressure. Clinics. 2010; 65 (3): 317- 325.
7. Cleroux J, Kouame N, Nadeau A, Coulombe D, Lacourciere Y. Aftereffects of exercise on regional and systemic hemodynamics in hypertension. Hypertension. 1992; 19 (2): 183- 191.
8. Monte SW, Jonathon WH, James RS. Cellular and molecular pathobiology of cardiovascular disease. San Diego, New York, Elsevier. 2014.
9. Sharief K.M, Hassan HA, Osman H, Ahmed AS. Ejection fraction rate for hypertensive patients using echocardiography. Med. Res. Chron. 2015; 2 (3): 322- 329.
10. Lakhdar N, Saad HB, DenguezliM, Zaouali M, Zbidi A, Tabka, et al. Effects of intense cycling training on plasma leptin and adiponectin and its relation to insulin resistance. ***Neuro Endocrinol Lett***. 2013; 34 (3): 229- 235.
11. Ahmadizad S, Moradi A, Nikookheslat S, EbrahiMI H, Rahbaran A, Connes PH. Effects of age on hemorheological responses to acute endurance exercise. ESCHM. 2011; 49 (1- 4): 165- 174.
12. Alis R, Sanchis- Gomar F, Primo- Carrau C, Lozano- Calve S, Dipalo M, Aloe R, et al. Hemoconcentration induced by exercise: Revisiting the dill and costill equation. Scand J Med Sci Sports. 2015; 25 (6): e630- 637.
13. Dill DB, Costill DL. Calculation of percentage changes in volumes of blood plasma and red cells in dehydration. J Appl Physiol. 1974; 37 (2): 247- 248.

14. Karampour S, Gaeini AA. The response of coagulation and anti-coagulant factors of elite athletes following acute resistance and high intensity interval exercises.J Sports Med Phys Fitness. 2017; 58 (1-2): 120- 126.
15. Zouhal H, Vincent S, Moussa E, Jacob C, Groussard C, Abderrahaman AB. Influence of training status on plasma volume variations and plasma lactate concentrations in response to supermaximal exercise. Bio Sport. 2007; 24 (4): 339- 356.
16. Eldour AAA, Khalafallah TO, Noja HM, Saad ESM, Elsayid M, Babker AMAAA. Fibrinogen levels in hypertensive and normotensive: A cross- sectional from el-obied city, sudan. JBM. 2016; 4: 28- 32.
17. Cortes- Canteli M, Zamolodchikov D, Jin Ahn HA, Strickland S, Norris EH. Fibrinogen and altered hemostasis in alzheimer's disease. J Alzheimers Dis. 2012; 32 (3): 599- 608.
18. Tabak O, Gelisgen R, Uzun H, Kalender B, Balci H, Curgunlu A. Hypertension and hemostatic/ fibrinolytic balance disorders. Clin Invest Med. 2009; 32 (6): E285- E292.
19. Ghaediyan S, Marefati H, Nabipur F, Naghizadeh MM. The effect of a moderate aerobic exercise on the blood coagulation markers in young non-athlete females. J Jahrom Univ Med Sci. 2012; 10 (2): 54- 60.
20. Maple- Brown LJ, Cunningham J, Nandi N, Hodge A, OdeaK. Fibrinogen and associated risk factors in a high-risk population: urban indigenous Australians, the DRUID study. Cardiovasc Diabetol. 2010; 9 (1): 69- 74.
21. Nascimento DC, Neto FR, Santana FS, Silva RAS, Santos- Neto LD, Balsamo S. The interactions between hemostasis and resistance training: a review. IJGM. 2012; 5: 249- 254.
22. Ahmadizad S, El-Sayed MS. The acute effects of resistance exercise on the main determinants of blood rheology. J Sports Sci. 2005; 23 (3): 243- 249.
23. Ribeiro J, Almeida DA, Ascensao A, Magalhaes J, Oliveira AR, Carlson J, et al. Hemostatic response to acute physical exercise in healthy adolescents. JSAMS. 2007; 10 (3): 164- 169.
24. Ikeda Y, Iwanaga S, Saito H, Katsuo S, Tanaka K, Davie EW. Recent advances in thrombosis and hemostasis. Japan: Springer. 2008.
25. Lichtin A, Bartholomew J. The coagulation consult: A case-based guide. New York, United Statesof America: Springer. 2014.
26. Tarsia J, Chang TR, Aysenne A, Boehme AK, Sartor AE, Albright KC, et al.Elevated plasma factor VIII in patients with ischemic stroke: Does it have any association with hypertensive heart disease? J Neurol Disord Stroke. 2013; 1 (3): 1027.
27. Shaz BH, Hillyer CD, Abrams CS, RoshalM. Transfusion medicine and hemostasis. clinical and laboratory aspects. (2nd Ed). New York, United States: Elsiver. 2013.
28. Kupchak BR, Creighton BC, Aristizabal JC, Dunn-Lewis C, Volk BM, Ballard KD, et al. Beneficial effects of habitual resistance exercise training of coagulation and fibrinolytic responses. Thromb Res. 2013; 31 (6): e227-e234.
29. Tinkham MH. Health promotion in cardiac rehabilitation patients through the use of a high- intensity interval training protocol. WJCD. 2014; 4: 493- 497.
30. Kolmos M, Krawcyk RS, Kruuse C. Effect of high- intensity training on endothelial function in patients with cardiovascular and cerebrovascular disease: A systematic review. SAGE Open Med. 2016; 4: 1- 13.