Original Research

Acute Effect of Probiotic Supplementation on Plasma Fibrinogen Levels of Young Soccer Players Following an Aerobic and Anaerobic Exercise

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Abstract

Introduction: The aim of this study was to evaluate the acute effect of probiotic supplementation on plasma fibrinogen levels of young soccer players following an aerobic and anaerobic exercise.

Method: Twenty-eight soccer players (Mean of age 20.68 ± 2.10 yrs., Height 1.73 ± 0.14 m, Weight 64.49 ± 7.39 kg and $Vo2_{max}$ 59.78 ± 5.30 ml/kg/min) were selected and randomly assigned into aerobic (n=14) and anaerobic (n=14) groups. Huff and RAST tests were used for aerobic and anaerobic training protocols, respectively. Probiotic (9¹⁰ units/g) and placebo capsules were used as double-blind method and counterbalance style in two stages (48 hours after the initial blood sampling and two weeks after the initial tests). Blood samples were taken in three stages before the supplementation, immediately after the tests, and in the last stage after two weeks immediately after the Huff & RAST tests. Data were analyzed by two-way mixed design or repeated measure for in-group and inter-group analysis at a significance level of P <0.05.

Result: Data analysis showed that aerobic and anaerobic exercise combined with probiotic supplementation had a non-significant effect on fibrinogen reduction in aerobic test ($p \ge 0.296$) and in anaerobic test ($p \ge 0.879$).

Conclusion: According to the findings of this study, it can be concluded that probiotic supplementation causes non-significant reduction of fibrinogen in response to an aerobic and anaerobic exercise session in soccer players. Besides, it is not likely to contribute to the rheology of blood and the reduction of blood clots in soccer players.

Key words: Probiotic, Exercise, Fibrinogen, Soccer

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Introduction

Now a day's soccer is one of the most popular sports in the international arena (Slimani, Znazen, Miarka, & Bragazzi, 2019). The aerobic basis of soccer is decisive for the athlete to face interspersed high intensity activities, including accelerations, running, changes of direction, jumping, lateral step, tackle, and technical skills specific to the game (Bangsbo, Nørregaard, & Thorsø, 1991). Soccer is one of the most sudden death team sports due to the nature of the aerobic and anaerobic exercises it involves (Maron et al., 1996).

Sudden death in athletes include hypertrophic cardiomyopathy (Maron, Nichols, Pickle, Wesley, & Mulvihill, 1984) and congenital anomalies of the coronary arteries (Cheitlin, De Castro, & McAllister, 1974), and disease affects the coronary arteries, atherosclerosis, thrombosis (Maron, Epstein, & Roberts, 1986). Sudden death in young athletes' events are rare, especially because the most common cause of sudden death in young athletes is sudden cardiac death (SCD) (Corrado, Basso, Rizzoli, Schiavon, & Thiene, 2003). There is strong evidence between physical activity and the reduction of mortality (Nocon et al., 2008). Regular physical activity may reduce the risk of SCD prevalence (Hull et al., 1994; Thompson et al., 2007), while irregular and intense physical activity may increase a risk of SCD (Siscovick, Weiss, Fletcher, & Lasky, 1984; Thompson et al., 2007). In three cases of SCD in athlete, early atherosclerosis coronary artery disease is the cause of sudden death in ages (Maron et al., 1996).

In 1998, the American Heart Association met to identify ways to help people who need primary prevention. One of the proposed strategies was a measurement of inflammatory indicators (Casas, Shah, Hingorani, Danesh, & Pepys, 2008; Geffken et al., 2001). According to these findings, some inflammatory indices are a predictor for cardiovascular disease. Increasing the plasma levels of inflammatory indicators can increase the risk of the plaque rupture. Some of these indicators include serum levels of amyloid, haptoglobin, white blood cells, albumin, sticky molecules, anti-trypsin, reaction protein C and fibrinogen (Hu, Meigs, Li, Rifai, & Manson, 2004).

Fibrinogen is the main protein for blood coagulation in plasma. The increase in fibrinogen plasma is a powerful predictor of a systemic heart and atherothrombosis disease (Taylor et al., 2021) and coronary artery disease (CAD) (Cicek, Bayil, Zer, Celik, & Geyikli, 2007; Diamond & Forrester, 1979; Isasi et al., 2000; Rana et al., 2011). Fibrinogen plays a key role in the coagulation, accumulation of platelets and fibrinolysis all of which are involved in thrombosis and excess coagulation (Isasi et al., 2000). Various factors affect inflammatory indicators, one of which is supplemental consumption Dabidi, Roushan, Gaeini, Ravasi, & Javadi, 2005).

Probiotics known as live microorganisms improve host performance by their influence over the intestines ("ICMR-DBT guidelines for evaluation of probiotics

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in food," 2011; Mazidi, Rezaie, Kengne, Mobarhan, & Ferns, 2016). Probiotics already are widely used in the form of products of fermented milk such as yogurt, or as a cultivation of dry ice (Ali, Velasquez, Hansen, Mohamed, & Bhathena, 2004; Schrezenmeir & de Vrese, 2001). The main probiotics bacteria related to dairy products include Lactobacillus acidophilus, Lactobacillus Casey and Bifid bacterium (Ali et al., 2004; Mazidi et al., 2016; Roberfroid, 2000; Schrezenmeir & de Vrese, 2001). In a study, consumption of yogurt containing Lactobacillus Casei prevented Pseudomonas Aeruginosa infection in young rats and reduced the risk of infection (Alvarez, Herrero, Bru, & Perdigon, 2001). Another study showed a significant improvement in lymphocytes, neutrophil, Immunoglobin A and C-reactive protein levels after high intensity interval training and a probiotic supplementation in young players (Jahani Qieqeshlaq, Abkar, & Heidari, 2016). Moreover, long-term probiotic dairy consumption (8 weeks) caused the reduction of LDL- cholesterol and increased fibrinogen (Agerholm-Larsen et al., 2000). Probiotic supplements can have a different effect on inflammatory indicators (Hatakka et al., 2003; Shoaei et al., 2015).

Regular training, even with the moderate levels of intensity, will result in enhanced aerobic capacity and less hemodynamic shear stress at a given workload. Moderate intensity training is indeed recommended for development of cardiovascular fitness, and CHD patients should avoid heavy exertion (Eriksson-Berg, Egberg, Eksborg, & Schenck-Gustafsson, 2002). Thus, the purpose of this study was to investigate the effect of probiotic supplemental consumption on plasma fibrinogen levels of young soccer players following a session of aerobic and anaerobic activity.

Methods and Materials

Research Design

A randomized controlled trial was carried out to determine whether probiotic supplemental consumption before a session of aerobic and anaerobic activity had an effect on serum levels of fibrinogen young soccer players. Participants in the counterbalance method were randomly divided into two groups of aerobic (n = 14) and anaerobic exercise (n = 14).

Participants and procedures

A semi-experimental study was conducted in 2017. For this aim, 28 soccer players with an age range of 18 to 24 years were selected from Jiroft city. A questionnaire was used for daily physical activity information. Besides, an informed consent form was taken from all participants. Furthermore, the purpose of the study was described to the patients.

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The intervention

The subjects performed 10 minutes of warm up, which was jagging and stretching exercises. Then, the subjects of the aerobic group performed the Rast test and the subjects of the anaerobic group performed the Haff test. At the end of the training session, 5 minutes of cool down was done. After two weeks of the second sampling, and with exchange for the supplement group with placebo group, all the early stages were repeated again and the third sampling was taken immediately after the Haff and Rast testing.

Biochemical Analyses

The initial sampling was taken forty-eight hours before the start of the protocol in fasting conditions. Then, the subjects (seven people from each group) consumed the probiotic supplement and placebo (one capsule daily after meals) for 48 hours. The second stage of blood sampling in fasting conditions was done immediately after Hoff and Rast tests. After two weeks, the third stage of blood sampling in fasting conditions was repeated only with changing the supplement and placebo groups immediately after the Hoff and Rast tests. The samples were analyzed with a fibrinogen kit. Evaluation of fibrinogen plasma levels was performed using the Dia-FIB kit with specifications (DIAGON Kft 1047 Budapest, Baross u, 48-52, HUNGARY).

Statistical Analysis

Mean and standard deviation were used to describe quantitative variables. Shapiro-Wilk test of normality, paired-samples t-test and statistical analysis were carried out using SPSS software version 24. The significance level was considered 0.05 for all tests.

Findings

In total, 28 soccer players (with the Mean \pm SD age 20.65 \pm 2.10 years, Height 1.73 \pm 0.14 meters, Body Weight 64.49 \pm 7.39 Kg and Vo2_{max} 59.78 \pm 5.30 ml.kg.min) were selected and distributed in two aerobic and aerobic groups. The findings indicated a 48-hour period of probiotic supplementation following a session of aerobic and anaerobic activity, the amount of Fibrinogen in the aerobic group (Figure 1) and the amount of Fibrinogen in anaerobic group (Figure 2) were non-significant change (P \geq 0.05).

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 Table 1- The results of analysis, probiotic supplementation on plasma Fibrinogen following a session of aerobic activity

Compare Aerobic Group	Mean	Df	t	р
Before- supplements	2.49-2.32	13	5.59	0.001
Before -placebo	2.49-2.38	13	1.81	0.093
Differences of Supplements - placebo	-0.06	13	-1.08	0.296



Figure 1- Comparing of difference, the placebo with the supplement in aerobic group

 Table 2- the results of analysis, probiotic supplementation on plasma Fibrinogen following a session of anaerobic activity

Comparison of anaerobic group	Mean	Df	t	р
Before- supplements	2.53-2.47	13	2.49	0.02
Before –placebo	2.53-2.48	13	0.64	0.53
Differences of Supplements - placebo	-0.01	13	-0.15	0.879



Anaerobic group

Figure 2- Comparing of difference, the placebo with the supplement in anaerobic group

Discussion

The results of the present study showed that an aerobic exercise session after using a probiotic supplement hasn't non-significant change of fibrinogen plasma levels in young players.

The results of Bizheh et al. and Ghanbari et al. are consistent with those of the present study (Bizheh & Jaafari, 2012; Ghanbari-Niaki, Behzad Khameslo, & Tayebi, 2013). However, the findings of Stratton et al. and Rshidelmir et al. are inconsistent with the present study's findings (A, Rashidlamir et al., 2011; Stratton et al., 1991).

In a study, Bizheh and Jaafari (2012) reported that long-term aerobic exercise increased aerobic capacity, red blood cell distribution and white blood cell count, and decreased body mass index and uric acid, but no change was observed in fibrinogen levels.

Another study showed that 4 weeks of aerobic training had no effect on plasma fibrinogen levels. Besides, the significant differences in body composition parameters were not observed between the experimental and control groups. However, total cholesterol levels (TC) and LDL-C and blood viscosity were significantly lowered in the experimental group compared to the control group (Ghanbari-Niaki et al., 2013).

A study done by Parsian (2013) aimed to compare the effect of endurance and resistance training on plasma fibrinogen in the non-athlete's young men. The

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results showed that plasma fibrinogen level reduced in endurance training compared with resistance training on the non-athlete young men

The study of Stratton et al. revealed that fibrinogen levels decreased significantly after 6 months' endurance training. C-reactive protein during testing has not changed (Stratton et al., 1991).

Regular aerobic activity by reducing catecholamine's stimulations increased blood flow in the muscles, and the increasing of blood volume leads to decrease fibrinogen levels (Furukawa, Kazuma, Kojima, & Kusukawa, 2008). Since fibrinogen changes depend on differences of the volume of plasma, therefore, the lack of fibrinogen change may be caused by the lack of plasma volume changes within the groups (Ahmadizad & El-Sayed, 2005). The similar results have shown that different training protocols have no significant effect on plasma Fibrinogen. However, some researchers have reported conflicting results. (Rankinen, Väisänen, Penttilä, & Rauramaa, 1995). It is likely that the changes of fibrinogen have depended to the type and severity of exercise and physical activity regardless of what kind of subjects is applied (Patelis, Karaolanis, Kouvelos, Hart, & Metheiken, 2016).

According to the results of previous studies, the age and sex of subjects and the type and duration and intensity of the exercise and the number of the subjects are effective factors on fibrinogen in response to aerobic exercise.

The results of the present study showed that acute anaerobic exercise after using a probiotic supplement hasn't significant change of plasma fibrinogen levels in young players. Some studies showed that acute exercise causes temporary decrease in blood coagulation and platelet function that the extent of these changes are significantly less in well-trained athletes than non-athletes. Therefore, a study evaluated the effect of anaerobic exercise on clotting factors in active women. The results showed which increases fibrinogen and increases platelets after testing RAST. The results revealed that Anaerobic power exercises causes the increase in platelets and fibrinogen levels in active women (Nazar Ali, 2011).

The fibrinogen is an important factor in the coagulopathy process and the primary determining factor of viscosity and blood flow. High fibrinogen levels increase the risk of cardiovascular disease (Kamath & Lip, 2003). Fibrinogen changes depend on the volume of blood plasma (Kamath & Lip, 2003). Therefore, some researchers showed the decreased and increased fibrinogen by using various training programs. It is said that these changes are due to the intensity of the exercises, type of activity, the amount of preparation, the duration of the exercise, the number of subjects, and taking supplements (Parsian, 2013).

The findings of this study showed that taking a probiotic supplement alone would not reduce of the plasma fibrinogen levels in young soccer players. In previous

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studies, the effect of probiotic use was applied. A study investigated the impact of 8 weeks of consumption of dairy products on cardiovascular disease risk factors. The results indicated that the dense cholesterol reduced and fibrinogen increased in overweight people with 450 ml consumption per day for 8 weeks (Agerholm-Larsen et al., 2000). Possible reason for the difference with the present study can be noted as the presence of non-athlete participants, a mixed sample of two genders, and that women were 2.5 times more than men were, and that also some were overweight and without doing aerobics and anaerobic tests as well as yogurt containing probiotics have been used.

A study entitled 'the influence of 8 weeks of intermittent exercises, with probiotic yoghurt consumption on immune cells, IGA and CRP in young soccer players' was conducted. So after the training program in the experimental group, the rate of lymphocyte, neutrophil, Immunoglobin A and C-reactive protein of rest, was a significant increase, and there was no evidence of any URTI. Exercise and consumption of probiotic supplements promote the performance of aerobic power, the immune system factors and reduce the risk of respiratory tract infections in the ST Group. As a result, it is recommended daily use in athletes who performed extreme physical exercises (Jahani Ghaeh Ghashlagh, Abcar, & Haydari, 2016). Another study showed that probiotic yogurt consumption in 30 girl swimmers has caused to decrease certain symptoms of respiratory infections and reduce the duration of some of the symptoms such as wheezing and earache and $VO2_{Max}$; However, a 1000 m record of front crawl and a reduction of symptoms of digestive problems in athletes who consume this yoghurt type is not statistically significant (Salarkia, Ghadamli, Zaeri, & Sabaghian Rad, 2013). In the above study, the advantages of probiotics for swimming athletes, reduction of respiratory infections and ear pain and improvements in maximum rate of oxygen consumption are viewed that probably these benefits will be for the present study.

Conclusion

Based on the results of the present study, a 48-hour consumption of probiotics alone caused a non-significant decrease in soccer players. Probably it can't prevent thrombosis and blood rheology in soccer players.

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References

- 1. A, Rashidlamir, A, Hashemi Javaheri, & M, Jaafari. (2011). The effect of regular aerobic training with weight loss on concentrations of fibrinogen and resistin in healthy and overweight men. *Tehran University Medical Journal*, 68(12), 710-717.
- Agerholm-Larsen, L., Raben, A., Haulrik, N., Hansen, A. S., Manders, M., & Astrup, A. (2000). Effect of 8 week intake of probiotic milk products on risk factors for cardiovascular diseases. *Eur J Clin Nutr*, 54(4), 288-297. doi: 10.1038/sj.ejcn.1600937
- Ahmadizad, S., & El-Sayed, M. S. (2005). The acute effects of resistance exercise on the main determinants of blood rheology. J Sports Sci, 23(3), 243-249. doi: 10.1080/02640410410001730151
- Ali, A. A., Velasquez, M. T., Hansen, C. T., Mohamed, A. I., & Bhathena, S. J. (2004). Effects of soybean isoflavones, probiotics, and their interactions on lipid metabolism and endocrine system in an animal model of obesity and diabetes. *J Nutr Biochem*, 15(10), 583-590. doi: 10.1016/j.jnutbio.2004.04.005
- Alvarez, S., Herrero, C., Bru, E., & Perdigon, G. (2001). Effect of Lactobacillus casei and yogurt administration on prevention of Pseudomonas aeruginosa infection in young mice. *J Food Prot*, 64(11), 1768-1774. doi: 10.4315/0362-028x-64.11.1768
- 6. Bangsbo, J., Nørregaard, L., & Thorsø, F. (1991). Activity profile of competition soccer. *Can J Sport Sci*, *16*(2), 110-116.
- 7. BIZHEH, N., & JAAFARI, M. (2012). EFFECTS OF REGULAR AEROBIC EXERCISE ON CARDIORESPIRATORY FITNESS AND LEVELS OF FIBRINOGEN, FIBRIN D-DIMER AND URIC ACID IN HEALTHY AND INACTIVE MIDDLE AGED MEN. JOURNAL OF SHAHREKORD UNIVERSITY OF MEDICAL SCIENCES, 14(3), -.
- Casas, J. P., Shah, T., Hingorani, A. D., Danesh, J., & Pepys, M. B. (2008). C-reactive protein and coronary heart disease: a critical review. *J Intern Med*, 264(4), 295-314. doi: 10.1111/j.1365-2796.2008.02015.x
- Cheitlin, M. D., De Castro, C. M., & McAllister, H. A. (1974). Sudden death as a complication of anomalous left coronary origin from the anterior sinus of Valsalva, A not-so-minor congenital anomaly. *Circulation*, 50(4), 780-787. doi: 10.1161/01.cir.50.4.780
- Cicek, H., Bayil, S., Zer, Y., Celik, A., & Geyikli, I. (2007). Comparison of Lipoprotein(a) levels between elderly and middle-aged men with coronary artery disease. *Ann N Y Acad Sci*, 1100, 179-184. doi: 10.1196/annals.1395.016
- Corrado, D., Basso, C., Rizzoli, G., Schiavon, M., & Thiene, G. (2003). Does sports activity enhance the risk of sudden death in adolescents and young adults? *J Am Coll Cardiol*, 42(11), 1959-1963. doi: 10.1016/j.jacc.2003.03.002
- 12. DABIDI ROUSHAN, V.A., GAEINI, A.A., RAVASI, A.A., & JAVADI, EBRAHIM. (2005). THE EFFECT OF THE CONTINUOUS TRAINING OF CRP OF STRAIN WISTAR 14848 RATS. *OLYMPIC*, *13*(2 (SERIAL 30)), -.
- Diamond, G. A., & Forrester, J. S. (1979). Analysis of probability as an aid in the clinical diagnosis of coronary-artery disease. *N Engl J Med*, 300(24), 1350-1358. doi: 10.1056/nejm197906143002402

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- 14. Eriksson-Berg, Margita, Egberg, Nils, Eksborg, Staffan, & Schenck-Gustafsson, Karin. (2002). Retained fibrinolytic response and no coagulation activation after acute physical exercise in middle-aged women with previous myocardial infarction. *Thrombosis research*, *105*(6), 481-486.
- Furukawa, F., Kazuma, K., Kojima, M., & Kusukawa, R. (2008). Effects of an offsite walking program on fibrinogen and exercise energy expenditure in women. *Asian Nurs Res (Korean Soc Nurs Sci)*, 2(1), 35-45. doi: 10.1016/s1976-1317(08)60027-4
- Geffken, D. F., Cushman, M., Burke, G. L., Polak, J. F., Sakkinen, P. A., & Tracy, R. P. (2001). Association between physical activity and markers of inflammation in a healthy elderly population. *Am J Epidemiol*, 153(3), 242-250. doi: 10.1093/aje/153.3.242
- Ghanbari-Niaki, Abbass, Behzad Khameslo, Mostafa, & Tayebi, Seyed Morteza. (2013). Effect of Pyramidal Training on Plasma Lipid Profile and Fibrinogen, and Blood Viscosity of Untrained Young Men. *Annals of Applied Sport Science*, 1(3), 47-56.
- Hatakka, K., Martio, J., Korpela, M., Herranen, M., Poussa, T., Laasanen, T., . . . Korpela, R. (2003). Effects of probiotic therapy on the activity and activation of mild rheumatoid arthritis--a pilot study. *Scand J Rheumatol*, 32(4), 211-215. doi: 10.1080/03009740310003695
- 19. Hu, F. B., Meigs, J. B., Li, T. Y., Rifai, N., & Manson, J. E. (2004). Inflammatory markers and risk of developing type 2 diabetes in women. *Diabetes*, *53*(3), 693-700. doi: 10.2337/diabetes.53.3.693
- Hull, S. S., Jr., Vanoli, E., Adamson, P. B., Verrier, R. L., Foreman, R. D., & Schwartz, P. J. (1994). Exercise training confers anticipatory protection from sudden death during acute myocardial ischemia. *Circulation*, 89(2), 548-552. doi: 10.1161/01.cir.89.2.548
- 21. ICMR-DBT guidelines for evaluation of probiotics in food. (2011). *Indian J Med Res*, 134(1), 22-25.
- Isasi, C. R., Starc, T. J., Tracy, R. P., Deckelbaum, R., Berglund, L., & Shea, S. (2000). Inverse association of physical fitness with plasma fibrinogen level in children: the Columbia University BioMarkers Study. *Am J Epidemiol*, 152(3), 212-218. doi: 10.1093/aje/152.3.212
- Jahani Ghaeh Ghashlagh, Gholamreza, Abcar, Alireza, & Haydari, Hossain. (2016). The Effect of High-Intensity Intermittent Training (HIIT) and Consumption of Probiotic Supplement on Immune Cells, C – reactive Protein, and IgA in Young Football Player. *Qom Univ Med Sci J*, 10(8), 36-46.
- 24. JAHANI QIEQESHLAQ, GHOLAM REZA, ABKAR, ALI REZA, & HEIDARI, HOOSSEIN. (2016). THE EFFECT OF HIGH-INTENSITY INTERMITTENT TRAINING (HIIT) AND CONSUMPTION OF PROBIOTIC SUPPLEMENT ON IMMUNE CELLS, C - REACTIVE PROTEIN, AND IGA IN YOUNG FOOTBALL PLAYER. *OOM UNIVERSITY OF MEDICAL SCIENCES JOURNAL*, 10(8), -.
- 25. Kamath, S., & Lip, G. Y. (2003). Fibrinogen: biochemistry, epidemiology and determinants. *QJM*, *96*(10), 711-729. doi: 10.1093/qjmed/hcg129
- Maron, B. J., Epstein, S. E., & Roberts, W. C. (1986). Causes of sudden death in competitive athletes. J Am Coll Cardiol, 7(1), 204-214. doi: 10.1016/s0735-1097(86)80283-2

- Maron, B. J., Nichols, P. F., 3rd, Pickle, L. W., Wesley, Y. E., & Mulvihill, J. J. (1984). Patterns of inheritance in hypertrophic cardiomyopathy: assessment by M-mode and two-dimensional echocardiography. *Am J Cardiol*, 53(8), 1087-1094. doi: 10.1016/0002-9149(84)90643-x
- Maron, B. J., Shirani, J., Poliac, L. C., Mathenge, R., Roberts, W. C., & Mueller, F. O. (1996). Sudden death in young competitive athletes. Clinical, demographic, and pathological profiles. *JAMA*, 276(3), 199-204.
- 29. Mazidi, M., Rezaie, P., Kengne, A. P., Mobarhan, M. G., & Ferns, G. A. (2016). Gut microbiome and metabolic syndrome. *Diabetes Metab Syndr*, 10(2 Suppl 1), S150-157. doi: 10.1016/j.dsx.2016.01.024
- Nocon, M., Hiemann, T., Müller-Riemenschneider, F., Thalau, F., Roll, S., & Willich, S. N. (2008). Association of physical activity with all-cause and cardiovascular mortality: a systematic review and meta-analysis. *Eur J Cardiovasc Prev Rehabil*, 15(3), 239-246. doi: 10.1097/HJR.0b013e3282f55e09
- Parsian H, Zafari A. (2013). The effect of different types of exercise on plasma fibrinogen levels in non-athlete males. *European Journal of Experimental Biology*, 3(3), 246-230.
- 32. Parvaneh Nazar Ali, Parichehr Hanachi. (2011). To investigate the fibrinogen and some of coagulation factors in anaerobic exercise training women. *World Applied Sciences Journal*, 12(1).
- Patelis, N., Karaolanis, G., Kouvelos, G. N., Hart, C., & Metheiken, S. (2016). The effect of exercise on coagulation and fibrinolysis factors in patients with peripheral arterial disease. *Exp Biol Med (Maywood)*, 241(15), 1699-1707. doi: 10.1177/1535370216660215
- 34. Rana, J. S., Arsenault, B. J., Després, J. P., Côté, M., Talmud, P. J., Ninio, E., ... Boekholdt, S. M. (2011). Inflammatory biomarkers, physical activity, waist circumference, and risk of future coronary heart disease in healthy men and women. *Eur Heart J*, 32(3), 336-344. doi: 10.1093/eurheartj/ehp010
- 35. Rankinen, T., Väisänen, S., Penttilä, I., & Rauramaa, R. (1995). Acute dynamic exercise increases fibrinolytic activity. *Thromb Haemost*, 73(2), 281-286.
- Roberfroid, M. B. (2000). Prebiotics and probiotics: are they functional foods? *Am J Clin Nutr*, 71(6 Suppl), 1682S-1687S; discussion 1688S-1690S. doi: 10.1093/ajcn/71.6.1682S
- 37. Salarkia, Nahid, Ghadamli, Leili, Zaeri, Farid, & Sabaghian Rad, Leila. (2013). Effects of probiotic yogurt on performance, respiratory and digestive systems of young adult female endurance swimmers: a randomized controlled trial. *Medical Journal of the Islamic Republic Of Iran*, 27(3), 141-146.
- Schrezenmeir, J., & de Vrese, M. (2001). Probiotics, prebiotics, and synbiotics-approaching a definition. Am J Clin Nutr, 73(2 Suppl), 361S-364S. doi: 10.1093/ajcn/73.2.361s
- Shoaei, T., Heidari-Beni, M., Tehrani, H. G., Feizi, A., Esmaillzadeh, A., & Askari, G. (2015). Effects of Probiotic Supplementation on Pancreatic β-cell Function and Creactive Protein in Women with Polycystic Ovary Syndrome: A Randomized Doubleblind Placebo-controlled Clinical Trial. *Int J Prev Med*, *6*, 27. doi: 10.4103/2008-7802.153866

- Siscovick, D. S., Weiss, N. S., Fletcher, R. H., & Lasky, T. (1984). The incidence of primary cardiac arrest during vigorous exercise. *N Engl J Med*, 311(14), 874-877. doi: 10.1056/nejm198410043111402
- Slimani, M., Znazen, H., Miarka, B., & Bragazzi, N. L. (2019). Maximum Oxygen Uptake of Male Soccer Players According to their Competitive Level, Playing Position and Age Group: Implication from a Network Meta-Analysis. *J Hum Kinet*, 66, 233-245. doi: 10.2478/hukin-2018-0060
- Stratton, J. R., Chandler, W. L., Schwartz, R. S., Cerqueira, M. D., Levy, W. C., Kahn, S. E., . . . Abrass, I. B. (1991). Effects of physical conditioning on fibrinolytic variables and fibrinogen in young and old healthy adults. *Circulation*, 83(5), 1692-1697. doi: 10.1161/01.cir.83.5.1692
- 43. Taylor, A. G., Ignaszewski, A. I., Bredin, S. S. D., Hill, J. S., Shellington, E. M., & Warburton, D. E. R. (2021). High Intensity Interval Training Leads to Similar Inflammatory Activation as Seen With Traditional Training in Chronic Heart Failure. *Front Cardiovasc Med*, 8, 752531. doi: 10.3389/fcvm.2021.752531
- 44. Thompson, P. D., Franklin, B. A., Balady, G. J., Blair, S. N., Corrado, D., Estes, N. A., 3rd, . . . Costa, F. (2007). Exercise and acute cardiovascular events placing the risks into perspective: a scientific statement from the American Heart Association Council on Nutrition, Physical Activity, and Metabolism and the Council on Clinical Cardiology. *Circulation*, 115(17), 2358-2368. doi: 10.1161/circulationaha.107.181485