Iranian Heart Journal; 2021; 22 (3)

Original Article

Serum Concentrations of Pentraxin3 in Patients With Acute Coronary Syndrome: A Case-Control Study

Mohammad Shojaei[1], MD; Karamatollah Rahmanian[1*], MD; Kavoos Solhjoo[1], PhD; Abdolreza Sotoodeh Jahromi[1], MS

ABSTRACT

Background: Cardiovascular diseases are the first and the most common cause of death in Iran. Pentraxin3 (PTX3) is an inflammatory marker that increases in patients with acute myocardial infarction. This study aimed to compare the PTX3 level among patients with acute coronary syndrome (ACS).

Methods: The present study enrolled 130 patients with ACS and 82 subjects as the control group. Within 12 hours of the onset of chest pain, 5 mL of blood was obtained from the antecubital vein. Then, serum was separated by centrifugation and stored at –70 °C until the measurement of PTX3. The level of PTX3 was measured using an enzyme-linked immunosorbent assay kit. Data were recorded and analyzed by SPSS version 16.0. A *P*-value of less than 0.05 was considered statistically significant.

Results: The distribution of age, sex, diabetes mellitus, hypertension, and hyperlipidemia was similar in both the ACS and control groups, but it was not similar for smoking. Serum PTX3 was significantly higher in the ACS group. The serum PTX3 level was higher in the subgroup with ST-segment elevation myocardial infarction than in the subgroups with unstable angina pectoris, stable angina pectoris, and noncardiac diseases. Additionally, patients with unstable angina pectoris had higher PTX3 than those with stable angina pectoris and noncardiac diseases.

Conclusions: Our results suggest that PTX3 may be released by systemic inflammation at the very onset of acute myocardial infarction. ***(Iranian Heart Journal 2021; 22(3): 64-73)***

KEYWORDS: Myocardial Infarction, STEMI, NSTEMI, Angina, Pentraxin3

[1] Research Centre for Non-Communicable Diseases, Medical School. Jahrom University of Medical Sciences, Jahrom, IR Iran.

***Corresponding Author**: Karamatollah Rahmanian, MD; Research Centre for Non-Communicable Diseases, Medical School. Jahrom University of Medical Sciences, Jahrom, IR Iran.
Email: rahmaniank47@yahoo.com **Tel:** +989173155578

Received: April 19, 2020 **Accepted:** August 18, 2020

Cardiovascular diseases, particularly coronary artery disease (CAD), are the most common cause of death in the world and Iran. [1, 2] This problem causes a great deal of disability and imposes a high cost on the health system. It is well documented that atherosclerotic progression is attributable to the chronic inflammatory process [3] because of various inflammatory mediators involved in atherosclerosis. [4-6] Several inflammatory mediators are the potential markers for the diagnostic and predictive factors of cardiovascular diseases such as myocardial infarction (MI), unstable angina pectoris (UAP), and cardiac failure. [7-9] Pentraxin3 (PTX3) is a sensitive and independent inflammatory marker [10] that is a glycoprotein belonging to the long pentraxin family. PTX3 is produced by macrophages and vascular endothelial cells [11, 12] in response to inflammatory incitements, and they specifically exist at high levels in cardiac muscles. [13-15] Thus, PTX3 is especially found in vascular and inflammatory cells, and it exists in human atherosclerotic lesions. [16] High circulating PTX3 levels are observed in acute coronary syndrome (ACS). [17] Matsuura et al [18] suggested that PTX3 levels in coronary artery plaques were higher among patients with UAP than in patients with stable angina pectoris (SAP). Several studies have suggested that PTX3 is prominent in patients with UAP [19, 20] and acute MI. [21-23] Serum PTX3 levels are greater in both non–ST-segment elevation myocardial infarction (NSTEMI) and ST-segment-elevation myocardial infarction (STEMI) than in patients admitted to the hospital without any heart disease. [24] Conversely, although the serum PTX3 level is associated with cardiovascular and all-cause mortality, it is not related to angina or acute MI. [25] Inoue et al, [26] in their review article, suggested that serum PTX3 was a useful marker and recommended that the use of it as a cardiovascular disease marker needed further research.

In Jahrom, near one-fifth of women and men (21.1%) aged 30 years and over had angina according to the Rose questionnaire. [27] Additionally, at least 50% of the subjects had 1 or 2 risk factors for CAD (50.9% in women and 51.1% in men). [28] Nonetheless, one of the most important health problems relating to ischemic heart disease is hypertension. [29]

In the current study, we sought to determine the serum level of PTX3 among patients with ACS and compare this level with that in a control group. We also compared the PTX3 level between 3 subgroups of ACS and 2 subgroups of the control group (totally, 5 subgroups).

METHODS

The current case-control study recruited patients with a diagnosis of ACS admitted to the cardiac care unit (CCU) of 2 hospitals (Motahari and Peymanieh) in the Iranian city of Jahrom. The control comprised SAP patients and individuals without cardiac diseases. In this analytical study, 212 subjects, consisting of 130 ACS subjects (54 STEMI, 26 NSTEMI, and 50 UAP cases) and 82 controls (42 SAP and 40 noncardiac diseases [NCD] cases) were included. Patients with typical chest pain who came to the hospitals within 12 hours after the onset of chest pain and were admitted to the CCU were enrolled in the study. The diagnosis of acute MI was established according to the guidelines of the American College of Cardiology/American Heart Association (ACC/AHA). NSTEMI was defined as typical chest pain lasting for more than 30 minutes and a depressed ST-segment on electrocardiography (ECG) associated with elevated cardiac enzymes. STEMI was defined as typical chest pain lasting for more than 30 minutes and an elevated ST-segment in at least 2 leads on ECG associated with

cardiac enzyme elevation. Angina pectoris was diagnosed based on the criteria introduced by the World Health Organization. UAP was defined as enhancing chest pain with a new increase in frequency and duration lasting for more than 15 minutes or occurring at rest or throughout slight exertion. These symptoms were joined with ST-segment depression and any changes in the biochemical indicators of the necrosis of the myocardium, including creatine phosphokinase and troponin T. Patients with typical angina triggered by exertion or emotional stress and associated with ECG change were considered to have SAP. Subjects who were without a history of CAD, autoimmune disorders, and renal and hepatic diseases were defined as NCD. The diagnosis of diseases (NSTEMI, STEMI, UAP, and SAP) was approved by cardiologists.

Patients with a history of hepatic cirrhosis, chronic renal failure (serum creatinine >2.0 mg/dL), autoimmune disorders, neoplastic diseases, inflammatory disorders, cardiac surgery during the preceding 3 months, and the existence of left bundle branch block on ECG were excluded from the study.

In each case, 5 mL of blood was obtained from the antecubital vein within 12 hours of the onset of chest pain, and the blood was drawn into ethylenediaminetetraacetic acid (EDTA) tubes on ice. Afterward, serum was separated by centrifugation and stored at –70 °C until the measurement of the PTX3 level. PTX3 was measured using an enzyme-linked immunosorbent assay (ELISA) kit (CAT.NO: E1938Hu, Shanghai Crystal Day Biotech Co, Ltd, China, http://www.bt-laboratory.com). The lower limit of PTX3 detection was 0.1 ng/mL as described in the manufacturer's order.

Factors such as age, sex, and a history of chronic and inflammatory diseases were recorded in a questionnaire.

Informed written consent was obtained from all the participants, and the Ethics Committee of Jahrom University of Medical Sciences, Iran approved this study (ethical code: IR.SBMU.RAM.REC 13940229). The study procedure conforms to the ethical guidelines of the 1975 Declaration of Helsinki.

All data were recorded and analyzed using Statistical Package for the Social Sciences (SPSS), version 16.0 (SPSS Inc, Chicago, IL, USA). The Kolmogorov–Smirnov test was used to check normality. Categorical and continuous variables were reported as the percentage and the mean ± the standard deviation (SD), respectively. Firstly, we compared the data distribution of each studied variable such as PTX3, age, sex, hypertension, diabetes mellitus, hyperlipidemia, and smoking between the ACS and control groups. Then we compared the data distribution of the studied variables between the 5 study subgroups. To compare categorical (qualitative) and quantitative variables between the ACS patients and the control group, we used the χ^2 test and the Student *t* test or the Mann–Whitney *U* test. To compare categorical and continuous variables between the 5 study subgroups, we utilized the χ^2 test and the one-way ANOVA or Kruskal–Wallis test. A *P*-value of less than 0.05 was considered statistically significant.

RESULTS

The clinical characteristics and PTX3 levels of the study population are presented in Table 1. According to the χ^2 test, classical characteristics such as sex, age, hypertension, diabetes mellitus, and hyperlipidemia were not statistically significantly different between the ACS patients and the control subjects, whereas the difference in smoking was statistically

significant between the ACS and control groups (P <0.05). The most common disease in the ACS and control groups was hypertension (43.8% and 34.1%, respectively).

The Mann–Whitney U test showed that circulating PTX3 levels were significantly higher in the ACS patients than in the controls (P <0.001).

As is shown in Table 2, according to the χ^2 test, the distributions of sex, hypertension, diabetes mellitus, hyperlipidemia, and tobacco use were significantly different within the 5 study subgroups (ie, STEMI, NSTEMI, UAP, SAP, and NCD); nevertheless, the age distribution was not significantly different between the subgroups. There were more men in the STEMI and NSTEMI subgroups than in the other subgroups (P =0.035). The prevalence of hypertension was significantly lower in the NCD subgroup (P <0.001). Hypertension was the most common (56.0%) among the UAP patients. The prevalence of diabetes mellitus (P <0.018) and hyperlipidemia (P <0.001) was significantly lower in the NCD subgroup than in the other 4 subgroups. Diabetes mellitus (35.7%) and hyperlipidemia (50.0%) were the most common in the SAP patients. The rate of smoking was lower in the NCD subjects (12.5%) and the SAP patients (14.3%) than in the other 3 subgroups (P <0.001), with the prevalence of smokers being higher in the STEMI patients (50.0%).

According to the results of the Kruskal–Wallis test, the serum concentration of PTX3 was significantly different between the 5 study subgroups (P <0.001). However, based on the Man–Whitney U test, the serum PTX3 level was higher in the STEMI patients than in the UAP patients (P =0.040), the SAP patients (P =0.010), and the NCD individuals (P <0.001) but was not different from the level in the NSTEMI patients (P =0.052). Further, the level of serum PTX3 in the patients with UAP was significantly higher (1.23 ng/mL) than that of the NCD subjects (P =0.031).

Table 3 demonstrates the differences in the serum concentration of PTX3 between the study groups based on sex. According to the Mann–Whitney U test, in the ACS patients, both men (P =0.006) and women (P =0.012) had higher PTX3 levels than the control subjects. PTX3 was, however, higher in the men than in the women in the ACS group (P =0.014), while the difference was not statistically significant between the men and women in the control group.

When the subjects were divided into 5 subgroups and the Mann–Whitney U test was applied, the serum PTX3 level was similar in both men and women (P >0.05). According to the Kruskal–Wallis test, the concentration of PTX3 in the men was not significantly different between the 5 study subgroups (P =0.068), while in the women, this level was significantly different between the 5 study subgroups (P =0.009).

According to the Mann–Whitney U test, in the men, the STEMI patients had higher PTX3 levels than the NCD individuals (P =0.005. Therefore, in the women, the STEMI patients had higher PTX3 levels than the UAP patients (P =0.043), the SAP patients (P =0.027), and the NCD subjects (P <0.001). Moreover, the serum PTX3 level in the UAP patients was more than that in the NCD individuals (P =0.035).

Table 1. Percentage or the mean of the variables in the patients with acute coronary syndrome and the control group

Groups / Variables	Acute Coronary Syndrome (n= 130)		Control (n= 82)		*P*-value
	Number	Percentage	Number	Percentage	
Female	44	33.8	37	45.1	0.100*
Hypertension	57	43.8	28	34.1	0.160*
Diabetes mellitus	29	22.3	17	20.7	0.786*
Hyperlipidemia	40	30.8	21	25.6	0.419*
Smoking	47	36.2	11	13.4	< 0.001*
	Mean	Standard Deviation	Mean	Standard Deviation	
Age, y	58.7	12.0	59.8	10.1	0.491**
PTX3, ng/mL	8.15	4.52	6.49	2.02	< 0.001***

* Comparison of 2 groups using the χ^2 test
** Comparison of 2 groups using the Student t test.
** Comparison of 2 groups using the Mann–Whitney *U* test
PTX3, Pentraxin3

Table 2. Comparison of the percentage or the mean of the variables between the 5 study groups

Groups / Variables	STEMI (n =54)	NSTEMI (n =26)	UAP (n =50)	SAP (n =42)	NCD (n =40)	*P*-value
Female, %	12 (22.2)	8 (30.8)	24 (48.0)	20 (47.6)	17 (42.5)	0.035*
HTN, %	21 (38.9)	8 (30.8)	28 (56.0)	23 (54.8)	5 (12.5)	< 0.001*
DM, %	11 (20.4)	7 (26.9)	11 (22.0)	15 (35.7)	2 (5.0)	0.018*
HLP, %	13 (24.1)	9 (34.6)	18 (36.0)	21 (50.0)	0 (0.0)	< 0.001*
Smoking, %	27 (50.0)	8 (30.8)	12 (24.0)	6 (14.3)	5 (12.5)	< 0.001*
Age, y	59.8 ± 12.6	56.5 ± 12.1	58.8 ± 11.3	60.5 ± 9.9	59.1 ± 10.4	0.681**
PTX3, ng/mL	9.08 ± 6.16	7.34 ± 1.63	7.57 ± 3.12	7.09 ± 2.07	5.86 ± 1.78	< 0.001***

ACS, Acute coronary syndrome; HLP, Hyperlipidemia; DM, Diabetes mellitus; HTN, Hypertension; NCD, Noncardiac disease; NSTEMI, Non–ST-segment elevation myocardial infarction; STEMI, ST-segment elevation myocardial infarction; SAP, Stable angina pectoris; UAP, Unstable angina pectoris; PTX3, Pentraxin3

* Comparison of 5 groups using the χ^2 test
** Comparison of 5 groups using the one-way ANOVA test
*** Comparison of 5 groups using the Kruskal–Wallis test

Table 3. The mean (±SD) serum concentration of pentraxin3 (ng/mL) by sex in the study groups

Parameters	Male	Female	*P*-value
ACS	8.69 (5.32)	7.09 (1.90)	0.014*
Control	6.78 (2.43)	6.14 (1.31)	0.153*
P-value	0.006*	0.012*	
STEMI	9.41 (6.91)	7.90 (1.67)	0.458*
NSTEMI	7.51 (1.58)	6.98 (1.80)	0.456*
UAP	8.35 (3.77)	6.73 (1.99)	0.061*
SAP	7.56 (2.48)	6.57 (1.40)	0.122*
NCD	6.03 (2.19)	5.63 (1.01)	0.488*
P-value	0.068**	0.009**	

ACS, Acute coronary syndrome; NCD, Noncardiac disease; NSTEMI, Non–ST-segment elevation myocardial infarction; STEMI, ST-segment elevation myocardial infarction; SAP, Stable angina pectoris; UAP, Unstable angina pectoris; SD, Standard deviation

* with the Mann–Whitney *U* test
** with the Kruskal–Wallis test

DISCUSSION

In the present study, we analyzed the association between the serum level of PTX3 and ACS and its subgroups to determine which ACS subgroup(s) would experience an elevation in PTX3. Our results demonstrated that the serum concentration of PTX3 was significantly higher in ACS patients than in control subjects. In addition, the serum PTX3 level rose higher in STEMI patients than those in the other subgroups except the NSTEMI subgroup. Furthermore, our UAP patients had significantly higher PTX3 levels than our NCD subjects. The distribution of sex was significantly different between the study groups. Men with ACS had higher PTX3 levels than women with ACS. In women, the PTX3 level was higher in ACS patients than in the controls, in STEMI patients than in NSTEMI, UAP, and NCD subjects, and in UAP patients than in NCD subjects.

Our results suggest that PTX3 may act as a predictive marker for MI and angina pectoris, especially for STEMI and UAP. Two-thirds of patients who are annually admitted to hospitals in the United States with ACS are diagnosed with UAP or NSTEMI. [30] Thus, a well-timed diagnosis is necessary to reduce morbidity and mortality. Biochemical markers and ECG findings are pivotal to the evaluation of suspected ACS patients. Although patients with UAP do not have any cardiac damage, cardiac indicators are not discovered in the blood, hence the need for other indicators to predict UAP.

Our results confirmed that ACS enhances serum PTX3. Similarly, previous reports have demonstrated the relationship between PTX3 and ACS or CAD. [17, 31, 32] Wu et al [33] and Ustundag et al [24] detected that circulating PTX3 was considerably higher in their ACS patients than in their control group. In contrast to our study, several investigators have observed no difference between ACS and NCD groups with regard to serum PTX3 levels. [34]

We found that PTX3 was higher in STEMI patients than in the UAP, SAP, and NCD subgroups but not the NSTEMI subgroup. The plasma PTX3 concentration of patients with acute MI was higher than that of patients with unstable angina. [33] In agreement with our result, El Melegy et al [35] and Peri et al [21] found that serum PTX3 levels were higher in patients with STEMI than in control subjects. Yamasaki et al [36] and Ustundag et al [24] found that the PTX3 level in STEMI patients was significantly higher than that in the normal control group. One of the main findings of our study was that the serum concentration of PTX3 did not significantly differ between patients with STEMI and those with NSTEMI. Similar to our result, Ustundag et al [24] found that serum PTX3 levels were not significantly different between their STEMI and NSTEMI groups.

The PTX3 level was not higher in our NSTEMI patients than in our UAP, SAP, and NCD subgroups. The mean PTX3 level at baseline was similar in both NSTEMI and SAP groups. [37] Conversely, in the study by Ustundag et al, [24] elevated PTX3 levels were determined to be significantly higher in patients with NSTEMI than in the control group. Similarly, in another study, serum PTX3 levels showed an increasing tendency in NSTEMI patients compared with healthy controls. [38]

Our results suggest that high serum PTX3 levels are associated with UAP but not with SAP. In a previous study, the level of serum PTX-3 was significantly higher in the UAP group than in the control group, [24] which chimes in with our result. Likewise, Inoue et al [20] detected a significantly higher PTX3 level in patients with UAP than in a normal group. In contrast, in a study conducted by Soeki et al, [39] the results revealed that the serum PTX3 level was similar in patients with angina pectoris and control subjects.

We found that PTX3 was not different between SAP cases and NCD subjects. Similarly, several investigators have observed no differences between SAP and NCD groups concerning serum PTX3 levels. [34, 39] Nevertheless, in a study conducted by Karakas et al, [40] the PTX3 level was increased in the SAP group by comparison with the control group.

In previous investigations, immunohistochemical assays of progressive atherosclerotic lesions have indicated that PTX3 expression is higher in the lumen and within atherosclerotic plaques in human and animal models. [41, 42] Cholesterol accumulations in the vascular intima layer are associated with the immuno-inflammatory process, increasing monocyte/macrophage and endothelial cell activation and, thereby, producing PTX3. Interleukin-1 and tumor necrosis factor-alpha are the main applicant factors for PTX3 regulation. [41] In patients with severe atherosclerosis, the rupture of the vascular intima is associated with increased plasma PTX3 after 15 minutes. [43] Moreover, the serum PTX3 level rises swiftly in the early stage of ischemic heart disease, [21, 23, 44] which suggests the probable role of PTX3 in MI.

In a previous study, PTX3 had a role as an early marker of ischemic cardiac damage insofar as the PTX3 level peaked 7.5 hours after admission to the intensive care unit in patients with acute MI. [21] Shim et al [45] reported that the serum PTX3 level rose to 2.33 ng/mL within 2 hours after arrival at the emergency room.

To date, the PTX3 level has been proposed as a risk predictor for acute MI [21] and a biomarker of adverse outcomes in patients with UAP, [19] MI, [44] and heart failure. [46] According to a previous investigation, femoral and coronary PTX3 levels in SAP patients with triple-vessel disease were higher than those with patent vessels, as well as those with single or double-vessel disease. [47]

Our study has some limitations. Firstly, the sample size of patients with NSTEMI was small. Secondly, we could not measure abdominal visceral obesity, which can affect the serum PTX3 level. [31, 45] Thirdly, the fact that the present study was performed in a single department means that we managed to provide data regarding only a single time-point measurement for each patient.

CONCLUSION

Our findings demonstrated that PTX3 was higher in patients with ACS. Furthermore, the level of PTX3 in STEMI and UAP cases was higher than that in NCD subjects during a 12-hour period following the onset of chest pain, suggesting that PTX3 may be released by systemic inflammation at the initial onset of acute MI.

Acknowledgements

The protocol of the study was supported by Jahrom University of Medical Sciences. We are grateful to the participants and the medical and nursing staff, who assisted in this project.

Conflict of interest

Authors have no conflicts of interest.

REFERENCES

1. Dahlof B. Cardiovascular disease risk factors: epidemiology and risk assessment. The American Journal of Cardiology. 2010;105:3A-9A.

2. Ahmadi A, Soori H, Mobasheri M, Etemad K, Khaledifar A. Haert failure, the outcomes, predictive and related factors in Iran. J Mazandaran Univ Med Sci. 2014;24:180-8.

3. Lusis AJ. Atherosclerosis. Nature. 2000;407:233-41.

4. Libby P, Pidker PM, Hansson GK. Inflammation in atherosclerosis: from pathophysiology to practice. J Am Coll Cardiol. 2009;54:2129-38.

5. Hodžić E, Hasković E, Duraković M, Fočak M. Troponin and C-reactive protein in risk stratification after myocardial infarction. Acta facultatis medicae Naissensis. 2017;34(3):213-20.

6. Jahromi AS, Shojaie M, Madani A. Cardiotrophin-1 in patients with acute myocardial infarction. American Journal of Applied Sciences. 2010;7(9):1190-4.7.

7. Koo BK, Choi DH, Ryu SK, et.al. Role of inflammation on coronary artery disease in Koreans. Korean Circ J. 2002;32:988-95.

8. Liuzzo G, Biasucci LM, Gallimore JR, Grillo RL, Rebuzzi AG, Pepys MB, et al. The prognostic value of C-reactive protein and serum amyloid a protein in severe unstable angina. N Engl J Med. 1994;331:417-24.

9. Shojaei M, Erfanian S, Taghipour N, Jahromia AS, Khoshfetrat M, Madani A, et al. Serum levels of β2-Microglobulin and high sensitive C-reactive protein in ST-elevated and non. ST-elevated myocardial infarction. Pakistan Journal of Medical and Health Sciences. 2018;12:880-3.

10. CieSlik P, Hrycek A. Long pentraxin 3 (PTX3) in the light of its structure, mechanism of action and clinical implications. Autoimmunity. 2012;45(2):119-28.

11. Maseri A, Fuster V. Is there a vulnerable plaque? Circulation. 2003;107(16):2068-71.

12. Garlanda C, Bottazzi B, Bastone A, Mantovani A. Pentraxins at the crossroads between innate immunity, inflammation, matrix deposition, and female fertility. Annu Rev Immunol. 2005;23:337-66.

13. Mantovani A, Garlanda C, Bottazzi B. Pentraxin 3, a non-redundant soluble pattern recognition receptor involved in innate immunity. Vaccine. 2003;21(suppl 2):S43-S7.

14. Napoleone E, Di Santo A, Bastone A, Peri G, Mantovani A, de Gaetano G, et al. Long Pentraxin PTX3 Upregulates Tissue Factor Expression in Human Endothelial Cells. A Novel Link Between Vascular Inflammation and Clotting Activation. 2002;22(5):782-7.

15. Mantovani A, Garlanda C, Bottazzi B, Peri G, Doni A, Martinez de la Torre Y, et al. The long pentraxin PTX3 in vascular pathology. Vascul Pharmacol. 2006;45:326-30.

16. Norata GD, Garlanda C, Catapano AL. The long pentraxin PTX3: a modulator of the immunoinflammatory response in atherosclerosis and cardiovascular diseases. Trends in Cardiovascular Medicine. 2010;20:35-40.

17. Kume N, Mitsuoka H, Hayashida K, Tanaka M. Pentraxin 3 as a biomarker for acute coronary syndrome: Comparison with biomarkers for cardiac damage. Journal of Cardiology. 2011;58(1):38-45.

18. Matsuura Y, Hatakeyama K, Imamura T, Tsuruda T, Shibata Y, Kodama T, et al. Different distribution of pentraxin 3 and C-reactive protein in coronary atherosclerotic plaques. Journal of Atherosclerotic and Thrombosis. 2012;19(9):837-45.

19. Matsui S, Ishii J, Kitagawa F, Kuno A, Hattori K, Ishikawa M, et al. Pentraxin 3 in unstable angina and non-ST-segment elevation myocardial infarction. Atherosclerosis. 2010;210(1):220-5.

20. Inoue K, Sugiyama A, Reid PC, Ito Y, Miyauchi K, Mukai S, et al. Establishment of a high sensitivity plasma assay for human pentraxin3 as a marker for unstable angina pectoris. Arterioscler Thromb Vasc Biol. 2007;27:161-7.

21. Peri G, Introna M, Corradi D, Iacuitti G, Signorini S, Avanzini F, et al. PTX3, A Prototypical Long Pentraxin, Is an Early Indicator of Acute Myocardial Infarction in Humans. Circulation. 2000;102:636-41.

22. Barbati E, Specchia C, Villella M, Rossi ML, Barlera S, Bottazzi B, et al. Influence of Pentraxin 3 (PTX3) Genetic Variants on Myocardial Infarction Risk and PTX3 Plasma Levels. PLoS ONE. 2012;7(12):e53030.

23. Salio M, Chimenti S, De-Angelis N, Molla F, Maina V, Nebuloni M, et al. Cardioprotective Function of the Long Pentraxin PTX3 in Acute Myocardial Infarction. Circulation. 2008;117(8):1055-64.

24. Ustundag M, Orak M, Guloglu C, Sayhan MB, Alyan O, Kale E. Comparative diagnostic accuracy of serum levels of neutrophil activating peptide-2 and pentraxin-3 versus troponin-I in acute coronary syndrome. Anadolu Kardiyol Derg. 2011;11:588-94.

25. Jenny NS, Arnold AM, Kuller LH, Tracy RP, Psaty BM. Associations of pentraxin 3 with cardiovascular disease and all-cause death: the Cardiovascular Health Study. Arterioscler Thromb Vasc Biol. 2009;29:594–9.

26. Inoue K, Kodama T, Daida H. Pentraxin 3: A Novel Biomarker for Inflammatory Cardiovascular Disease. International Journal of Vascular Medicine. 2012;2012:e657025.

27. Shojaei M, Rahmanian K, Moayedy-Rad M. Association of Rose angina with cardiovascular risk factors among men and women: a population-based study. Jentashapir J Health Res. 2014;5(1):477-82.

28. Shojaei M, Sotoodeh-Jahromi A, Rahmanian K, Madani A. Gender Differences in the Prevalence of Cardiovascular Risk Factors in an Iranian Urban Population. OnLine Journal of Biological Sciences. 2015;15(3):178-84.

29. Rahmanian K, Shojaie M. The prevalence of pre-hypertension and its association to established cardiovascular risk factors in south of Iran. BMC Research Notes. 2012;5:386.

30. Yamashina A, Tomiyama H, Arai T, Hirose K, Koji Y, Hirayama Y, et al. Brachial-ankle pulse wave velocity as a marker of atherosclerotic vascular damage and cardiovascular risk. Hypertens Res. 2003;26:615– 22.

31. Barazzoni R, Aleksova A, Carriere C, Cattin MR, Zanetti M, Vinci P, et al. Obesity and high waist circumference are associated with low circulating pentraxin-3 in acute coronary syndrome. Cardiovascular Diabetology. 2013;12:167.

32. Guo T, Huang L, Liu C, Shan S, Li Q, Ke L, et al. The clinical value of inflammatory biomarkers in coronary artery disease: PTX3 as a new inflammatory marker. Exp Gerontol. 2017;97:64-7.

33. Wu L-P, Song X-F, Zhang S-Q, Tang J-F, Yang P-L. The Relationship of Pentraxin-3 with Acute Coronary Syndrome and Coronary Artery Lesion. Chinese Journal of Arteriosclerosis. 2007;12:016.

34. Özer MR, Ergin M, Kılınç İ, Dündar ZD, Özer N, Önal MA, et al. Diagnostic and Prognostic Significance of Neutrophil Gelatinase-Associated Lipocalin and Pentraxin-3 in Acute Coronary Syndrome. Eurasian J Emerg Med. 2017;16: 12-8.

35. El-Melegy EK, E.A B, El-Kersh AM, EL-Shafey WH, Fareed WA. Pentraxin 3 genotyping in relation to serum levels of pentraxin 3 in patients with acute ST-segment elevation myocardial infarction. Clin Trials Regul Sci Cardiol. 2016;13:6-13.

36. Yamasaki T, Koizumi T, Tamaki T, Sakamoto A, Kikutani T, Sano K, et al. Differing Behavior of Plasma Pentraxin3 and High-Sensitive CRP at the Very Onset of Myocardial Infarction with ST-segment Elevation. Angiol. 2013;1:108.

37. Saygı S, Kırılmaz B, Tengiz İ, Türk UO, Yıldız H, Tüzün N, et al. Long pentraxin-3 measured at late phase associated with GRACE risk scores in patients with non-ST elevation acute coronary syndrome and coronary stenting. Arch Turk Soc Cardiol. 2012;40(3):205-12.

38. Eggers KM, Armstrong PW, Califf RM, Johnston N, Simoons ML, Venge P, et al. Clinical and prognostic implications of circulating pentraxin 3 levels in non ST-elevation acute coronary syndrome. Clin Biochem. 2013;46(16-17):1655-9.

39. Soeki T, Niki T, Kusunose K, Bando S, Hirata Y, Tomita N, et al. Elevated concentrations of pentraxin 3 are associated with coronary plaque vulnerability. Journal of Cardiology. 2011;58(2):151-7.

40. Karakas MF, Buyukkaya E, Kurt M, Motor S, Akcay AB, Buyukkaya Ş, et al. Serum Pentraxin 3 Levels Are Associated With the Complexity and Severity of Coronary Artery Disease in Patients With Stable Angina Pectoris. Journal of Investigative Medicine. 2013;61(2):278–85.

41. Rolph MS, Zimmer S, Bottazzi B, Garlanda C, Mantovani A, Hansson GK. Production of the long pentraxin PTX3 in advanced atherosclerotic plaques. Arterioscler Thromb Vasc Biol. 2002;22(5):e10-e4.

42. Norata GD, Marchesi P, Venu VKP, Pasqualini F, Anselmo A, Moalli F, et al. Deficiency of the long pentraxin PTX3 promotes vascular inflammation and atherosclerosis. Circulation. 2009;120(8):699-708.

43. Kotooka N, Inoue T, Fujimatsu D, Morooka T, Hashimoto S, Hikichi Y, et al. Pentraxin3 is a novel marker for stent-induced inflammation and neointimal thickening. Atherosclerosis. 2008;197(1):368-74.

44. Latini R, Maggioni AP, Peri G, Gonzini L, Lucci D, Mocarelli L, et al. Prognostic significance of the long pentraxin PTX3 in acute myocardial infarction. Circulation. 2004;110:2349-54.

45. Shim B-J, Jeon H-K, Lee S-J, Kim S-S, Park M-Y, Lee D-H, et al. The Relationship Between Serum Pentraxin 3 and Central Obesity in ST-Segment Elevation Myocardial Infarction Patients. Korean Circ J. 2010;40:308-13.

46. Suzuki S, Takeishi Y, Niizeki T, Koyama Y, Kitahara T, et.al. Pentraxin 3, a new marker for vascular inflammation, predicts adverse clinical outcomes in patients with heart failure. Am Heart J. 2008;155:75–81.

47. Haybar H, Davoodi M, Shahlaee A, Eslami.Shahr.Babaki A, Fazelinezhad Z, Azarian M, et al. The implication of calcium score and pentraxin-3 in non-invasive identification of significant coronary artery stenosis in chronic stable angina pectoris. World Journal of Cardiovascular Diseases. 2013;3:433-41.