INVESTIGATING THE RELATIONSHIP BETWEEN SERUM PENTRAXIN3 LEVEL AND ANGIOGRAPHIC FINDINGS IN PATIENTS WITH CORONARY ANGIOGRAPHY

HABIB HEYBAR[1], AHMADREZA ASSAREH[1], SOMMAYEH JALALI[2]*

[1]Cardiovascular Research Center, Ahvaz Jundishapur University of Medical Science, Ahvaz, Iran. [2]Department of Cardiology, Ahvaz Jundishapur University of Medical Science, Ahvaz, Iran. Email: sommayeh.jalali@gmail.com

ABSTRACT

Objective: Pentraxin3 (PTX3) is an inflammatory single-phase mononuclear polysorbate glycoprotein, synthesized by endothelial, macrophages, and mildew cells; based on reports and research findings, it is also believed to be synthesized in the tissue of atherosclerotic lesions of arterial arteries. Therefore, PTX3 can be considered as a more specific marker for atherosclerosis. The present study examines the relationship between PTX3 serum levels and coronary angiography findings.

Methods: A total of 100 patients with stable cardiac status under elective coronary angiography were studied. Meanwhile, serum levels of PTX3 were measured, along with coronary angiography, in these patients. Finally, the relationship between the serum level of this marker and the severity of the angiographic findings of these individuals was compared and contrasted.

Results: out of 100 patients examined in the present study, 57 subjects (57.6%) were male and 42 subjects (42.4%) were female. The mean age of participants turned out to be 53±9.16, and the mean serum level of PTX3 was 5.91±12.5. The mean serum level of PTX3 turned out to be lower in patients with normal angiography than in those with coronary artery disease (p<0.0001). Smoking and age did not affect the mean serum levels of this marker. Furthermore, a higher serum level of PTX3 was associated with a higher syntax score in the angiography (p<0.0001).

Conclusion: Serum levels of PTX3 can have a predictive value in the diagnosis of coronary artery disease in patients with stable cardiovascular symptoms.

Keywords: Pentraxin, Coronary angiography, Syntax score.

INTRODUCTION

Coronary artery disease is currently the most common cause of death in most parts of the world, both developed and developing countries, including Iran; it accounts for 40% of all deaths in these countries [1,2].

Inflammatory processes play a key role in the emergence and development of atherosclerosis [3]. Atherosclerosis or hardness of the arteries is the name of a type of disease in the veins, which is characterized by the deposition of lipids and other substances in the internal wall tissue of some arteries. The result of this process is the formation of fibrous-lipid plaques (atroma), which develops with increasing age, leading to stenosis and inflammation and, finally, coronary artery disease [4]. Pentraxin3 (PTX3) is an inflammatory single-phase mononuclear polysorbate glycoprotein, synthesized by endothelial, macrophages, and mildew cells [5]. PTX3 is released from platelet-induced neutrophils in the coronary artery bypass (CAD) graft [6], and acts through inflammatory processes in the CAD; it, even, acts as a prognostic factor for CAD admission [7]. Interestingly, the production of PTX3 in the tissue of atherosclerotic lesions of arterial arteries has also been reported [8]. Some studies have associated high levels of PTX3 with unstable angina [9] and adverse outcomes following myocardial infarction [10]. Compared with high-sensitivity C reactive protein (HsCRP) protein, PTX3 has been shown to be more specific in vascular inflammation and has been associated with the progression of atherosclerosis and vascular disease independently [11]. However, the precise role of PTX3 in the pathogenesis of cardiovascular disease requires further exploration [12].

Inflammation plays an important role in each stage of the onset and progression of atherosclerosis. Therefore, many studies have

already been conducted to find an inflammatory marker as predictive and prognostic of coronary artery disease. The most prominent inflammatory marker that has ever been studied is CRP. The accumulation of CRP in atherosclerotic plaques has been proven. There is also a positive direct correlation between serum CRP and cardiovascular risk. CRP, which is a member of PTX series, as a non-specific marker, has a pentameric structure and is synthesized in the liver in response to inflammatory processes and is a non-specific marker [12,13].

PTX3 was initially identified as an inflammatory marker initiating inflammatory response; however, since it was later on identified specifically as an inflammatory marker in response to vascular injury, it became a reliable indicator in the prediction of the possibility of obstruction and vascular damage.

Many studies have, so far, been done on the role of PTX3 in acute coronary and myocardial infarction and its comparison among stable and unstable patients. In addition, other studies which have been conducted on patients with stable heart conditions, the level of PTX3 in the majority of cases was administered locally and during invasive angiographic procedures, such as the femoral artery.

It seems that serum level can be used as a marker to predict coronary artery involvement in patients undergoing elective coronary angiography. Since there is no comprehensive study conducted on stable patients on this issue in this epidemiological area, the present study was conducted to find a relationship between serum PTX3 level and coronary angiography findings in subjects undergoing elective angiography.

METHODS

A total of 100 patients referred to educational centers of Golestan and Imam Khomeini Hospitals of Ahvaz, with stable cardiac status were considered candidate based on initial examination, exercise tests, myocardial perfusion scan, and cardiologist diagnosis of elective angiography; these subjects were categorized into three groups of one, two, and three vessels on the basis of the number of vessels involved. Demographic information of patients, including age, sex, and medications, was collected through a questionnaire. PTX3 serum level was determined in Pardis campus according to enzyme-linked immunosorbent assay (ELISA) method. Furthermore, the patient's syntax score was calculated by the software and recorded in the questionnaire.

Considering the potential for interference with the level of PTX3, the main exclusion criteria included the presence of glucose metabolism disorder such as diabetes mellitus impaired fasting glucose, impaired glucose tolerance, heart failure (EF <50%), and kidney failure (GFR <60). The serum level of PTX3 was measured along with coronary angiography in these subjects. PTX was measured and examined through ELISA method and CUSABIO BIOTECH CO, Ltd., Japan kit; finally, the relationship between average serum level of this marker and the severity of angiographic findings was determined based on the presence or absence of coronary involvement, the number of vessels involved and the severity of the conflict according to SYNTAX score.

Statistical analysis

Quantitative variables are used to illustrate descriptive results. The qualitative variables are presented as percentages. For analytical analysis, ANOVA tests were used to compare the serum level of PTX3 in three groups; additionally, Chi-square and independent t tests were used to compare the results of three groups.

Ethical considerations

1. The researcher introduced himself for the volunteers, explained the objective of the research, assured them about the confidentiality of the information, and obtained their written consent.
2. All forms used for collecting information form patients are anonymous.
3. Participation in research for all eligible patients is entirely optional and free.
4. Patients are not charged for injected serums, and the research was conducted entirely free.

Findings

Out of 100 patients examined in the present study, 57 subjects (57.6%) were male and 42 subjects (42.4%) were female. The mean age of participants turned out to be 53±9.16, and the mean serum level of PTX3 was 5.91±12.5. The qualitative results of the study included mean age, sex percentages of patients, mean PTX3 serum level, and syntax score of patients, all of which are indicated in following Tables 1-6 and graphs.

The mean PTX3 serum level difference was 1.18±2.4 between two sexes, which showed a significant difference between the two sexes in terms of serum level of this marker (p value = 0.042).

According to the findings of the present study, the mean syntax score difference turned out to be 13.6140±1.38 among male and 1.32±8.2857 among female subjects.

One-way ANOVA test was used to examine the difference between the levels of PTX3 in different stages of vessel involvement, the results of which are shown in the following table; as you can see, there was a significant difference in serum levels of PTX3, compared to other groups, at least in the groups with normal coronary angiography (p<0.0001). There was also a significant difference between three and two vessels groups in the level of PTX3 in the coronary angiography (p=0.037).

In addition, the relationship between syntax score difference and the number of involved vessels turned out to be significant, meaning that, at least in two groups, there is a significant difference between the score of the patients' syntax and the number of vessels involved.

In fact, the results showed that the syntax score of groups with normal angiography and minimal CAD was significantly lower than three blood vessels groups.

DISCUSSION

The present study suggests that serum levels of PTX3 can be a valuable marker for differentiating patients with normal coronary angiography from those with coronary involvement. However, this study provided no differentiation between patients with coronary involvement on the basis of the number of involved vessels or PTX3 rate. It has been shown that the serum level of PTX3 in patients with three vessels is significantly higher than those with double-vessel involvement. It was,

Table 1: The relationship between smoking and the number of vascular involvement in angiography

Smoking status	The number of vessels					Total
	Normal (%)	Minimal (%)	One vessel	Two vessels	Three vessels	
Smoking						
Smoking						
Count	10	3	9	5	6	33
% within smoking	30.3	9.1	27.3	15.2	18.2	100.0
% within number of vessels	30.3	15.8	42.9	41.7	42.9	33.3
% of total	10.1	3.0	9.1	5.1	6.1	33.3
No smoking						
Count	23	16	12	7	8	66
% within smoking	34.8	24.2	18.2	10.6	12.1	100.0
% within number of vessels	69.7	84.2	57.1	58.3	57.1	66.7
% of total	23.2	16.2	12.1	7.1	8.1	66.7
Total						
Count	33	19	21	12	14	99
% within smoking	33.3	19.2	21.2	12.1	14.1	100.0
% within number of vessels	100.0	100.0	100.0	100.0	100.0	100.0
% of Total	33.3	19.2	21.2	12.1	14.1	100.0

Table 2: The mean serum levels of pneumotoxic based on patients' gender

Variable	Levene's test for equality of variances		T-test for equality of means						95% confidence interval of the difference	
	F	**Significant**	**t**	**df**	**p value**	**Mean difference**	**Standard error difference**		**Lower**	**Upper**
PTX3	3.789	0.054	2.066	97	0.042	2.44331	1.18286		0.09565	4.79096

Table 3: The relationship between serum levels of PTX3 and the number of involved vessels

(I) number of vessels	(J) number of vessels	Mean difference (I-J)	Standard error	Significant	95% confidence interval	
					Lower bound	**Upper bound**
Normal	Minimal	−6.62203*	1.31574	0.000	−10.2817	−2.9624
	One vessel	−6.95892*	1.27536	0.000	−10.5062	−3.4116
	Two vessels	−5.78023*	1.54014	0.003	−10.0640	−1.4964
	Three vessels	−10.98368*	1.45724	0.000	−15.0369	−6.9305
Minimal	Normal	6.62203*	1.31574	0.000	2.9624	10.2817
	One vessel	−0.33689	1.44659	0.999	−4.3605	3.6867
	Two vessels	0.84180	1.68467	0.987	−3.8440	5.5276
	Three vessels	−4.36165	1.60923	0.060	−8.8376	0.1143
One vessel	Normal	6.95892*	1.27536	0.000	3.4116	10.5062
	Minimal	0.33689	1.44659	0.999	−3.6867	4.3605
	Two vessels	1.17869	1.65333	0.953	−3.4199	5.7773
	Three vessels	−4.02476	1.57638	0.088	−8.4094	0.3599
Two vessels	Normal	5.78023*	1.54014	0.003	1.4964	10.0640
	Minimal	−0.84180	1.68467	0.987	−5.5276	3.8440
	One vessel	−1.17869	1.65333	0.953	−5.7773	3.4199
	Three vessels	−5.20345*	1.79735	0.037	−10.2027	−0.2042
Three vessels	Normal	10.98368*	1.45724	0.000	6.9305	15.0369
	Minimal	4.36165	1.60923	0.060	−0.1143	8.8376
	One vessel	4.02476	1.57638	0.088	−0.3599	8.4094
	Two vessels	5.20345*	1.79735	0.037	0.2042	10.2027

*The mean difference is significant at the 0.05 level

Table 4: The relationship between the score of syntax and the number of vessels involved in angiography

Multiple comparisons

Dependent variable: Syntax score

Tukey HSD

(I) number of vessels	(J) number of vessels	Mean difference (I-J)	Standard error	Significant	95% confidence interval	
					Lower bound	**Upper bound**
Normal	Minimal	−15.00000*	1.66526	0.000	−19.6318	−10.3682
	One vessel	−17.19048*	1.61415	0.000	−21.6801	−12.7008
	Two vessels	−15.41667*	1.94927	0.000	−20.8384	−9.9949
	Three vessels	−20.92857*	1.84434	0.000	−26.0585	−15.7986
Minimal	Normal	15.00000*	1.66526	0.000	10.3682	19.6318
	One vessel	−2.19048	1.83087	0.753	−7.2829	2.9020
	Two vessels	−0.41667	2.13220	1.000	−6.3472	5.5139
	Three vessels	−5.92857*	2.03671	0.036	−11.5936	−0.2636
One vessel	Normal	17.19048*	1.61415	0.000	12.7008	21.6801
	Minimal	2.19048	1.83087	0.753	−2.9020	7.2829
	Two vessels	1.77381	2.09253	0.915	−4.0464	7.5940
	Three vessels	−3.73810	1.99514	0.339	−9.2875	1.8113
Two vessels	Normal	15.41667*	1.94927	0.000	9.9949	20.8384
	Minimal	0.41667	2.13220	1.000	−5.5139	6.3472
	One vessel	−1.77381	2.09253	0.915	−7.5940	4.0464
	Three vessels	−5.51190	2.27481	0.118	−11.8392	0.8153
Three vessels	Normal	20.92857*	1.84434	0.000	15.7986	26.0585
	Minimal	5.92857*	2.03671	0.036	0.2636	11.5936
	One vessel	3.73810	1.99514	0.339	−1.8113	9.2875
	Two vessels	5.51190	2.27481	0.118	−0.8153	11.8392

*The mean difference is significant at the 0.05 level. According to the results of the present study, there is, also, a significant relationship between syntax score and PTX3 serum level of the patients (p<0.05; r=0.89)

also, found that mean serum level of PTX3 in patients with significant vascular involvement was considerably higher among males. However, there was no relationship between smoking and the serum level of this marker.

Polat Nerkiz *et al*. showed that PTX3 is a useful pre-angiography predictor of vascular involvement [14]. According to results of this study, increase in the number of involved vessels caused the level of this serum to higher, which did not turn out to be consistent with the findings of the present study, according to which PTX3 serum level was significantly lower in two groups with normal angiography, in comparison to other groups. In addition, the level of this marker in patients with two blood vessels involved was considerably higher than those with three vessels involved.

Based on the results of Liu Haibo *et al*. study, which was conducted in 2014 under the title of "Evaluating PTX3 as a predictive marker of post-vascular metastatic events after the implementation of the DES stent," high level of this marker is highly efficient in predicting possible major cardiovascular events only hours after the instalment of the DES stent [15]. The present study differed from this study in several ways. First, only patients who were candidates for PCI were evaluated in this study and this marker was not considered in patients with stable cardiac status. However, according to the results of the present study, PTX3 can be used as a marker for treating patients with vascular disorder even without intervention or the necessity of implementing PCI.

A study conducted by Marie Tomandlova *et al*. in 2015 found that high levels of serum PTX3 can predict 1-year mortality of patients with STEMI; these patients are more likely to be afflicted with ventricular dysfunction after MI, causing their mortality to go higher and higher after 1 year [16]. However, both the nature and examined population of the present study differed hugely with their study.

Marie's study examined the prognostic impact of PTX3 in regard to cardiovascular events; but, the present study looked at the predictive role and diagnostic value of this marker. In addition, while their study examined only patients with unstable cardiovascular status, ours was specifically conducted on those with stable cardiac conditions. A simple comparison of the findings of these two studies indicates that carrying out further research will provide immeasurable help in determining and introducing PTX3 as a predictive and prognostic marker for both stable and unstable patients with heart problems.

In a cross-sectional study conducted on patients with STEMI in 2016 by Alipour-Parsa *et al*., following results were obtained. Patients with higher serum levels of PTX3 experienced more serious involvement in coronary angiography than the other groups; they were in more urgent need of PCI and intervention, in comparison to those with normal serum level; patients with higher level of PTX3 had lower EF, higher GRACE scores, and higher grade Killip class in comparison with those with normal PTX3 level [17]. Our study also found that people with higher PTX3 had higher syntax score, which means that, in addition to the prognostic value of this marker in cardiovascular complications, it is possible that even the severity of coronary artery disease and the probability of need for PCI can be predicted. This study determined serum levels of 0.29 ng/dl and above as a cut point predictor of high-intensity coronary involvement. However, the present study focused merely on the numerical relationship between the level of this marker and the prediction of coronary involvement and the threshold and the cutoff point were not specified for the probable differentiation of healthy patients from patients with coronary involvement [18,19].

With regard to the above findings, carrying out further research will provide immeasurable help in determining and introducing PTX3 as a predictive and prognostic marker for both stable and unstable patients with heart problems.

However, the results of the present study indicated that a low level of serum PTX3 has a predictive value for, at least, predicting normal coronary artery and no significant involvement. Actually, this marker seems to be more specific rather than sensitive in diagnosing and predicting critical coronary artery disease. Perhaps in the future, this marker can be used to reject coronary artery disease in patients with low to moderate risk, with atypical symptoms or those who have non-invasive results in non-diagnostic cases.

However, the present study had, also, some weaknesses. First, this study was conducted on patients with the stable cardiovascular disease, and it cannot be claimed whether PTX3 serum would have the same prognostic value for patients with a critical cardiovascular condition or not. However, some studies conducted on unstable patients have shown that this marker not only has no prognostic value, it might actually

Table 5: The relationship between PTX3 serum level and syntax score

Correlations		
PTX3	**PTX3**	**Syntax score**
Pearson correlation	1	0.898**
Significant (two-tailed)		000
N	99	99
Syntax score		
Pearson correlation	0.898**	1
Significant (two-tailed)	0.000	
N	99	99

Statistical analysis showed that syntax score and serum level of PTX3 did not differ significantly between smokers and non-smokers (p=0.6, 0.4)

Table 6: The relationship between PTX3 serum level and syntax score with smoking

Independent samples test									
	Levene's equality of variances		T-test for equality of means					95% confidence interval of the difference	
	F	**Significant**	**t**	**Df**	**p value**	**Mean difference**	**Standard error difference**	**Lower**	**Upper**
PTX3									
Equal variances assumed	1.933	0.168	−0.837	97	0.405	−1.05636	1.26256	−3.56220	1.44947
Equal variances not assumed			−0.938	86.168	0.351	−1.05636	1.12580	−3.29431	1.18158
Syntax score									
Equal variances assumed	1.397	0.240	−0.501	97	0.617	−1.07576	2.14528	−5.33355	3.18203
Equal variances not assumed			−0.537	76.911	0.593	−1.07576	2.00379	−5.06590	2.91438

exacerbate their critical condition and necessitate the implementation of PCI in these patients.

Another weakness of our study was that a cut-off point and a specific number could not be determined to predict coronary artery disease or a small probability of coronary involvement, and it would not be possible to identify a certain level PTX3 that could reject coronary disorder with absolute certainty.

One of the strengths of the present study is that the necessity of coronary angiography was initially determined by non-invasive methods and medical examinations, increasing the specificity of PTX3 serum level in rejection of coronary artery disease. Another strength of the present study is simultaneous study of other factors, such as age, sex, smoking, and the severity of vascular involvement, based on the diameter of the lumen, apart from the examination of the number of vessels involved, and their relationship with PTX3 level, which had not been done in former researches.

CONCLUSION

PTX3 serum levels can be predictive of coronary heart disease in patients with the stable cardiovascular condition. In addition, the serum level of this marker is lower in patients with normal angiography, in comparison to those with coronary artery diseases. Serum level of this marker is, also, higher in males and patients with significant traceability. However, smoking and age had no effect on the mean serum levels of this marker in the present study.

CONFLICTS OF INTEREST

All authors have none to declare

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