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The Relationship Between Pentraxin 3 Levels and Diabetic Retinopathy in Patients with Type 2 Diabetes

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ABSTRACT

Background: Diabetic retinopathy (DRP) is one of the most common microvascular complications of diabetes. Microvascular complications of diabetes, such as diabetic macular edema and proliferative DRP, are among the major causes of vision loss in the active working-age population. Pentraxin 3 (PTX3) is a protein that is rapidly released during local inflammatory processes in the body. Increased inflammation in diabetes damages the capillaries in the eye, thereby laying the groundwork for retinopathy.

Materials and Methods: A total of 82 participants were included in the study. Twenty of these were healthy volunteers. Of the 62 diabetic patients, 41 had DRP and 21 did not. PTX 3 levels were compared between the groups with DRP, without DRP, and the healthy group. The patient group comprised 28 patients with non-proliferative DRP (NPDRP), 13 patients with proliferative DRP (PDRP) and 21 diabetic patients without DRP. The PTX 3 levels of the four groups were compared to assess the severity of DRP. PTX 3 levels in patient serum samples were determined using the ELISA method.

Results: PTX3 levels did not show a statistically significant difference between the three study groups. It has been observed that PTX3 levels decrease as the severity of retinopathy increases in patients with diabetes; however, this decrease is not statistically significant. The reduction was not statistically significant, even when compared with the healthy control group.

Conclusion: PTX3 levels did not increase in patients with DRP. Furthermore, PTX3 levels did not rise as the severity of DRP increased.

Keywords: diabetes mellitus, diabetic complications, diabetic retinopathy, pentraxin 3

Introduction

Diabetic retinopathy (DRP) is a microvascular complication of diabetes. Microvascular complications of diabetes such as diabetic macular edema and proliferative DRP are among the leading causes of vision loss in working-age population. These complications require regular monitoring and treatment.[1] Irreversible vision can occur in patients who are not monitored regularly or managed properly.[2]

Pentraxin 3 (PTX3) is from a subgroup of pentraxins referred to as long pentraxins. PTX3 is an acute phase reactant structurally and functionally similar to C-reactive protein (CRP), although PTX3 differs from CRP in its gene organization and chromosomal location and cellular origin, inducibility and ligand binding characteristics. PTX3 activates the complement system via classical, alternative or lectin pathways. PTX3 can be used to measure disease severity in inflammatory or infectious conditions. PTX3 has been considered as a rapid marker of innate immunity and primary local activation of inflammation.[3]

PTX3 has been used as a marker in the differential diagnosis of chronic inflammatory

conditions as well as an acute phase reactant during exacerbations. Previous studies on PTX3 demonstrated that PTX3 levels increased with the violence of inflammatory response and PTX levels correlated with disease activity level in several rheumatic conditions. PTX3 levels were significantly higher in patient groups compared to control groups in studies in patients with rheumatoid arthritis or familial Mediterranean fever.[4,5]

PTX3 is released by two structures in the retinal tissue: retinal pigment epithelial cells and vascular endothelial cells.[6]

This protein produced in the eye plays a role in tissue homeostasis by alleviating overactivation of the complement system in a neurodegenerative ophthalmic condition referred to as macular degeneration, which is of the major basis of eyesight loss in older adults.[7]

Currently, very limited data are available on the role of PTX3 in the pathogenesis of DRP. There are controversial data on potential associations between plasma PTX3 concentrations and disease status.[8,9]

Age-related macular degeneration and DRP have been linked to cellular and molecular components of major inflammatory pathways that also involve PTX3, which has long been recognized as an important mediator of vascular or complement-related inflammation and has recently been implicated in retinal neurodegeneration.[10,11]

However, local PTX3 grades in the ocular fluid of diabetic patients with DRP are greater compared to diabetic patients without DRP or non-diabetic volunteers.[12] Despite these data, biological connection of PTX3 in DRP has remained unknown.

Materials and Methods

This cross-sectional study was managed by the Internal Medicine and Ophthalmology Clinics. This study contained total of 82 individuals who presented to our hospital between November 2019 and October 2020; 41 DRP, 21 diabetic patients without DRP, and 20 healthy volunteers.

All participants underwent a complete ophthalmological exam in the Ophthalmology Clinics. Chronic diseases and previous medications were recorded. All patients exhibiting evidence of DRP in the fundoscopic exam underwent a Fundus Fluorescein Angiography (FFA) to determine the stage of DRP. Diabetic retinopathy was divided into two categories based on FFAs findings. Patients with hyperfluorescence leakage due to neovascularization in FFA were considered proliferative DRP (PDRP) (13 patients), and patients without leakage were considered non-proliferative DRP (NPDRP) (28 patients). Blood samples for serum PFX3 testing were collected from all study participants in the Internal Medicine Clinics. Body mass index (BMI) was calculated in the study population using the formula kg/m^2.

Adult individuals identified with Type 2 DM were included in the study. Pregnant women and minors, with a history of coronary artery disease, cerebrovascular or peripheral artery disease, type I diabetes mellitus, patients with macrovascular complications (diabetic foot, chronic kidney and/or liver failure) were not included. Patients with uveitis, glaucoma, and non-diabetic retinopathy were also excluded from the study.

The study was approved by the Clinical Research Ethics Committee of Hitit University (Decision date: 18.09.2019, Decision number: 50) and was conducted in line with the principles of the Declaration of Helsinki. All study participants gave informed consent.

Laboratory analysis

Once the routine tests were performed, remnant blood specimens were centrifuged for 10 minutes at 3.500 Relative Centrifugal Force (RCF). Centrifuged serum was placed in Eppendorf tubes and was frozen at -80 °C for testing. Serum samples and kits were allowed to stand at room temperature (+25 °C). PTX3 serum levels were measured utilizing the Enzyme-Linked Immunosorbent Assay (ELISA).

Pentraxin-3 analysis

The Human Pentraxin 3 ELISA kit of the Bioassay Technology (BT) Laboratory was used and PTX3 results were expressed in µg/mL.

Statistical Analysis

Statistical analyses were performed using the SPSS (Version 22.0, SPSS Inc., Chicago, IL, USA) software package. The Kolmogorov Smirnov test evaluated the conformity of the groups to normal distribution. Continuous variables were expressed as means ± standard deviations in normally distributed groups, and continuous variables that did not follow normal distribution were expressed as medians. The Student's t-test was used for the comparisons between patient and control groups if the variables were normally distributed, and the The Mann-Whitney U test was used to compare groups for variables that do not follow a normal distribution. The chi-square test was performed for the comparison of categorical variables between groups. The One-way ANOVA was used for three-way comparisons of the groups with normally distributed data and the Kruskal-Wallis test was used for non-normally distributed data. The Pearson's test was used if the data showed normal distribution in correlation analysis; otherwise, the Spearman's correlation test was used. Any p value less than 0.05 ($p<0.05$) was considered statistically significant.

Results

The study population consisted of 82 individuals. 62 were diabetic patients, and 20 were healthy volunteers without any underlying disease. Of the 62 diabetic patients, 41 had retinopathy, while 21 did not. Among 41 patients with DRP, 28 had NPDR and 13 had PDR.

There were no significant differences between the study groups in terms of age, BMI, systolic and diastolic blood pressure values (Table 1).

An analysis of biochemical data revealed that fasting blood glucose (FBG) and HbA1c values were remarkably higher in

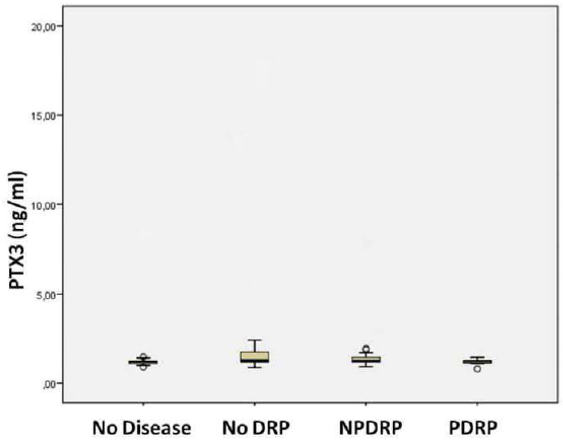

Figure 1. PTX3 levels by disease severity

PTX-3: pentraxin 3; DRP: Diabetic retinopathy; NPDRP: non-proliferative DRP; PDRP: proliferative DRP

patient groups with diabetes +/- DRP compared to healthy control group ($p < 0.001$ for both FBG and HbA1c). However, these two parameters did not significantly differ between the patient group with DRP and the patient group with diabetes without DRP ($p > 0.05$). Lipid parameters were similar among study groups. Moreover, serum creatinine levels did not statistically significantly differ among three study groups and PTX3 levels did not statistically significantly differ among three study groups (Table 1).

PTX3 levels were found to reduce as the severity of retinopathy increased in patients with diabetes, although this reduction was not statistically significant. The reduction was not statistically significant even in comparison with the healthy control group (Table 2) (Figure 1).

Discussion

Study groups did not significantly differ in age and gender distribution in our study. PTX3 levels did not significantly differ among three study groups ($p = 0.081$). PTX3 levels were found to reduce as the severity of retinopathy increased. However, this reduction was not statistically significant ($p = 0.065$).

Diabetes is a complex metabolic disorder. Hyperglycemia results in oxidative stress in retinal tissues, triggering an inflammatory response in patients with diabetes.[13] Numerous studies have shown that inflammatory processes play a central role in the various pathogenic mechanisms underlying DRP.[14-16]

As a glycosylated protein, PTX3 is produced acutely during inflammatory reactions. Increased oxidative stress in retinal tissues activates inflammatory signaling pathways in diabetic conditions and various inflammatory cytokines, such as IL-1 and TNF-α, are secreted. PTX3 molecules are locally expressed by immune and non-immune cells at infectious sites and protect the host against opportunistic bacteria in those sites.[17]

In addition to its role in natural immunity against infections, it has been observed to activate inflammation in several in vitro models such as myocardial infarction, gut ischemia or acute lung injury models.[18-20]

Evidence suggests that PTX3 is found in the eyes of humans and is synthesized by various cell types, such as retinal pigment epithelial cells, endothelial cells and myeloid cells. Produced locally, this protein plays a role in tissue homeostasis; for instances, by alleviating the excessive activation of the complementary system, PTX3 can mitigate age-related macular degeneration (AMD), which is a neurodegenerative condition and one of the main causes of visual impairment in older people.[21]

Table 1. Demographic clinical and biochemical characteristics of study participants

Variables	Diabetes with DRP (n=41)	Diabetes without DRP (n=21)	Control (n=20)	p-value
Gender, female/male	21/20	14/7	13/7	0.448
BMI, kg/m2	30 ± 4.6	31.8 ± 5.6	28.3 ± 3.4	0.069
Age, years	60.14 ± 8.82	60.19 ± 10	57.10 ± 6.95	0.400
SBP, mmHg	127.6 ± 12.3	126.5 ± 10.4	125.4 ± 9.6	0.424
DBP, mmHg	78.1 ± 8.8	76.3 ± 7.8	75.6 ± 7.4	0.321
Total Cholesterol, mg/dL	222 ± 59	207 ± 41	220 ± 37	0.540
Triglycerides, mg/dL	203 ± 171	169 ± 63	152 ± 71	0.316
LDL-cholesterol, mg/dL	131 ± ?	120 ± 32	138 ± 31	0.334
HDL-cholesterol, mg/dL	49 ± 28	53 ± 13	51 ± 7	0.401
FBG, mg/dL	203 ± 102	177 ± 71	98 ± 10	<0.001
HbA1c, %	9.30 ± 2.54	8.14 ± 1.77	5.17 ± 0.34	<0.001
Creatinine, mg/dL	0.77 ± 0.16	0.74 ± 0.19	0.78 ± 0.17	0.772
PTX-3, ng/mL	1.47 ± 0.16	3.18 ± 0.95	1.65 ± 0.33	0.081

FBG: fasting blood glucose; LDL: low density lipoprotein; HDL: high density lipoprotein; BMI: body mass index; DBP: diastolic blood pressure; SBP: systolic blood pressure; PTX-3: pentraxin 3; DRP: Diabetic retinopathy; NPDRP: non-proliferative DRP; PDRP: proliferative DRP

†For FBG and HbA1c, the p-value is reported as pairwise comparisons rather than an overall value: Diabetes without DRP vs. Control, $p < 0.001$; Diabetes with DRP vs. Control, $p < 0.001$

Table 2. PTX3 levels by disease severity

Variable	PDRP group (n:13)	NPDRP group (n:28)	Diabetes without DRP group (n:21)	Control group (n:20)	p-value
PTX3 (ng/mL)	1.19±0,04	1.60±0.23	3.18±0.95	1.65±0.33	0.065

PTX-3: pentraxin 3; DRP: Diabetic retinopathy; NPDRP: non-proliferative DRP; PDRP: proliferative DRP

A study conducted on diabetic patients in Egypt found that serum PTX3 levels were substantially more elevated with DRP than without the DRP; a cut-off value of 1150 pg/mL (1.15 ng/ml) provided a sensitivity of 93.3% and a specificity of 72%.[22] In contrast to that research, serum PTX3 levels were higher in the group of patients without DRP compared to the group of patients with DRP in our study, although intergroup difference was not statistically significant.

In a meta-analysis of 15 studies, Mohammadpour Fard et al. demonstrated that PTX3 was a promise biomarker for the prompt recognition and follow-up of DRP.[23] Moreover, considering that PTX3 concentrations were substantially elevated in the PDRP and NPDRP, they emphasized potential clinical utility of PTX3 in detecting the condition and assessing disease severity. However, in our study, PTX3 levels were found to reduce as the severity of retinopathy increased, although this reduction was not statistically significant. In a meta-analysis conducted by Mohammadpour Fard and colleagues, four clinical trials were reviewed to investigate circulating PTX3 concentration levels in patients with PDRP and NPDRP; the findings suggested a probable increase in PTX3 levels in PDRP patients compared with NPDRP patients, but, as with the results of our study, the increase was not statistically significant.[23]

Despite the large body of evidence demonstrating the release of PTX3 by various leukocytes, including monocytes, macrophages, dendritic cells and neutrophils, in the presence of infections or sepsis, investigations into blood PTX3 levels in diabetics have failed to arrive at a definitive result.[21,24]

However, PTX3 levels in the aqueous humor were found to be higher in patients with diabetes compared to controls without diabetes.[12] It was remarkable that there were no differences between patients with diabetes with DRP and with diabetes without DRP. The findings confirm significance of PTX3 initial phases of DRP, as reflected by the locally elevated PTX3 levels in the ocular compartment.[21]

In our study, no significant difference was found between patient with DRP and without DRP in PTX3 levels. However, we could not determine whether PTX3 levels were increased in the aqueous humor or not, as we were not able to measure PTX3 levels in the aqueous humor.

However, serum PTX3 levels (3.18 ± 0.95 ng/ml) were higher in the group of patients without DRP than in the group with DRP. The findings might indicate that PTX3 levels might have increased in the aqueous humor previously and PTX3 might play a role during early stages of DRP.

Although the root cause of these inconsistencies between the studies could not be determined, sample sizes, race or specimen (plasma vs. aqueous humor) differences could play a role in conflicting results.

PTX3 can be secreted by various cell types in sites of inflammation sites and plasma PTX3 concentrations are highly sensitive to systemic conditions. Therefore, a more detailed analysis of the aqueous humor during different disease stages will be crucial to the investigation of the potential role of PTX3 in the development of DRP.[25]

In a study, Jiang Y et al. suggested that PTX3 might have a significant inhibiting effect on angiogenesis in the retina.[25] Neovascularization is a complex process involving multiple signaling pathways, including, epidermal growth factor (EGF), VEGF, insulin-like growth factor 1 receptor (IGF1R), platelet-derived growth factor (PDGF) and others. Conversely, PTX3 expression was upregulated on high glucose situations and the inhibition of PTX3 expression upregulated fibroblast growth factor-(FGF) mediated angiogenesis whereas excess expression of PTX3 suppressed FGF-mediated angiogenesis. In light of these findings, further research is required to demonstrate potential effects of PTX3 on DRP and retinal neovascularization.[26]

Further studies are needed to observe PTX3 expression in retinal tissue in diabetic mice at different disease stages, PTX3 overexpression in animal models of oxygen-induced retinopathy and effects of PTX3 overexpression on retinal neovascularization.[25]

Limitations of our study includes our inability to measure PTX levels in the aqueous humor and limited number of patients in the PDRP group The small sample size (n=13) in the PDRP subgroup is one of the limitations of the study. Lipid metabolism markers, CRP and other markers similar to CRP were not included in our study and this might be another limitation of our study.

Conclusion

This study did not reveal any significant intergroup differences in serum PTX3 levels at any stage of diabetic retinopathy. However, based on the results of our study, we believe that there is no association between serum PTX3 levels and retinopathy in patients with type 2 diabetes, independently from macrovascular disease. Further studies with larger sample size and measurements of PTX3 levels in the aqueous humor are needed to determine if PTX3 contributes to the pathogenesis of DRP.

References

1. Arıkan Yorgun M, Öner S, Mendi ZN, Yıldız Taşçı Y, Toklu Y. Diyabetik Retinopati Hastalarında COVID-19 Salgını Kaynaklı Anksiyetenin Retina Kliniği Takiplerine Etkisinin Değerlendirilmesi. MN Oftalmoloji.

2023;30(2):101-106.

2. Bresnick G, Cuadros JA, Khan M, et al. Adherence to ophthalmology referral, treatment and follow-up after diabetic retinopathy screening in the primary care setting. BMJ Open Diabetes Res Care. Jun 2020;8(1) doi:10.1136/bmjdrc-2019-001154

3. Daigo K, Inforzato A, Barajon I, et al. Pentraxins in the activation and regulation of innate immunity. Immunol Rev. Nov 2016;274(1):202-217. doi:10.1111/imr.12476

4. Sharma A, Khan R, Gupta N, et al. Acute phase reactant, Pentraxin 3, as a novel marker for the diagnosis of rheumatoid arthritis. Clin Chim Acta. May 2018;480:65-70. doi:10.1016/j.cca.2018.01.035

5. Gok M, Sirkeci O, Kara M, et al. Evaluation of pentraxin-3 in familial Mediterranean fever patients during attack and attack-free periods. Bratisl Lek Listy. 2018;119(8):490-493. doi:10.4149/BLL_2018_089

6. Woo JM, Kwon MY, Shin DY, Kang YH, Hwang N, Chung SW. Human retinal pigment epithelial cells express the long pentraxin PTX3. Mol Vis. 2013;19:303-10.

7. Swinkels M, Zhang JH, Tilakaratna V, et al. C-reactive protein and pentraxin-3 binding of factor H-like protein 1 differs from complement factor H: implications for retinal inflammation. Sci Rep. Jan 26 2018;8(1):1643. doi:10.1038/s41598-017-18395-7

8. Zhou W, Hu W. Serum and Vitreous Pentraxin 3 Concentrations in Patients with Diabetic Retinopathy. Genet Test Mol Biomarkers. Mar 2016;20(3):149-53. doi:10.1089/gtmb.2015.0238

9. Yang HS, Woo JE, Lee SJ, Park SH, Woo JM. Elevated plasma pentraxin 3 levels are associated with development and progression of diabetic retinopathy in Korean patients with type 2 diabetes mellitus. Invest Ophthalmol Vis Sci. Aug 26 2014;55(9):5989-97. doi:10.1167/iovs.14-14864

10. Stravalaci M, Davi F, Parente R, et al. Control of Complement Activation by the Long Pentraxin PTX3: Implications in Age-Related Macular Degeneration. Front Pharmacol. 2020;11:591908. doi:10.3389/fphar.2020.591908

11. Haapasalo K, Meri S. Regulation of the Complement System by Pentraxins. Front Immunol. 2019;10:1750. doi:10.3389/fimmu.2019.01750

12. Mutlu M, Yuksel N, Takmaz T, Dincel AS, Bilgihan A, Altinkaynak H. Aqueous humor pentraxin-3 levels in patients with diabetes mellitus. Eye (Lond). Oct 2017;31(10):1463-1467. doi:10.1038/eye.2017.87

13. Rubsam A, Parikh S, Fort PE. Role of Inflammation in Diabetic Retinopathy. Int J Mol Sci. Mar 22 2018;19(4)doi:10.3390/ijms19040942

14. Shafabakhsh R, Aghadavod E, Mobini M, Heidari-Soureshjani R, Asemi Z. Association between microRNAs expression and signaling pathways of inflammatory markers in diabetic retinopathy. J Cell Physiol. Jun 2019;234(6):7781-7787. doi:10.1002/jcp.27685

15. Dehdashtian E, Mehrzadi S, Yousefi B, et al. Diabetic retinopathy pathogenesis and the ameliorating effects of melatonin; involvement of autophagy, inflammation and oxidative stress. Life Sci. Jan 15 2018;193:20-33. doi:10.1016/j.lfs.2017.12.001

16. Wang M, Wang Y, Xie T, et al. Prostaglandin E(2)/EP(2) receptor signalling pathway promotes diabetic retinopathy in a rat model of diabetes. Diabetologia. Feb 2019;62(2):335-348. doi:10.1007/s00125-018-4755-3

17. Porte R, Silva-Gomes R, Theroude C, et al. Regulation of inflammation and protection against invasive pneumococcal infection by the long pentraxin PTX3. Elife. May 24 2023;12doi:10.7554/eLife.78601

18. Salio M, Chimenti S, De Angelis N, et al. Cardioprotective function of the long pentraxin PTX3 in acute myocardial infarction. Circulation. Feb 26 2008;117(8):1055-64. doi:10.1161/CIRCULATIONAHA.107.749234

19. Souza DG, Amaral FA, Fagundes CT, et al. The long pentraxin PTX3 is crucial for tissue inflammation after intestinal ischemia and reperfusion in mice. Am J Pathol. Apr 2009;174(4):1309-18. doi:10.2353/ajpath.2009.080240

20. Deban L, Russo RC, Sironi M, et al. Regulation of leukocyte recruitment by the long pentraxin PTX3. Nat Immunol. Apr 2010;11(4):328-34. doi:10.1038/ni.1854

21. Stravalaci M, Ferrara M, Pathak V, et al. The Long Pentraxin PTX3 as a New Biomarker and Pharmacological Target in Age-Related Macular Degeneration and Diabetic Retinopathy. Front Pharmacol. 2021;12:811344. doi:10.3389/fphar.2021.811344

22. Dobriceanu RC, Meca AD, Boboc IKS, et al. Pentraxin-3 as a Biomarker in Diabetes Mellitus: Insights into Inflammation, Vascular Complications, and Modulation by Antidiabetic Medications. Biomedicines. Apr 7 2025;13(4)doi:10.3390/biomedicines13040891

23. Mohammadpour Fard R, Sherafat NS, Rashno M, Bahreiny SS. Evaluating pentraxin 3 as a diagnostic biomarker for diabetic retinopathy: a systematic review and meta-analysis. Diabetol Metab Syndr. Jul 16 2025;17(1):273. doi:10.1186/s13098-025-01849-8

24. Porte R, Davoudian S, Asgari F, et al. The Long Pentraxin PTX3 as a Humoral Innate Immunity Functional Player and Biomarker of Infections and Sepsis. Front Immunol. 2019;10:794. doi:10.3389/fimmu.2019.00794

25. Jiang Y, Xing X, Niu T, et al. Protective effect of pentraxin 3 on pathological retinal angiogenesis in an in vitro model of diabetic retinopathy. Arch Biochem Biophys. Aug 15 2022;725:109283. doi:10.1016/j.abb.2022.109283

26. Rodrigues PF, Matarazzo S, Maccarinelli F, et al. Long Pentraxin 3-Mediated Fibroblast Growth Factor Trapping Impairs Fibrosarcoma Growth. Front Oncol. 2018;8:472. doi:10.3389/fonc.2018.00472