ASSOCIATION OF INFLAMMATORY MARKERS WITH PHYSICAL ACTIVITY, FAMILY HISTORY AND OTHER DIABETIC COMPLICATIONS IN PATIENTS OF DIABETIC RETINOPATHY

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ABSTRACT

Objective: To study the association of inflammatory markers with physical activity, family history and other complications among patients of diabetic retinopathy.

Study Design: Cross sectional comparative study.

Place and Duration of Study: Department of Biochemistry and Molecular Biology, Army Medical College, Rawalpindi in collaboration with Armed Forces Institute of Ophthalmology (AFIO) and Military Hospital Laboratories, Rawalpindi from Jan 2016 to Jun 2016.

Material and Methods: A total of 90 diagnosed patients of diabetic retinopathy of ages 40-70 years were enrolled from Armed Forces Institute of Ophthalmology, Rawalpindi. Their inflammatory markers (ESR and CRP) were assessed and their levels were compared with their physical activity, family history and other complications of diabetes already developed in them. These were then compared with those of 90 normal healthy controls enrolled from general population using independent student's t test and one way Anova test for scale variables and Chi square test for nominal variables.

Results: Both patients and controls were age and gender matched with mean age of 60 ± 8.9 years in patients and 59 ± 13.02 years in controls. Among 90 patients enrolled 51(56.7%) were males and 39 (43.3) were females. And among 90 controls 49 (54.4%) were males and 41(45.6%) were females. An inverse association was observed between inflammatory markers and physical activity with a *p*-value of 0.001. On the contrary a strong positive association was observed between inflammatory markers and family history and complications of diabetes with a *p*-value 0.001.

Conclusion: There is an inverse association of inflammatory markers with physical activity and a direct association of these with family history and complications of diabetes among patients of diabetic retinopathy.

Keywords: C-reactive protein, Diabetic foot, Erythrocyte sedimentation rate, Nephropathy, Peripheral neuropathy.

INTRODUCTION

Diabetes mellitus is now a global health challenge. It is also a serious pathology of South Asia with special concern inurban areas of Pakistan[1]. The dilemma lying with the disease is that hyperglycemia being asymptomatic; the disease is mostly diagnosed with already developed complications. The hyperglycemia in diabetes mellitus leads to development of microvascular complications of diabetes including retinopathy, neuropathy and nephropathy. Various pathways contributing in this respect are polyol pathway, protein kinase C activation, oxidative stress and advanced glycation end (AGE) products formation[2].

One third of the patients suffering from diabetes develop retinopathy as a complication[3]. Diabetic retinopathy is the leading cause of blindness in middle aged adults[4]. It is the most frequently occurring micro vascular complication of diabetes[5]. Patients of diabetes are 25 times more prone to become blind as compared to normal healthy population[6]. It is estimated that patients of diabetic retinopathy are expected to

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rise from 126.6 million in 2011 to 191 million by 2030 worldwide[7].

Pathological changes at structural and molecular level in retinopathy are now being linked to inflammation[8]. Thus both inflammation and endothelial dysfunction are suspected to be the contributing factors in development of diabetic retinopathy[9].

Dysfunctional retinal endothelium plays a crucial role in development of various stages of diabetic retinopathy. Various contributing factors in this regard are reduced bioavailability of nitric oxide, hyperglycemia, insulin resistance, hyper-lipidemias, systemic inflammation and weight alternations in diabetic patients[6].

C-reactive protein (CRP) being an important and common inflammatory marker has been found to have strong association with diabetic retinopathy[10]. Patients with elevated plasma CRP levels are 2.6 times more likely to develop proliferative diabetic retinopathy than those having low plasma CRP levels[11]. Erythrocyte sedimentation rate is a nonspecific inflammatory marker. It has also been found to be raised in micro vascular complications of diabetes[12].

Among the three microvascular complications of diabetes, retinopathy is considered to be most debilitating as it leads to blindness severely compromising the quality of life of the patient.

The main aim of our study was to analyze the contribution of inflammation in the development of complications of diabetes like retinopathy. We also focused on association of inflammatory markers with certain parameters like family history, physical activity and complications of diabetes mellitus.

The significance of this study is that it will link the inflammatory mechanisms with progression of diabetic retinopathy with reference to physical activity, family history and development of other complications among patients of type 2 diabetes mellitus.

MATERIAL AND METHODS

This was a cross sectional comparative study conducted at the Department of Biochemistry and Molecular Biology, Army Medical College, Rawalpindi. Patients were enrolled from Armed Forces Institute of Ophthalmology (AFIO) after permission from Commandant AFIO for a time tenure of 6 months (January 2016 to June 2016). Formal approval was also taken from ethical review committee, Army medical College. Non probability purposive sampling was done for this purpose.

Ninety diagnosed patients of diabetic retinopathy of ages 40-70 years were enrolled from AFIO. Written informed consent was taken from all patients. Their biochemical parameters i.e inflammatory markers (CRP and ESR) were assessed. ESR was measured using Westergren method and CRP was assessed by CRP latex test kit (Cat No. CRP/012) following standard protocol of the kit. Their detailed history was taken regarding their physical activity, family history and other diabetic complications. Then the association of inflammatory markers was assessed with all these parameters seperately.

Table-I: Association of ESR with physical activity by applying one way Anova test.

Physical activity	None	Infrequent Exercise	Daily walk <30 min	Daily walk >30 min	Jogging	Running	*p* value
ESR	29.4 ± 8.70	23.9 ± 7.96	18.66 ± 10.07	12 ± 5.4	10.9 ± 4.13	21.88 ± 9.67	<0.001

Table-II: Association of CRP with physical activity by applying Chi square test.

Physical Activity	None	Infrequent exercise	Daily walk <30min	Daily walk >30min	Jogging	Running	*p* value
Positive	9	19	24	0	0	0	<0.001
Negative	15	45	44	20	4	0	

The patients excluded from the study were those having retinopathy due to some other cause and patients on any anti-inflammatory therapy.

Data were analyzed on SPSS-22. Mean and standard deviation were calculated for quantitative data. Percentages were assessed for qualitative data. Means of numerical data were assessed by independent student's t test and one way Anova test. Categorical data was compared by applying Chi square test.

RESULTS

A total of 90 patients of ages 40-70 years were enrolled in the study. Among which 51 (56.67%) were males and 39 (43.3%) were females. Among 90 controls 49 (54.4%) were males and 41 (45.56%) were females. Mean ages were 60 ± 8.9 years in cases and 59 ± 13years in controls.

Chi square test was applied to determine association between CRP and family history of DM among patients of diabetic retinopathy. CRP was significantly associated with family history <0.001. In patients with positive family history CRP was positive among 38 patients and negative among 52 patients. While in patients with negative family history CRP was positive among 14 patients and negative among 76 patients.

ESR levels were compared with diabetic complications and it was found that the values were markedly raised in peripheral neuropathy, diabetic foot and stroke (fig-1).

CRP levels when assessed showed negative CRP values in patients of diabetic retinopathy with no complicationsand positive CRP values were seen in mostly in patients having peripheral

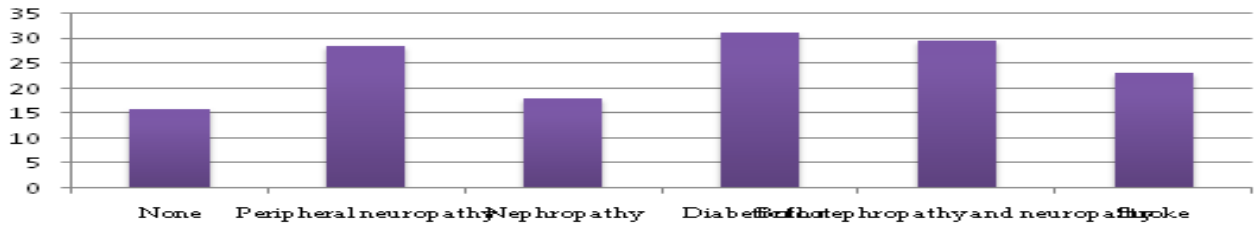

Figure-1: Association of ESR with complications of diabetes mellitus by applying one way anova test.

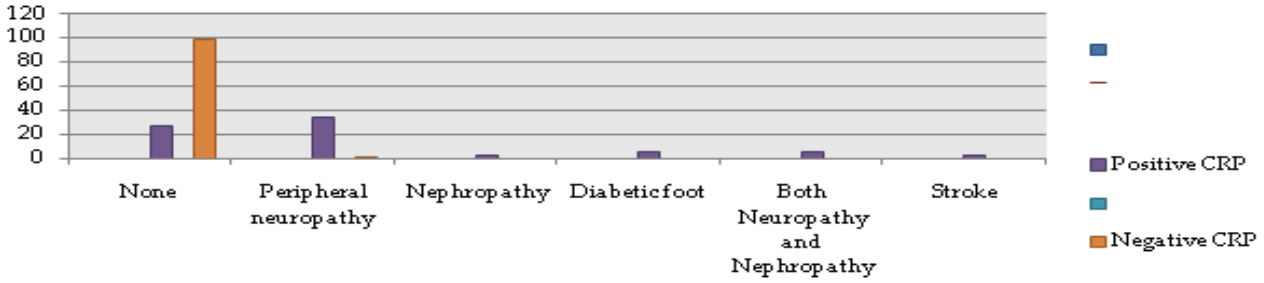

Figure-2: Association of CRP with complications in patients of diabetes mellitus by applying chi square test.

The ESR and CRP levels were assessed regarding physical activity among cases and controls (table-I & II).

In patients when association of ESR was seen with family history by applying student's t test , those with positive family history were having ESR levels 25.06 ± 8.98 and those with negative family history were having values 18.87 ± 8.80 with a *p*-value<0.001.

neuropathy and diabetic foot (fig-2).

DISCUSSION

In Pakistani population when we assessed the association of inflammatory markers with daily physical activity we observed that a negative association exists. More a person is active, less are his levels of inflammatory markers whereas more a person is sedentary more are

hislevels of the markers. Loprinzi, et al suggested an inverse association between CRP and physical activity among diabetics of Baltimore, USA in his study[13].

Hamer, et al conducted a study in UK and reported an inverse relationship between inflammatory markers and physical activity among type 2 diabetics[14].Autenreith, et al reported an inverse relationship between inflammatory markers (CRP and Fibrinogen) with physical activity among American diabetics[15].

When we assessed the association of inflammatory markers with family history, a strong positive association was observed. This predicts that inflammatory mechanisms also affect an individual at his genetic level and would lead to some permanent changes that may be inherited by their future generations. Bener, et al reported in their study that there are significant maternal effects in transmission of type 2 Diabetes Mellitus in the young thus family history also has a very strong impact[16].

As far as the levels of inflammatory markers are related to diabetic complications, a strong positive association has been seen. People having higher ESR values and positive CRP are more likely to develop complications of diabetes as compared to those who are vice versa. This indicates that inflammatory markers have a positive role in development of all types of diabetic complications.

Matrina, et al reported a positive association between raised inflammatory markers and retinopathy, a complication of diabetes[6]. Fransisco, et al reported that inflammatory markers are highly depressed in diabetics with healing foot ulcers. This correlates with our study in the context that our diabetic patients with diabetic foot had raised ESR and positive CRP values.

Sinha, et al reported that in African Americans and Hispanic diabetics developing chronic kidney disease have positive CRP levels[17]. Carlsson, et al in their research revealed that inflammatory markers can be a predictor of cardiovascular abnormalities among type 2 diabetics[18].

One aspect of our study is that as inflammatory markers are the pioneers of diabetic complications, they can be considered as prediabetic markers for early diagnosis of the disease[19]. Moreover by keeping their levels low we can prevent the deleterious complications that adversely affect the quality of life of diabetics. If we see in context of therapeutic implementation anti-inflammatory therapies can be protective for slow progression or even prevent diabetic complications[9].

CONCLUSION

The findings suggest a statistically significant inverse relationship between inflammatory markers and physical activity and a strong positive association between inflammatory markers and family history and complications of diabetes.

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CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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