ORIGINAL ARTICLE

Anticardiolipin Antibodies as Additional Risk Factor in Proliferative Diabetic Retinopathy

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ABSTRACT

Aim: In patients of proliferative diabetic retinopathy (PDR) the prevalence of anticardiolipin antibodies (aCL) account as high-risk criterion (HRC).[1]

Methods: Both groups of Diabetic and non diabetics patients contain PDR by way of HRC and were compared for anticardiolipin antibodies presence.

Results: Amongst the 40 patients, 9(22.5%) of the diabetic subjects having PDR with HRC had anticardiolipin antibodies positive results. There were no significant relationships of (aCL) antibodies with type of diabetes or gender. By using Pearson's association test, no significant relations of (aCL) antibodies with diabetes or age of subject would be establish. Statistically significant difference was found in all subjects with positive results of (aCL) had PDR along with HRC.

Conclusion: Presence of anticardiolipin antibodies (aCL) may signify as a supplementary risk factor for PDR.

Keywords: Proliferative diabetic retinopathy, Anticardiolipin antibodies, Antiphospholipid antibodies (APLA), Intravitreal vascular endothelial growth factor, high-risk criterion.

INTRODUCTION

Diabetic retinopathy (DR) is account as principal reason of blindness in the functioning people of the Western world; the pervasiveness of which is powerfully associated to the period of diabetes and the control of glucose level. In emergency diabetic management, the objective of treatment is to attain near-normal blood glucose control which may put off or impediment the commencement of DR. In attendance of plenty confirmation that multiple factors like genetic, growth factor, and metabolic factors plays a major role in development of microangiopathy. Adding together, intra-vitreal vascular endothelial growth factor (VEGF) has been initiate to be connected to PDR action[3]. On close by cellular membranes the auto-antibodies which are Antiphospholipid antibodies (APLA) mark one or few additional phospholipids or PL-binding proteins. It is postulated that (APLA) together with (aCL), are notice in many diseases, but only those initiate in connection with autoimmune disease necessitate the existence of phospholipid binding serum protein[beta-2 glycoprotein I (B2GPI)]. Understanding (aCL), has been the focus of considerable importance due to their conventional role in the pathology of anti-phospholipid syndrome (APS), it is an autoimmune disorder connected with venous and arterial thrombosis and repeated loss of fetus. Anticardiolipin antibodies are against the complex of cardiolipin and the plasma protein cofactor (B2GPI). Presently, B2GPI is considered as the accurate antigenic objective for a CL antibodies. In the walls of blood vessels the immunological marker has been reported for short time period. The incidence of autoantibodies to antigens of endothelial cell surface area may commence vascular injury. Current confirmations recommend that diabetic retinopathy may due to an autoimmune progression. Antiphospholipids antibodies (APLA), together with Anticardiolipin antibodies, are auto-antibodies that mark one or more phospholipids or PL-binding proteins nearby on cellular membranes which may be linked with venous and/or arterial thrombosis. Immunological system may take part an important role in the pathogenesis of diabetic micro-angiopathy by means of deposition of immune complexes[4]. There is a documented involvement between aCL antibodies occurrence and a vascular occlusive disease. The reason of this study was to establish the incidence of anticardiolipin aCL antibodies in patients having proliferative diabetic retinopathy (PDR) with high-risk criteria (HRC) and to inspect whether anticardiolipin aCL antibodies occurrence may be significant to the pathogenesis of DR[5].

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MATERIAL AND METHODS

This study was permitted by the human ethical committee and all participants were signed the written and informed consent before they enters into this study. A large number of patients of DM were screened for signs of PDR along with HRC. According to National Group of Diabetes patients are classified. Thru color fundus examination the morphology of retinal vasculature was assessed. According to the Diabetic Retinopathy Study Research Group criteria, (HRC) were defined. The exclusion criteria includes poor glycemic control HbA1c >9.0%), essential hypertension BP

>140/90), hypercholesterolaemia (>5.7mmol/L), smoking and eye hazy media[6]. Forty patients of diabetes were register in this study. Forty two similar diabetic subjects free of diabetic retinopathy were elected as control group. All 82 patients undergo ophthalmological assessment which includes slit lamp, visual acuity, and fundal lens examination. 5 ml of intra venous blood sample was taken from each patient who further centrifuged and extracted sera were stored in -80C. These Serum samples were examined for anticardiolipin aCL antibodies (IgG & IgM) were resolute by means of Enzyme-Linked Immuno-Sorbent Assay (ELISA) method. Patients having >10 GPL unit/ml (1 GPL unit is 1 microgram of IgG antibody) were consider as positive result for IgG aCL antibodies and negative results when the level <10 GPL unit/ml. Patients were considered positive for IgM aCL antibodies when it was >7.0 MPL unit/ml (1 MPL unit is 1 microgram of IgM antibody) and negative when the titer was <7.0 MPL units/ml. For quantitative variables in descriptive statistics, the mean, range and standard deviation (σ) are used to give details of central tendency and distribution. Dissimilarity among the means of the independent samples was examined by the Student's t tests. Multiple tests includes Pearson's correlation & Fisher's exact probability tests were used to contrast study and control groups and also to test connection among aCL and other variables like age, sex, duration of illness diabetes type, and incidence of PDR by means of HRC. If ($P < 0.05$) all tests were considered significant[7].

RESULTS

Total eighty two (82) diabetic patients were included in this study (39 males, 43 female's age ranges between 24–66 years). Thirty eight included patients were diagnosed type I diabetics while other 44 patients were type II diabetes. Forty (40) patients having PDR with HRC while other forty two (42), patients had no diabetic retinopathy. Statistically there is no difference between age, gender, and diabetes type in both groups**.** Eight patients reported positive for aCL antibodies. No significant association among aCL antibodies with gender and diabetes type appeared in Fisher's exact probability test. No significant association among aCL antibodies with diabetes duration and patient age by using Pearson's correlation test. Eight out of 82 diabetic patients (9.7%) were positive for aCL (IgG) antibodies. while three (3.6%) had positive aCL (IgM) antibodies. 20% of patients having PDR with HRC were positive for aCL. Most recurrent antibody type was (IgG) and are more common in type I diabetes than type II diabetes. Six patients were having type I diabetics (Three of them had both antibodies IgG and IgM and three had IgG antibody only) while two patients were having type II diabetes (IgG antibody only). Not any of diabetic retinopathy free patients was positive for aCL antibodies. The incidence of aCL was identify in 8 (20%) patients (four males and four females) have PDR along with HRC. Statistically significant Fisher's exact probability test ($P = 0.01$). In type I diabetes mellitus patients, aCL was found in 33.3% proliferative diabetic retinopathy patients with HRC, and 9.0% aCL antibodies found in type II diabetes mellitus had PDR along with HRC

Table: 1 Patients characteristic (control group) free of diabetic retinopathy and having PDR with HRC and diabetics

P value	Diabetic patients free of diabetic retinopathy	PDR patients with HRC
Age (years)	45.1±16.0	47.5± 14.2
Gender (M/F) 0.4	20(51.2)/22(58)	19(51.1)/21(48.8)
Duration years Mean± SD 0.3	13.1±2.7	14± 3.1
Median	15	14
Range	9-20	10-18
Type of diabetes (1/2) 0.1	20(47.6%)/22(52.3%)	18(45%)/22(55%)
Total	42(51.2%)	40(48.7%)

Table: 2 Incidence of aCL antibodies (control group) free of diabetic retinopathy and having PDR with HRC and diabetics.

Diabetics with HRC	Type 1 Diabetics free of retinopathy	Type 1 Diabetics Having PDR with HRC	Type 2 diabetics free of retinopathy	Type having PDR Having PDR
IgG (9%)	0	6(33%)	0	2
IgM(0)	0	3(16.6%)	0	0
Total	20	18	22	22

DISCUSSION

In maintaining Hemostasis vascular endothelium plays a major role. Endothelial cell dysfunction and vascular damage occurs near the beginning in the path of diabetic micro-angiopathy. As a consequence these changes may results alteration of endothelium from a thrombo-resistant into a thrombo-genic surface. Vascular injury is inititiated by means of autoantibodies to endothelial cell surface antigens. It is likely that the communication of endothelial cell anion phospholipid with circulating B2GPI stimulate formation of a neo epitope that present identification specificity for aCL. The B2GPI has been revealed to be essential for the anticardiolipin-mediated for its patho-physiological effect. However, there is no reliable interpreter of thrombotic proceedings in a patient having positive aCL antibodies, aCL antibodies are found in the immunoglobulin (Ig) classes IgG, IgM and IgA[8]. The IgA antibodies are significant in the African population .In the current study IgG and IgM were considered significant. It demonstrates the association among IgM, aCL antibodies and in venous thrombosis. In adding together, aCL antibodies may have connected with occlusive ocular diseases. The most characteristic feature in patient with positive aCL antibodies was vasculitis in retinal walls about (60%). The most significant pervasiveness of aCL antibodies which is statistically proven is established in patients having retinal vascular occlusive disorders in the deficiency of main accepted risk factors for retinal thrombosis. A synchronized bilateral central retinal vein

occlusion was found to be connected with aCL antibodies in a patients having leukemia. The frequency of aCL, IgG was elevated in patients with Behcet's disease with non-occlusive thrombosis than in patients with retinal occlusive events. Even though aCL antibodies have been related with a great quantity of diseases, reported only few researches contains these antibodies in DR subjects[9]. In the present study aCL antibodies found in both type I and type II diabetes having PDR with HRC were studied and they both differ in their auto antibodies, immune-genetics and they did not contribute to the loci in genetic vulnerability. In one of the known research study, they institute that the predominance of IgG aCL antibodies in both diabetics type I and type II were to be 8.8% while on the other hand the incidence of IgM aCL was to be 5.8%. In type I diabetes having vascular complications the serum levels of IgM aCL antibodies has been found to be more prevalent as compared without complication. The frequency of (APLA) has been found to be uniformly elevated in both types I and type II diabetics along with retinopathy. The most reasonable justification for endothelial proliferation and neo vascularizations in the retina is due to ischemia in the internal layers secondary to retinal capillary bed closure in some parts.[10] The neo vascularization-stimulating factor is produced by ischemia in retina, which is competent to act locally and disseminate thru the vitreous to different areas of the retina, optic disc, and in the anterior chamber. For diabetic microangiopathy the immunological basis has been recommended by some researchers presenting an amplified deposition of Ig's and Ag–Ab complexes in small blood vessels basement membrane that the production of decarboxylase auto-antibodies, glutamic acid, which may contributing for the avoidance of retinopathy. On the basis of autoimmunity finding as antipericyte and antiendothelial cell autoantibodies in diabetic subjects circulation the (DR) has been recommended as autoimmune disorder. More confirmation suggests the existence of autoimmune process in the proliferative stage of DR. Raising serum levels of tumor necrosis factor-alpha (TNFα) interleukin-8 (IL-8) soluble interleukin-2 receptor in diabetic patients, also had increased vitreous concentration of the (IL-6) and (IL-8) in patients with PDR. In this current study, there are significantly raised levels of aCL in subjects having PDR with HRC suggestive of that aCL may possibly characterize an added risk factor for (PDR) proliferative diabetic retinopathy[11]. The pathophysiological change of vascular endothelium from anti-thrombotic to a pro-thrombotic state may be more prominent in patients with positive anticardiolipin and higher concentrations of immune complexes, in view of the fact that they acquire the capability not only to stimulate platelet activation and its aggregation and also triggers the complement system by means of the classical pathway. Consequently, a probable collaboration among antibodies generation alterations in Hemostasis and endothelial stress has been recommended[12].

CONCLUSION

Further clarifications are required on the basis of investigations thru different immunochemical techniques whether this autoimmune response is the reason, there complications and infuriating factors of this disease. With the perceptive of innovative cellular and molecular processes, latest inventions of therapeutic approach may be envisaged.

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