ORIGINAL ARTICLE

Ischemia Modified Albumin Levels in Diabetes Mellitus Patients with and without Diabetic Retinopathy

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ABSTRACT

Objective: To determine and compare the levels of ischemia modified albumin (IMA) in healthy individuals, diabetes without retinopathy, and diabetic having no proliferative and proliferative retinopathy.

Study Design: Cross sectional comparative study.

Place and Duration of study: Diabetic Clinic, Lahore General Hospital from September 2104 to May 2015.

Materials and Methods: Sixty subjects were divided into three groups with 20 subjects in each. Group I was control group, included healthy subject, Group II included diabetics without retinopathy and group III included diabetics with retinopathy which comprised of both diabetics with proliferative and non-proliferative diabetic retinopathy. Indirect method using a 90 % D lens was used to diagnose diabetic retinopathy by a consultant ophthalmologist. The levels of IMA were measured by a colorimetric albumin cobalt binding assay and the values were presented as absorbance units. Data was analyzed using IBM SPSS version 23.

Results: Out of 66 % of diabetics individuals 33% were diabetics without retinopathy and 33 % were diabetics with retinopathy out of which 55% had proliferative diabetic retinopathy (PDR) and 45% had non proliferative diabetic retinopathy (NPDR). Low levels of IMA were seen in 33% of diabetics without retinopathy and significantly higher levels of IMA were seen in 27 % of diabetics with proliferative diabetic retinopathy.

Conclusion: We conclude from our study that the levels of IMA raise with the progression of the disease, higher levels of IMA are seen in diabetics with proliferative as compared to non proliferative diabetic retinopathy and as compared to diabetic without retinopathy.

Key Words: *Albumin, Diabetes Mellitus, Diabetic Retinopathy, Ischemia, Oxidative Stress*.

Introduction

Diabetes mellitus is globally a major public health priority.[1] The complications of the disease are broadly classified as acute and late complications. which are further classified as microvascular and macrovascular complications.[2] Among the commonest microvascular complications is diabetic retinopathy, which eventually leads to blindness in most cases.[3]

The diabetic retinopathy is classified according to Early Treatment Diabetic Retinopathy Study (ETDRS-the modified Airlie House Classification). Diabetic retinopathy advances from very mild retinopathy, to Non proliferative diabetic retinopathy (NPDR) to Proliferative Diabetic Retinopathy (PDR) in which proliferation of the new blood vessels, in the retina and vitreous gel occurs, thus filling the eye .[4,5,6,]

Human serum albumin has N –terminal which has a tendency to cohere metal ions such as nickel, iron and cobalt. Exposure of human serum albumin to ischemia or oxidative stress leads to biochemical degradation of N terminal thus decreasing its affinity for the metal ions. This human serum albumin having reduced ability to cohere to metal ions is called as ischemia modified albumin. [7]

Initially serum IMA was well thought-out as a valuable indicator for acute coronary syndrome and cardiac ischemia.[8] However, now IMA is also known as an indicator of oxidative stress.[9] Study in the patients of diabetes have shown higher levels of IMA as compared to controls , which result due to uninhibited oxidative stress, on the endothelial cell because of hyperglycemia and subsequently

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Funding Source: NIL; Conflict of Interest: NIL
Received: September 16, 2020; Revised: June 10, 2021
Accepted: July 06, 2021

released reactive oxygen species modifies the albumin.[10] Increased levels of IMA have been seen in patients with diabetic retinopathy as compared to diabetics without retinopathy however very limited literature is available for the levels of IMA in different stages of diabetic retinopathy. A study done by Reddy et al, showed increased levels of IMA in diabetics suffering from PDR when compared with diabetics with NPDR. The succession of the disease from NPDR to PDR results in increased production of reactive oxygen species thereby increasing the levels of serum IMA in diabetics with PDR.[11]

A study done by Gulpamuk et al, suggested that levels of IMA can be used as a biomarker to determine the damage due to tissue ischemia in DM and to classify the different stages of DR, in the future.[12]

Diabetes and its complications considerably influence the life of the patient. Till now no economical marker is available for the early detection of the progression of diabetic retinopathy to proliferative diabetic retinopathy. So, the aim of the study was to determine and compare levels of IMA in healthy individuals, diabetics without retinopathy and diabetics with NPDR and PDR.

Materials and Methods

This comparative and cross-sectional study was carried in diabetic clinic of Lahore General Hospital on 60 subjects including both males and females from September 2014 to May 2015. Sample size came out to be 20 in each group with the power of study=90. Subjects were selected by Nonprobability, purposive sampling. The protocol of this research was accepted by the members of ethical review committee of the Post Graduate Medical Institute of Lahore. The subjects of the study were split into three groups. The control Group 1 consisted of 20 normal healthy adults, group 2 was of 20 diabetic patients without retinopathy and group 3 had 20 diabetic patients with retinopathy out of which 11 had proliferative diabetic retinopathy and 9 had no proliferative diabetic retinopathy. Presence or absence of diabetic retinopathy was diagnosed by an ophthalmologist on slit lamp through an indirect method using a 90D lens. Subjects with history of smoking, hypertension, end stage renal disease, diabetic foot, autonomic neuropathy, liver cirrhosis, acute coronary syndrome, and cerebrovascular occlusion were excluded from the study based on history and clinical examination. Each participant was briefed about the study and then written informed consent was taken.

4 ml of blood sample was collected from antecubital vein under aseptic conditions and was put in gel vial (yellow top) for measurement of IMA. Sample was then routinely centrifuged within 1 hour of collection for 15 minutes at 3000 revolutions per minutes and aliquots of serum samples were stored at -20 °C for a maximum of one week before IMA measurement. Serum levels of IMA were measured by colorimetric method explained by Bar-Or et al and results were reported in absorbanse units,

Data was analyzed using SPSS version 23 and was explored for normality by ShapiroWilk's statistics test of normality. Data came out to be non-parametric. Kruskal wallis test and Mann Whitney U test was applied to compare the parameters among the groups and two groups respectively, and the value of p< 0 .05 was taken as statistically significant

Results

Comparison of the levels of IMA in the three groups showed a significant difference of P<0.00 respectively. Fifty five percent of the population of diabetic retinopathy group had PDR and 45 percent had NPDR (Table I). Comparison of serum IMA levels in group I and diabetics with proliferative retinopathy and no proliferative diabetic retinopathy revealed a significant difference as shown in table II. Comparison of serum IMA between the diabetics without retinopathy and diabetics with PDR revealed a significant difference. However, when IMA of diabetics without retinopathy was compared with NPDR a nonsignificant difference was seen as shown in Table III. When the levels of IMA were compared between diabetics with no proliferative and proliferative diabetic retinopathy a significant difference was revealed as shown in Table IV.

Table I: Frequency Distribution of Study Population

Type of diabetic retinopathy	Frequency	Percentage %
Healthy individuals	20	33%
Diabetics without retinopathy	20	33%
PDR	11	18%
NPDR	9	15%
TOTAL	60	100%

Table II: Comparison of IMA Levels between Healthy Controls, Diabetic with PDR And NPDR

Parameter	Group I n=20	Group III	P value
Ischemia modified Albumin (Absorbance units)	0.51(0.43-0.54)	PDR n=11 0.65(0.61-0.72)	0.00
		NPDR n=9 0.60(0.56-0.72)	0.03

Table III: Comparison of IMA Levels between Diabetics without Retinopathy and Diabetic with PDR and NPDR

Parameter	Group II n=20	Group III	P value
Ischemia modified Albumin (Absorbance units)	**0.59(0.53-0.61)**	PDR n=11 0.65(0.61-0.72)	0.00
		NPDR n=9 0.60(0.56-0.72)	0.44

Table IV: Comparison of Ischemia Modified Albumin Levels in Diabetics with PDR and NPDR

Parameter	PDR n=11	NPDR n=9	P value
Ischemia Modified Albumin Absorbance Units (ABSU)	0.65(0.61-0.72)	0.60(0.56-0.72)	0.03

Discussion

Oxidative stress induced by high blood glucose level in diabetic patients is a leading cause of many ocular degenerative changes, to reduce the hazardous effects of diabetes mellitus on vision an effective screening marker should be introduced to assess the progression of diseases to the proliferative diabetic retinopathy which is a leading cause of blindness. Our study shows high levels of IMA in diabetics with NPDR, and PDR are seen as compared to controls group. Reddy VS et al, 2016 in one of his study concluded that the levels of ischemia modified albumin were higher in patients with NPDR as compared to control group, this supports the idea that there is a role of oxidative stress in the development of diabetic retinopathy.[11] Gaonkar B et. al 2020 in his study concluded that the concentration of oxidative stress markers are higher in patients with proliferative diabetic retinopathy as compared to controls, the results of his study support our study as there is high level of IMA in diabetic with PDR as compared to controls.[13] Retina has a large amount of polyunsaturated fatty acid, and also has maximum capacity of oxygen uptake and glucose utilization as compared to any other tissue in the body, which renders retina susceptible to oxidative stress.[14]

In our study there was non-significant difference in the level of IMA in patients without diabetic retinopathy with Non proliferative diabetic retinopathy. Our result is in correlation with the result shown by Bozkurl et al in 2019 on a group of diabetics without retinopathy and diabetics with non-proliferative diabetic retinopathy in which that the concentration of an oxidative stress marker rises in proportion to the severity of the DR, but the comparison did not show the significant difference.[15] Gulpamuk et al, 2018 in one of his research concluded that increase in oxidative stress in diabetics leads to increase levels of oxidative stress markers such as IMA in diabetics having proliferative retinopathy when compared to diabetics without retinopathy.[12]

The progression of the disease from NPDR to PDR causes a noteworthy rise in the levels of oxidative stress which is reflected by high levels of IMA in our study in diabetics with proliferative diabetic retinopathy as compared to diabetics with non-proliferative diabetic retinopathy. This result is similar to the results seen by Gulpamuk et al in 2018 in which increase in levels of serum IMA were seen in PDR patients as compared to those having NPDR thus indicating underlying ischemia and subclinical inflammation.[12]

Thus, we can say as there is progression of disease from non-proliferative to proliferative diabetic retinopathy there is more oxidative stress leading to underlying ischemia and subclinical inflammation. So, increased level of ischemia modified albumin can be taken as a marker of Proliferative diabetic retinopathy patients as compared to those with Non proliferative diabetic retinopathy

Limitations and Recommendations

Follow-up of the patients with NPDR should have been done in order to see the alteration in the levels of IMA so that the disease may not progress to PDR. In further studies Antioxidants levels and lipid profile should be estimated to evaluate the oxidative status of the body.

Conclusion

We conclude from our study that the levels of IMA raise with the progression of the disease, higher levels of IMA are seen in diabetics with proliferative

as compared to non proliferative diabetic retinopathy and as compared to diabetic without retinopathy.

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