Research Article

Study of glycated haemoglobin, lipid profile and uric acid levels in diabetic retinopathy

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Abstract: Diabetic patients with and without complications show a difference in serum uric acid pattern in relation to duration of disease along with glycemic status, lipid derangements and complications associated with the disease. HbA1c studies were taken to know the blood sugar levels for the past 3 months to assess the glycemic control. Study of lipid profile is also taken to assess the micro vascular complications like Retinopathy in diabetic cases. Behaviour of uric acid levels may indicate the ongoing pathophysiology in diabetes in relation to glycemic control, onset and progression of complications such as retinopathy. The present study consists of 75 cases of chronic diabetes with retinopathy as a complication in the age of 45-75 years. The values are compared with the values of 50 apparently healthy non-diabetics which will fall on the same age group. All the subjects were from ophthalmology department of Govt. General Hospital, Kakinada and also from Nayana Eye Care Hospital, Kakinada. The Mean, SD Values of HbA1C were high in whole blood group of diabetic retinopathy cases, 8.903, +1.549 as compared to control group. The Mean, SD values of uric acid of diabetic retinopathy cases are 4.796, +0.944, which doesn’t show much difference with control group, It shows that poor glycemic control plays a major role on the onset and progression of diabetic retinopathy. In diabetic retinopathy statistically significant lipid profile changes observed. Serum uric acid level has not shown statistically significant changes in diabetic retinopathy. It shows that uric acid values have no significance.

Keywords: HbA1C, lipid profile, uric acid, diabetic retinopathy

INTRODUCTION

Diabetes Mellitus is a global health problem. It is potentially life threatening metabolic syndrome. There are nearly 171 million diabetics worldwide in 2000 with the number projected to almost 2.5 times, about 366 million by the year 2030 (prevalence rate of 4.4%) with the greatest number of cases expected in China and India. India had 32 million diabetics in the year 2000 a number, which is expected to become triple by 2030 when they would constitute about 80 million. Diabetic retinopathy is responsible for 4.8% of the 37 million cases of blindness due to eye diseases throughout the world (i.e. 1.8 million persons).

Diabetic retinopathy is one of the commonest problems in East Godavari District, Andhra Pradesh. Diabetes mellitus is a potentially life threatening metabolic syndrome, characterized by hyperglycemia due to absolute or relative insulin deficiency, causes profound alterations in both micro and macro vasculature affecting nearly every organ of the body.

Diabetes magnifies the risk for vascular diseases several fold, and thus vascular complications are major cause of morbidity and mortality worldwide. There has been a dramatic increase in the prevalence of diabetes globally, expected to reach pandemic proportions by 2030. In India economic drift and its consequent lifestyle have lead to an alarming increase in the prevalence of diabetes, which has now become the greatest health hazard.

Although renal and arterial diseases are the main causes of death in diabetics, the ocular complications of the disease are a major determinant of disability. Diabetics are about 15 times more likely to go blind than non-diabetics and this disease accounts to about 7% of the newly registered blind. Hyperglycemia, increased reactive oxygen species, decreased nitric oxide, increased fatty acids alter the vascular responses, and are the underlying pathogenic mechanisms of chronic vascular complications.

The main causes of blindness in diabetic patients are retinal disease, accounting for about 80% and cataract formation which accounts for the majority of the remaining 20%. Other ophthalmic conditions to which diabetics are liable include optic neuritis and
extra ocular muscle palsy, both of which usually have a favourable prognosis.

Both longitudinal and cross-sectional studies have shown that best predictor of diabetic retinopathy is duration of the disease.

The prevalence of retinopathy determined by these studies varies slightly, but most agrees that for insulin dependent diabetes mellitus; there is virtually no clinically apparent diabetic retinopathy for 4-5 years after the initial diagnosis of diabetes. After 5-10 years of duration about 25-50% of the patients will have some retinopathy and very few, if any will have proliferative retinopathy has been reported to be between 18 and 40% [1].

Similar results have been obtained for type II (non-insulin-dependent) diabetes, but in such patients the time of onset and therefore the duration of disease are more difficult to determine precisely.

It is recommended the patients with type I diabetes mellitus be referred for ophthalmologic examination within 3 years after diagnosis and re-examined on at least on annual basis. Type II diabetic patients should be referred for ophthalmologic examination at the time of diagnosis and re-examined at least annually.

The prevalence of proliferative retinopathy in type I diabetics with 15 years of systemic disease is 50%. While the prevalence of proliferative disease at 15 years is much less in type II diabetics, the prevalence of macular edema as a function of the duration of systemic disease is the same in both groups.

Despite all of these theoretic benefits, clinical trials have thus far failed to show a reduction in the incidence of diabetic retinopathy or neuropathy with the use of aldose reductase inhibitors, possibly because an effective aldose reductase inhibitor with few systemic side effects has yet to be developed.

Vascular endothelial growth factor, which inhibits the growth of retinal endothelial cells in vitro, has recently been implicated in diabetic retinopathy. This factor is found in the vitreous of patients with diabetic retinopathy and decreases after pan retinal photocoagulation. Further, experimental intravitreal injections of vascular endothelial growth factor produce retinal ischemia and micro angiopathy in primates.

One of the early symptoms of diabetic retinopathy is poor night vision (dark adaptation) and poor recovery from bright lights (photo stress). Blue-yellow discrimination is affected earlier and more severely than is red-green discrimination. One of the earliest electro physiologic abnormalities seen in diabetic patients without ophthalmoscopically visible retinopathy is diminution of the amplitude of the oscillatory potentials of the electroretinogram at a time when both the a and b waves are normal. This abnormality probably reflects ischemia in the inner nuclear layer of the retina. The first point of attack of hypoxia is oxidative phosphorylation of cells resulting in increased anaerobic glycolysis, decreased generation of ATP and increased accumulation of lactic acid.

Secondly ischemia induced depolarization of retina causes excessive release of Glutamate, which overexcites NMDA-receptors and abnormally large influxes of intra-cellular Calcium ion (Ca++). Third phenomenon of cellular ischemia is activation of endogenous phospholipase, degradation of membrane phospholipids, formation of arachidonic acid, eicosanoids and oxygen derived free radicals. Ultimately hypoxic cells secrete VEGF to revascularize patients who have had insulin-dependent diabetes mellitus (IDDM) for 5 years or less rarely show any evidence of diabetic retinopathy. However, 27% of those who have had IDDM for 5 to 10 years and 71% to 90% of those who have had IDDM for longer than 10 years have diabetic retinopathy.

After 20 to 30 years, the incidence rises to 95%, and about one third to one half of these patients have proliferative diabetic retinopathy. Determining the role of duration of diabetes as a predictor of retinopathy in non-insulin dependent mellitus (NIDDM) is more difficult because of the uncertainty of onset in many patients.

The decades-old controversy as to whether or not good metabolic control prevents the development or progression of retinopathy was finally laid to rest by the Diabetes Control and Complications Trial (DCCT) and the Oslo study.

Retrospective studies using measurements of Glycosylated haemoglobin (HbA1C) to evaluate relatively long-term glycaemic control have suggested that, chronic hyperglycemia is closely related to the development of diabetic retinopathy; it proved that strict blood sugar control reduces the risk of development and progression of diabetic retinopathy. The benefits of rigorous control of blood glucose do not extend to eyes with advanced diabetic retinopathy. Even patients who are made normoglycemic by pancreatic transplantation continue to show progression of retinopathy. Elevated serum cholesterol is a strong predictor for the rate of visual loss. Patients with elevated total cholesterol and low-density lipoprotein cholesterol are much more likely to have severe, hard exudates in the macula, and this correlates strongly with visual loss.

Experimental section
The present study was conducted in the Department of Biochemistry, Rangaraya medical college, Kakinada, from patients of Government

General Hospital (GGH), Kakinada, East Godavari District, and Andhra Pradesh.

The present study consists of 75 cases of chronic diabetes with retinopathy as a complication in the age of 45-75 years. The values are compared with the values of 50 apparently healthy non-diabetics which will fall on the same age group.

All the subjects were from ophthalmology department of Govt. General Hospital, Kakinada, who attended for checkups and treatment. And also from Nayana Eye Care Hospital, Kakinada, which is super specialty Eye Hospital in coastal districts.

Demographic and clinical data were collected from the above two hospitals. Blood samples were obtained from Vene Puncture from antecubital veins of upper limbs on the test groups. Consent was obtained from both cases and control groups.

Anticoagulated whole blood is analysed for glycated haemoglobin HbA1c. plasma was separated and analyzed by using standard methods.

Keeping in view of risk of diabetes patient with retinopathy were studied with the following objectives.

- To study the glycated haemoglobin (HbA1c) levels in Diabetic Retinopathy.
- To study Lipid Profile levels in Diabetic Retinopathy.
  - Cholesterol Levels in Diabetic Retinopathy.
  - Triglyceride levels in Diabetic Retinopathy.
  - HDL Cholesterol levels in Diabetic Retinopathy.
  - LDL Cholesterol levels in Diabetic Retinopathy.
- To study Serum Uric acid levels in Diabetic Retinopathy.

Methods of estimation

- Measurement of HbA1c (glycated haemoglobin) by turbidimetric method (Siemens Dimension Xpand plus)
- Principles of Procedure:
  - The polyhepten reacts with excess (free) anti-HbA1c antibodies to form an insoluble antibody-polyhepten complex. The rate of this reaction is measured turbidimetrically at 340nm and blanked at 700nm and is inversely proportional to the concentration of HbA1c in the sample.
  - Anti HbA1c – antu body (excess) + poly hepten Ab/polyhepten complex. (Absorbs at 340nm)
  - Estimation of serum cholesterol – CHOD PAP method
  - The triglycerides method is based on an enzymatic procedure
  - The AHDL assay measures HDL cholesterol levels directly without the need for sample pre-treatment or specialized centrifugation steps
  - Estimation of uric acid uricase/pod, End Point Assay
  - The ALDL Cholesterol assay is homogenous method for directly measuring LDL-C levels in human sera or plasma, without the need for any off-line pre-treatment or centrifugation step present study.

RESULTS AND DISCUSSION

Table 1: showing mean, SD values of various parameters in controls versus diabetic retinopathy cases

<table>
<thead>
<tr>
<th></th>
<th>Control Group</th>
<th>Diabetic Retinopathy Group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>HbA1C</td>
<td>5.878</td>
<td>0.391</td>
</tr>
<tr>
<td>CHOLESTEROL</td>
<td>156.98</td>
<td>24.94</td>
</tr>
<tr>
<td>TGL</td>
<td>128.28</td>
<td>30.54</td>
</tr>
<tr>
<td>HDL</td>
<td>44.86</td>
<td>8.18</td>
</tr>
<tr>
<td>LDL</td>
<td>101.48</td>
<td>17.14</td>
</tr>
<tr>
<td>SERUM URIC ACID</td>
<td>4.948</td>
<td>1.278</td>
</tr>
</tbody>
</table>

Table 2: t’-value and ‘p’-value of different parameters in study group

<table>
<thead>
<tr>
<th>PARAMETER</th>
<th>‘t’-Value</th>
<th>‘p’-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HB A1C</td>
<td>13.5082</td>
<td>&lt; 0.0001 ***</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>6.9390</td>
<td>&lt; 0.0001 ***</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>7.4286</td>
<td>&lt; 0.0001 ***</td>
</tr>
<tr>
<td>HDL</td>
<td>4.2602</td>
<td>&lt; 0.0001 ***</td>
</tr>
<tr>
<td>LDL</td>
<td>3.7776</td>
<td>&lt; 0.0002 ***</td>
</tr>
<tr>
<td>Uric acid</td>
<td>0.7642</td>
<td>Equal to 0.446 *</td>
</tr>
</tbody>
</table>
It can be deducted from the table 1 that the Mean, SD Values of HbA1C were high in whole blood group of Diabetic Retinopathy cases, 8.903, +1.549 as compared to control group Mean, SD value 5.878, +0.391. Similarly the Mean, SD values of Lipid Profile were high in Diabetic Retinopathy Cases when compared to control group 202.04 + 41.12, the Mean, SD value TGL 217.21, +80.8, the Mean, SD for LDL 120.69, +33.09. The Mean, SD values are of control group for Cholesterol 156.98, +24.94 for TGL 128.28, +30.54, for HDL 44.86, +8.18 and for LDL 101.48, +17.14.

The Mean, SD values of Uric Acid of Diabetic Retinopathy cases are 4.796, +0.944, which doesn’t show much difference with control group, whose Mean & SD Values are 4.948, +1.278. Study of Diabetic Retinopathy and Serum Lipids by D H W Su, et al show a positive relationship between serum cholesterol and low-density lipoprotein levels and retinal hard exudation [2]. Other studies show serum triglyceride levels as being important in the progression of retinopathy. Weber et al reported that serum triglycerides, but not cholesterol, were associated with diabetic retinopathy in children with Type 1 (insulin-dependent) diabetes mellitus [3].

Gordon et al found that the use of pravastatin for 1 year in patients with diabetes and moderately high total serum cholesterol levels did result in an improvement in diabetic retinopathy [4]. Behaviour of serum uric acid and lipid profile studied in relation to glycemic status in proliferative and non-proliferative diabetic retinopathy by Asha kiran et al.: [5]. High hemoglobin A1c level, high 2-hr blood glucose level, low uric acid level and positivity for proteinuria were found to be significantly associated for the development of diabetic retinopathy [6].

Behaviour of uric acid levels may thus indicate along with co-existence of lipid derangements, the ongoing patho physiology in diabetes in relation to glycemic control, insulin resistance, onset and progression of complications such as retinopathy and nephropathy. It is postulated that uric acid levels have tendency to decrease before complications like retinopathy complication sets in [7]. Similar studies of serum lipoprotein, cholesterol profile in diabetic retinopathy done by SP Dhir, Rajvir Dahiyan et al.: [8].

The level of non esterified fatty acids was significantly higher in diabetic with retinopathy as compared to without retinopathy. [9]. Lopes Virella et al.: [4] found inverse correlation of high density lipoprotein cholesterol (HDL-c) with poorly controlled diabetics [10].

Study on risk factors of poor control of HbA1c and diabetic retinopathy: Paradox with insulin therapy and high values of HDL in African diabetic patients is done by B Longo-Mbenza, MM et al.: [11]. Retinopathy and serum uric acid in diabetics by Feldman T [12]. Low serum uric acid (UA) levels have been reported in diabetics. In a group followed for 15 years it was reported that low UA levels preceded the onset of diabetic retinopathy. Multiple regression analysis showed that higher UA levels were related independently to high body mass index (overweight, obesity), and male gender [13]. Prevalence and 15-year incidence of retinopathy and associated characteristics in middle-aged and elderly diabetic men by LUTZA YANKO [14] Low serum uric acid appears to precede the incidence of diabetic retinopathy and to decline further as the disease progresses.

HbA1c levels were significantly elevated in Diabetic Retinopathy cases (p <0.0001) when compared to the controls. It shows that in diabetic cases poor glycemic control for prolonged period will lead to micro vascular changes and Retinopathy. Similar results were observed in the study of “Risk factors of poor control of HbA1C and Diabetic Retinopathy” by B Longo-Mbenza, MM Muaaka, G Mbenza.

The lipid profile studies shows the cholesterol levels increases in diabetic retinopathy shows statistically significant p value<0.0001. TGL levels increased will also show statistically significance p-value<0.0001. HDL levels decreased will also show statistically significance p-value<0.0001. LDL levels increased will also show statistically significance p-value<0.0002.

Similar results were observed in the study of “Diabetic Retinopathy and Serum Lipids 36” by D H W Su and K T Yeo. And also in the study of “Serum Lipoprotein Cholesterol Profile in Diabetic Retinopathy” by Dhir SP, Dahiya R, Ram J.

In the present study changes in the Serum Uric Acid levels were not significant (p-value = 0.446), when compared to the control group. It shows that the Uric Acid levels have no correlation in the Diabetic Retinopathy, in the present study. Similar observations were reported in the study of “Retinopathy and Serum Uric Acid in Diabetics ” by Feldman T, Weitzman S, Biedner B, saying that no relation of Uric Acid level variation for the age and duration of Diabetes, Glycated Haemoglobin in Diabetic Retinopathy cases.

CONCLUSION
The salient findings of the present study of Diabetic Retinopathy from the Bio-Chemical parameters are as follows:

The glycosylated haemoglobin levels were significantly elevated in the Diabetic retinopathy cases as compared to the controls. It shows that poor glycemic control plays a major role on the onset and progression of Diabetic Retinopathy.
The lipid profile study in Diabetic Retinopathy shows:

- Statistically significant elevation of Cholesterol level.
- Statistically significant elevation of TGL level.
- Statistically significant decreased HDL level.
- Statistically significant elevation of LDL level.

It shows that in Diabetic Retinopathy statistically significant Lipid Profile changes observed.

Serum Uric Acid level has not shown statistically significant changes in Diabetic Retinopathy. It shows that Uric Acid values have no significance in Diabetic Retinopathy in the present study.

Control of Diabetes Mellitus is most important factor associated with prevention of onset and progression of Retinopathy.

REFERENCE