Retinopathy and Microalbuminuria in Type 2 Diabetic patients.

Masoud R. Manaviat (1), Mohammad R Shoja(2) Mohammad Afkhami Ardekani (3)

Address: Diabetes Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.

Background: The aim of this study was to identify risk factors for the development of retinopathy and microalbuminuria and their correlation in diabetes type 2 patients.

Methods: In this cross sectional study 591 patients with diabetes type 2 were examined. Fundoscopy was performed by practising Ophthalmologist. The urinary albumin to creatinin ratio was assessed by clinitek 100 (Bayer corporation – USA). HbA1C, height, weight also was measured.

Results: The overall prevalence of retinopathy was 39.3% (232 patients), from this group 5.5% was PDR. Diabetic retinopathy had significant inverse correlation with BMI. (P=0.02) HbA1C was higher in patients with PDR (mean = 10.5) than in patients without retinopathy (mean=9.5) and this difference was statistically significant (P=0.001). The prevalence of microalbuminuria was 23.5% also 12.8% had macroalbuminuria. As expected diabetic retinopathy and renal involvement were strongly positively associated (P=0.001).

Conclusion: Microalbuminuria is associated with diabetic retinopathy in diabetes type 2 patients and is a reliable marker of retinopathy.

Keywords: Retinopathy – Microalbuminuria – Diabetes type II

Correspondance: Diabetes Research Center , Jomhoori Blvd, Yazd, Iran.

Tell: +98 3515258234

Fax: +983515258354

Email: m_r@manaviat

Email: M.R.SHOJA: (shoja99@ yahoo.com)
Introduction:

Diabetes mellitus is one of the most common metabolic diseases in which either the hormone insulin is lacking or the body’s cells are insensitive to insulin’s effects. The multisystem effects of diabetes such as retinopathy, nephropathy, neuropathy and cardiovascular disease are public health problems.

Diabetic retinopathy is one of the leading cause of blindness in the world that increases the chance of losing the sight about 25 folds compared to normal individuals. Using new surgical and/or medical techniques, the incidence of blindness can be reduced by 90%. Decrease in visual acuity in diabetic retinopathy is either associated with maculopathy or proliferative complications of it. Many studies underwent to find out the precipitated factors of retinopathy such as duration and type of diabetes, hyperglycemia, pregnancy, change in hormonal level, genetics and microalbuminuria.

The occurrence of microalbuminuria in type I diabetes is strongly predictive of renal and cardiovascular disease whereas in type II less association is observed.

The purpose of this study is to evaluate the incidence of microalbuminuria, macroalbuminuria and their relation to diabetic retinopathy and other risk factors such as hyperglycemia, hypertension in diabetes type II.

Method:

This cross-sectional study prepared for patients with type II diabetes whom presented to Yazd Center of Diabetes Research between years 2000 to 2001. Subsequent to completing preliminary questionnaires that included personal data, patient’s ophthalmologic examination and laboratory tests completed.

Clinitek 100 (made by Bayer Corporation-Elkhart, IN 46515, USA) was used to measure microalbuminuria. Three urine samples were taken in three to six months duration and if two samples were positive, microalbuminuria was affirmative. The device shows the ratio of albumin to creatinine in mg/g. If the ratio was less than 30 the patient is normoalbuminuric. Ratios between 30-300 are indicative of microalbuminuria and above 300mg/g considered macroalbuminuria.

Detailed assessment completed to exclude other possible causes of microalbuminuria. Ophthalmologic examination including visual acuity (by means of snellen charts), intraocular pressure (using Applanation Tonometry), fundoscopy (utilizing slit lam) and contact lenses) and indirect ophthalmoscopy completed. If required, fluorescein...
angiography was ordered. All the relevant examinations completed by an ophthalmologist. Patients were categorized according to their retinopathy.

No retinopathy
Mild Nonproliferative Diabetic Retinopathy (NPDR)
Moderate NPDR
Severe NPDR
Proliferative diabetic retinopathy (PDR)

Five minutes after resting in sitting position, patient’s blood pressure by mercury Sphygmomanometer was measured. BP ≥ 135/80 mmHg was considered abnormal.

Patient’s medications including hypertensive drugs were recorded. Body Mass Index (BMI) also documented. HbA1c was ordered and data was analyzed by chi-square and Fischer exact tests. P values < 0.05 were considered significant.

Results:

A total of 591 patients (346 females and 245 males) included in this study. Mean of age was 54.9±10.2 and patients diabetes duration were between 1 to 32 years (Mean = 10.2±6.6). Of the patients 39.4% had some degree of retinopathy; 19.1% had mild NPDR, 12% Moderate, 2.7% severe and 5.6% had PDR. 52 patients (13.3%) had CSME (Clinically Significant Macular Edema) of whom 1 with grade II, 35 grade III, 13 grade IV, and 3 had grade V retinopathy. About 200 of patients had BP ≥ 135/80 mmHg. There was no significant relationship (p=0.37) between high blood pressure and different degrees of retinopathy. Gender and type of retinopathy also had no significant correlation with grading of retinopathy. (p=0.31).

Relationship between different types of retinopathy and risk factors such as duration of diabetes, HbA1c, FBS, BMI, and age were significant. (Table1).

TABLE 1

<table>
<thead>
<tr>
<th>BETWEEN GROUPS</th>
<th>p value</th>
</tr>
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<tbody>
<tr>
<td>Duration of diagnosis</td>
<td>0.001</td>
</tr>
<tr>
<td>HbA1c</td>
<td>0.001</td>
</tr>
<tr>
<td>Mean FBS</td>
<td>0.001</td>
</tr>
<tr>
<td>BMI</td>
<td>0.028</td>
</tr>
<tr>
<td>Age</td>
<td>0.014</td>
</tr>
</tbody>
</table>

Examination of urine samples in 320 subjects (54.0%) showed normal range of albumin excretion (normoalbuminuria). Of patients 23.5% percent were microalbuminorirc and 12.8% had macroalbuminuria. Table 2 shows significant relationship between different grades of retinopathy and albuminuria. (p=0.001)
TABLE 2

<table>
<thead>
<tr>
<th>Albuminuria</th>
<th>Diabetic Retinopathy</th>
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<tbody>
<tr>
<td></td>
<td>Grade 0</td>
</tr>
<tr>
<td>Normoalbuminuria</td>
<td></td>
</tr>
<tr>
<td>230 (71.9%)</td>
<td>57 (17.8%)</td>
</tr>
<tr>
<td>Microalbuminuria</td>
<td></td>
</tr>
<tr>
<td>80 (57.9%)</td>
<td>25 (17.9%)</td>
</tr>
<tr>
<td>Macroalbuminuria</td>
<td></td>
</tr>
<tr>
<td>16 (21.1%)</td>
<td>20 (26.3%)</td>
</tr>
<tr>
<td>Not possible</td>
<td>32 (58.2%)</td>
</tr>
<tr>
<td>Total</td>
<td>358 (60.6%)</td>
</tr>
</tbody>
</table>

Discussion:

Numerous studies carried out to determine the incidence of retinopathy and albuminuria in diabetes Type II. These studies yielded different rates between 16 to 53.4%. Our study showed incidence rate of 39.4% which is somewhere in median range. The variation in rate could be as a result of different methods used in those studies, the population and or races involved, or variation in controlling blood sugar level. The incidences of microalbuminuria and macroalbuminuria in our study were 23.5% and 12.8% respectively. Parving et al reported the incidence rate of 22% of microalbuminuria in diabetes type II whereas Lunetta reported the incidence rate of 15%. The above-mentioned studies show that there is a significant relationship between the degree of retinopathy and albuminuria. However there are few studies oppose such relationship. Erasmus et al showed among 113 patients with NIDDM, the incidence rate of microalbuminuria was as high as 54% among males and 59% among females. Prevalences of retinopathy and hypertension were 16% and 41% respectively. They concluded that microalbuminuria may not predict retinopathy and occurs independently of either glycaemic control or elevated blood pressure levels. The population chosen for the study influences the different incidences achieved in various studies. For example, 5-6% of normal non-diabetes individuals in United Kingdom and United States of America have microalbuminuria whereas in South Korea this value is 12.2% and in Finland is 30-35%.

Our study showed that microalbuminuria in addition to HbA1c, BMI, and Length of illness, is a contributing factor in the degree of retinopathy (p=0.001) and this correlation can be explained by the common mechanism involved in tissue damage by all those factors. In addition to blood sugar level and blood pressure, there are also other factors to damage vessels in retina and kidney. For example, Klein et al showed that microalbuminuria could be seen in 29.2% of insulin taking patients and 22% of
non-insulin dependent patients. Therefore, insulin can also have a role in nephropathy.\textsuperscript{12}

In a study of 497 normal nondiabetic cases above 40 years in seoul Kim et al after regression analysis reported that fasting plasma level of insulin and systolic blood pressure have had independent correlation with micoralbumiuria\textsuperscript{11}. Besides common mechanisms, renal damage may accelerated retinopatuy with increased blood pressure and serum levels of fibrinogen and lipoproteins. Also microalbuminuria has direct correlation with incidence of coronary heart disease.\textsuperscript{4,13} Albuminuria also has been considered as a predictor of diabetic retinopathy, and coronary heart disease and therefore urine excretion of albumin is a sign of kidney involvement and can reflect generalized vessel damage throughout the body. Further prospective studies should be carried out to evaluate the effect of lowering albumin excretion on reducing vessel damage.

\textbf{Conclusion}:

Microalbuminuroa is associated cross sectionaly with the presence of retinopathy in persons with diabetes type II. These data suggest that microalbuminurinia may be a marker for the risk of proliferative retinopathy developing. If longitudinal studies confirm these findings diabetes patients who have microalbuminuria may benefit from close ophthalmologic follow up.

\textbf{List of abbreviations used}

BMI= Body mass index.
NPDR= Non proliferative diabetic retinopathy.
PDR= Proliferative diabetic retinopathy.

\textbf{Competing interest.} 
None declared.

\textbf{Authors' contributions}

MRM, the director of the project, participated in the design of the study and the examination of protocol. MAM, participated in the statistical analysis and the design of study. MRS, the manager of project, participated in the design of study and will coordinate the study. All authors have read and approved the final manuscript.

\textbf{Acknowledgements}

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