Original Research Article

Twenty years with type 2 diabetes: ocular and associated complications

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ABSTRACT

Purpose: To evaluate the incidence of ocular and renal complications in known patients of diabetes mellitus (DM) with more than 20 years of disease duration.**Materials and Methods:** A total of 50 patients diagnosed with Type 2 DM with disease duration of more than 20 years underwent ophthalmic evaluation and as well for renal status and biochemical analysis.**Results:** With a disease duration between 20 to 31 years, 84% (42/50) patients had a disease duration from 20 years to 25 years. The distribution of various stages of diabetic retinopathy (DR) showed that 1/5th of the study group had no DR. Only 10% had PDR. This data suggests that after 20 years of disease duration the number of subjects with no DR were double that of the severe stage of retinopathy which is PDR. In this study there were only 8/50 patients with CKD (16%).**Conclusion:** With increasing age there is surprisingly lesser incidence of complications of DM in this study group.© This is an open access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>) which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

1. Introduction

Diabetes mellitus (DM) is a one of the leading life style disorders affecting this part of the world.¹ The persistent hyperglycemia has been held responsible for the occurrence of various organ and tissue damage in diabetic patients. Eyes, kidneys and peripheral nerves that have been frequently damaged due to diabetes related micro-vessels alteration.²⁻⁴ Both DCCT (diabetes control and complications trial) and EDIC (epidemiology of diabetes interventions and complications) studies have also summarized that chronic glycaemia and duration of diabetes were the major factors in the pathogenesis of micro-vascular complications in their cohort of Type 1 diabetes.^{5,6} Furthermore, large vessels are also damaged causing severe diseases such as myocardial infarction, cerebral infarction

and gangrene. Park et al.⁷ in their study on DR and renal disease, found that longer duration of DM, poorer control of blood sugar and that baseline DR severity was associated with faster renal function decline. They found that NPDR (non proliferative diabetic retinopathy) had 2.9 times and PDR (proliferative diabetic retinopathy) had 16.6 times higher risk for CKD (chronic renal disease) progression.

The ocular manifestations of diabetes include all the tissues of the eye. Of these, diabetic retinopathy (DR) has been a major cause of avoidable blindness in both the developing and the developed countries. Among the independent risk factors for severity of DR has been duration of diabetes mellitus (DM), HbA1c, male gender and macro-albuminuria.⁷ It can be seen that duration of DM has been a constant underlying factor characterising the complications related to the same.

The advent of newer insulin preparations and newer drugs with different mechanism of actions coupled

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with early detection subsequent to increasing awareness have increased the longevity of diabetics. Apart from these factors, in the last three decades, the treatment strategies for DR have been revised which include early surgical interventions and pharmacotherapies besides laser photocoagulation.

The DCCT and EDIC studies have shown a decrease in the morbidity due to DM in patients with intensive treatment including the retinal complications. The Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR) XXIII report, had noted that those patients who had been diagnosed most recently with a similar duration of diabetes had a lower prevalence of PDR independently of glycosylated hemoglobin level, blood pressure level, and presence of proteinuria. This fact was attributed to the improvement in diabetes care.⁸ DCCT/EDIC studies have also supported the fact that intensive therapy aimed at achieving glycaemic levels as close to the non-diabetic range as safely as possible reduce the development and progression of all diabetes-specific complications by as much as 76%.^{5,6}

There have been many studies on the duration of disease and the incidence of retinopathy in type I disease but literature has not been enriched with observations on this aspect in subjects with type 2 disease. A hospital based cross-sectional study on diabetic patients visiting the outpatient department of ophthalmology was therefore conducted to evaluate the incidence of retinopathy, other ocular manifestations, status of glycaemic control and renal status in patients with type 2 DM having the disease of more than 20 years after diagnosis.

2. Materials and Methods

After obtaining institutional ethical clearance, and obtaining written consent patients diagnosed with type 2 DM at medicine/ endocrine OPDs of a tertiary care teaching hospital with disease duration of more than 20 years were enrolled in the study. The duration of the disease was ascertained from the documents available with the patients. These included OPD books/ In- patient discharge documents and medical documents of insurance patients. Patients with no available documents were excluded.

The enrolled patients were then subjected to complete ocular examination. Best corrected visual acuity (BCVA) in both eyes (unaided & aided), detailed anterior segment evaluation with diffuse illumination and by slit lamp bio-microscopy in particular for neo-vascularisation of iris (NVI), evaluation of anterior vitreous by slit-lamp bio-microscopy, fundus examination by direct ophthalmoscopy & by 90 D with slit lamp bio-microscopy and measurement of intra ocular tension with Goldmann applanation tonometer were performed. Fundus photography and fundus fluorescein angiography was performed as per requirement. The DR was classified as per the early Treatment of Diabetic

Retinopathy Study (ETDRS) classification.

A complete medical history for evidence of renal disease, hypertension, coronary arterial disease and cerebro-vascular disease was obtained. History of all medications taken by the patient and use of any ocular topical medication was obtained.

After completing the ophthalmic examination, the patients were subjected to laboratory investigations consisting of estimation of blood sugar levels, HbA1C, blood urea, serum creatinine and lipid profile.

The following were the inclusion/exclusion criteria:

2.1. Inclusion criteria

1. Patients diagnosed with type 2 DM from endocrine/medicine OPD.
2. Patients having type 2 DM 20 years or more based on available documentation.

2.2. Exclusion criteria

1. Patients with no documentation
2. Patients with NVI and NVG

The diagnosis of chronic kidney disease (CKD) was based on the evaluation done from the nephrology OPD. The ocular findings were correlated with HbA1C results and renal status. The data was tabulated and subjected to statistical analyses.

Evaluation of hypertension was excluded from the analysis as all the study population was hypertensive and on treatment. Total of 50 patients were studied.

3. Results

The age range of the study group was from 48 years to 85 years. Majority of the patients were within the age range of 61 to 70 years (52%) constituting half the study population. The mean age was 65.04 years (SD: 7.29). There was male preponderance (Table 1). When the criteria of age of the patient was compared with sex, lens status, retinal status, renal status and HbA1C, the same was not found significant. (Table 2).

Of the study group of 50 subjects, 10 patients (20%) had no DR, 17 (34%) had mild NPDR, 11 (22%) had moderate NPDR and 12 (24%) had Severe NPDR and PDR. The retinal status did not have any significance with the lens status. Retinal status has also not been related to age. The various stages of DR have been equally distributed across all ages. (Tables 2 and 5). The numbers of patients with any level of DR (Table 3) have been more among patients with the disease duration of 20-22 years. With increasing duration of disease, the percentage of any DR has been found to be decreasing with 16% (8/50). This fact has also been statistically significant.

The retinal status (Table 4) has also been statistically significant when compared to HbA1C levels. In this study group the 38% (19/50) had HbA1C of $\leq 6.5\%$. This included the all 20% (10/50) who had no retinopathy. The remaining 09 had only mild NPDR. Significantly, all the 31/50 study group that had retinopathy also had HbA1C of more than 6.5. Among these subjects with DR, 08 (25%) had mild NPDR. The remaining were having more severe stages of DR.

The retinal status when compared to the renal status has been quite significant (Table 5). This significance has been for the 07 cases that had CKD. All these had DR and 06 of them had severe NPDR to PDR. In comparison patients with mild and moderate NPDR (excepting 01) did not have CKD. Glycosylated Hb. (Table 4)

Glycosylated hemoglobin levels reflect the long-term glycemic control. The range of HbA1C levels has been from 6.5% to 11% with a mean of 7.74%. This probably refers to the glycemic control of the study population as a whole. In this study group, 62% had a good control. However, the difference between the two groups of $< 6.5\%$ and $> 6.5\%$ has not been statistically significant. HbA1C levels were not statistically significant when compared to age, sex and lens status. HbA1C levels were significant when compared with retinal status, renal status and duration of disease.

There were only 8/50 patients with CKD (16%). The renal parameters were statistically not significant with age, sex, lens status or duration of disease. The association of renal disease has been seen with all durations of disease. However they have been statistically significant when compared with various stages of DR. The renal parameters have also been statistically significant when compared to HbA1C levels (Table 6). All the 08 cases of CKD had more than 6.5% of HbA1C (Table 5). The range of disease duration was from 20 years to 31 years. Of the study group, 84% (42/50) were having disease duration of 20-25 years compared to 16% (8/50) of patients with 25-29 years of disease duration. This difference has been found to be statistically significant. The duration of the disease when compared to sex and lens status has not been significant and this stands to reason. The duration of disease when compared to renal status was also not significant.

4. Discussion

DM was detected from ages of 28 to 65 years since this study group was formed of patients with more than 20 years of disease duration. This data has been in consonance with the global study.⁸ The mean age of the study group of 65.04 years (SD: 7.29) has corroborated the increasing longevity of patients with DM.

Another inference based on the findings in this study on the statistically significant number of patients having a disease duration of 20 to 25 years is that if an analysis were to be done in long standing diabetics of more than 50 years

of age, the chances for them to have a disease duration of more than 20 years would be high.

Increasing age of the patient and increasing disease duration are two aspects. It was seen that increasing age had no correlation with any other parameter.

The male preponderance in this study has been a deviation. The reason for this could be the sample size as also the fact that this study was conducted at a service hospital where attendance by male patients would usually be heavy. However, the parameter of sex has not been found to be statistically significant when compared to all other parameters. This however has been in variance with studies wherein male sex has been considered to be a risk factor for DR.⁶ The data of this study suggests that after 20 years of disease duration the number of subjects with no DR have been double that of the severe stage of retinopathy which is PDR. However, the various stages of DR also have no statistical significance amongst them.

With increasing duration of disease, the percentage of any DR has been found to be decreasing in this study. This fact has also been statistically significant. This corroborates with the studies of Finn-Diane which has shown lesser DR in cases with more disease duration.⁹ However in those subjects who had DR, the severity was associated with HbA1C above 6.5% which however, is in consonance with existing knowledge.

The 16% CKD prevalence in this has been in consonance with the studies of Verdaguer.¹⁰ However, the renal parameters were statistically not significant with age, sex, lens status or duration of disease but with all durations of diseases as also with various stages of DR as with HbA1C of more than 6.5%. It may be seen that CKD was seen with cases with Moderate NPDR upwards which is in consonance with the available data on this aspect from various studies world over.⁷

HbA1C levels were significant when compared with retinal status, renal status and duration of disease which have already been discussed. It may be seen that higher stages of DR and CKD are associated with higher levels of HbA1C. When HbA1C is compared to the duration of disease it appears that with disease duration of 20 – 25 years, majority of the patients had a poorer control which was statistically significant.

The main thrust of this study has been the duration of disease. Majority of the patients 42/50 (84%) were having a disease duration from 20 to 25 years and when this was compared to the remaining 8/50 (16%), this difference was statistically significant with a p value of 0.01. This fact implies that majority of diabetics in this study had an average of 22 years of disease duration. Of these patients with disease duration of 20 to 25 years, there were 34 subjects with any retinopathy compared to 06 among patients with disease duration of more than 25 years. The duration of disease when compared to renal status is also

Table 1: Age & sex distribution

Sex	41-50	51-60	Age 61-70	71-80	81-90	Total
Female	01	06	03	03	0	13(26)
Male	01	06	23	06	01	37(74)
Total	02	12	26	09	01	50(100)

Table 2: Analyses of age with disease duration

Duration of Disease	41-50	51-60	Age 61-70	71-80	81-90	Total	P Value
20-22	02	11	13	05	0	31(62)	0.010
23-25	0	0	08	03	0	11(22)	
26-28	0	01	04	00	0	5(10)	
29-31	0	0	01	01	01	3(6)	
Total	02	12	26	09	01	50(100)	

Table 3: Table analyses of retinal status with disease duration

Hb A1c	Normal	Mild NPDR	Retinal Status Moderate NPDR	Severe NPDR	PDR	Total	P Value
≤6.5	10	09	0	0	0	19(38)	<0.001
>6.5	0	08	11	07	05	31(62)	
Total	10	17	11	07	05	50(100)	

Table 4: Analyses of Retinal status with HbA1C

Duration of Disease	Normal	Mild NPDR	Retinal Status Moderate NPDR	Severe NPDR	PDR	Total	p Value
20-22	04	11	09	04	03	31(62)	0.038
23-25	04	05	0	01	01	11(22)	
26-28	0	0	02	02	01	5(10)	
29-31	02	01	0	0	0	3(6)	
Total	10	17	11	07	05	50(100)	

Table 5: Analyses of retinal status with renal status

RFT	Normal	Mild NPDR	Retinal Status Moderate NPDR	Severe NPDR	PDR	Total	P Value
CKD	0	0	01	03	04	8	<0.001
WNL	10	17	10	04	01	42	
Total	10	17	11	07	05	50	

Table 6: Analyses of CKD with HbA1C

HbA1c	CKD	WNL	Total
≤6.5	0	19	19
>6.5	08 (p 0.016)	23	31
Total	08	42	50

not significant. This would indicate that apart from glycemic toxicity there are perhaps other features to account for renal disease in diabetics which may include concurrent morbidities and genetic predisposition also.

The data on the duration of disease shows a reduced percentage of patients with any DR and CKD. This is in consonance with the studies of The WESDR XXII which assessed the twenty-five-year progression of retinopathy in persons with type 1 diabetes¹¹ and the Finn-Diane study⁹ and the studies of James S et al.,¹²

There could be various reasons for this finding. Development of newer more effective insulin preparations and their easy availability and the provision of pens which are easy to carry could be a reason. One cannot also forget the genetic factors.^{13–15}

Hyperglycaemia appears to be the major modifiable risk factor for long-term complications of DM including diabetic macular edema¹⁶ but this factor explains only a modest fraction of overall risk for diabetes complications. It may be seen that in this study too, patients with longer duration of disease did have poorer HbA1C but the same did not correlate with DR or CKD.

A limitation of this study is the case numbers. A larger study would throw more light on this aspect of DM.

5. Conclusions

This study has shown that there is an increasing longevity among patients suffering from DM. Increase duration of disease may not necessarily mean increasing complications. While tight glycaemic control is a non-negotiable fact, occurrence of complications due to DM would require attention into other factors also.

6. Source of Funding

None.

7. Conflict of Interest

None.

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