

**Original Research Article** 

# A HOSPITAL BASED PROSPECTIVE STUDY TO CORRELATE THE SEVERITY OF DIABETIC RETINOPATHY WITH END STAGE OF RENAL DISEASE OF TYPE – II DIABETES MELLITUS PATIENTS AT TERTIARY CARE CENTER

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## ABSTRACT

**Background:** Diabetes is the most common disorder with ocular and renal manifestations. Renal disease and ocular complications in diabetes are frequently disturbing and destined to become one of the challenging problems of the future. This study is an attempt to access the ocular status, complications associated with CRF. It is intended to highlight the importance of ocular examination, to screen patients for any potential visual threat, so that necessary treatment or advice can be given, before they become irreversibly visually impaired.

**Material and Methods:** This is a hospital based prospective study done on 30 patients who were diagnosed end stage renal disease of diabetic etiology with or without hypertension. The onset of end stage renal disease was restricted to be less than six months. Patients with concomitant eye disease were also rejected. Patients underwent regular hemodialysis of once a week. The type of dialysis is bicarbonate, and few patients underwent acetone dialysis. Where acidosis is present only bicarbonate dialysis is done.

**Results:** Majority of the patients were in the age group 55-60 yrs, accounting to about 60%-men 33.33% & women 26.66%. Most of the patients were women, accounting for 56.66% of the total. 4 eyes with severe NPDR had progressed to very severe NPDR. Combined retinopathy was present in 12 Patients of the total. Grade I & Grade II were the majority. Drop in visual acuity in two eyes was due to hard exudates near the macula. 9 eyes that underwent photocoagulation were found to improve in visual acuity of 1-2 line.

**Conclusion:** Better understanding of importance of control of hypertension, improvement in hemodynamic monitoring, increased accessibility of dialysis units has improved the quality of life of people on dialysis and provide an opportunity for timely ophthalmological intervention.

Keywords: Hypertension, Type II diabetes, Visual acquity, Renal disease.

## **INTRODUCTION**

Eye is a mirror that reflects pathological changes occurring in many organs of the body. Numerous systemic disorders affect both eye and kidney. Examination of eye is an in dispensable part of the clinical assessment of a patient with renal disorders. CRF is irreversible and progressive process that result in END STAGE RENAL DISEASE (ESRD) where patient has to depend on renal replacement for survival.<sup>[1]</sup> Richard bright in 1836 first associated renal disease with blindness.<sup>[2]</sup> By ESRD 80% of pts will have secondary hypertension.<sup>[3]</sup> Ocular morbidity may be due to coexisting risk factors like hypertension, diabetes, uremia and anemia. Inflammatory reactions of conjunctiva and episclera can be associated with sudden marked raise in serum calcium.<sup>[4,5]</sup> Conjunctival degenerative changes (e.g) pinguecula are frequently seen in CRF.<sup>[6]</sup>

Diabetes is the most common disorder with ocular and renal manifestations.<sup>[7]</sup> Rubeosis iridis and neovascular glaucoma occur due to posterior segment pathology. Rising concentration of intracellular calcium might contribute to early cataract genesis and calcium deposit in lens.<sup>[8]</sup> Hypertension affects the eye and kidney in parallel and very often occurs along with diabetes. Hypertensive changes are particularly severe in renal failure. This has been attributed to the effects of retained nitrogenous products.<sup>[9]</sup> Accelerated Hypertension can result in optic disc edema.<sup>[10]</sup>

Renal disease and ocular complications in diabetes are frequently disturbing and destined to become one of the challenging problems of the future. Blindness due to proliferative retinopathy or maculopathy is approximately 5 times in diabetic patients with nephropathy compared with non albuminuric patients.<sup>[11]</sup>

In India majority of end stage renal disease patients are of type II diabetes. 5% of diabetic patients die of end stage renal disease. Diabetic retinopathy (DR) tends to deteriorate with falling renal function and poorly controlled blood pressure.<sup>[12]</sup> Diabetic Microangiopathy has been recognized as a major cause of kidney involvement in diabetes. Diabetic nephropathy ultimately leads to end stage renal disease. Both anterior and posterior optic neuropathy can occur in CRF, when hemoglobin level falls below 5gm% retinopathic features like retinal hemorrhages, hard and soft exudates and pallor of optic discs could be present.

The retinal arterioles look pale, and veins appear distended. Retinopathy is often asymptomatic in its most treatable stage. Delay in diagnosis can result in significant increase in patients' risk of visual loss. Type II DM accounts for 90% - 95% diabetes cases and differs from type I diabetes in average age of onset and etiology.<sup>[13]</sup>

Patients with type I diabetes, who are generally younger and are more likely to live long enough to benefit from tight glycaemic control, than patients with type II disease, who face a shorter life expectancy, because of their age and risk of cardiovascular disease.<sup>[14]</sup> For patients with coexistent disease, the delayed benefits of glycaemic control may be offset by the more immediate inconvenience, complications, and costs of intensive treatment and by the health effects of co morbid conditions. Ocular condition is also an indicator of metabolic control of the disease process. Similarly, an unknown case of chronic renal failure with its ocular complications, may first present to an ophthalmologist. This study is an attempt to access the ocular status, complications associated with CRF. It is intended to highlight the importance of ocular examination, to screen patients for any potential visual threat, so that necessary treatment or advice can be given, before they become irreversibly visually impaired.

## **MATERIALS AND METHODS**

This is a hospital based prospective study done on 30 patients who were diagnosed end stage renal disease of diabetic etiology with or without hypertension. The onset of end stage renal disease was restricted to be less than six months.

The following criteria were to be noted to fulfil the diagnosis of ESRD

- 1. Raised BUN about 100mg/dl at time of diagnosis.
- 2. Raised serum creatinine about 8mg/dl.
- 3. Signs and symptoms of Uraemia for more than 3 months.
- 4. Known diabetic for more than 5yrs with retinopathy.
- 5. Only NIDDM patients were included.

### Inclusion Criteria

Patients with minimum 5-year duration of DM giving informed consent for participation in the study were enrolled.

## **Exclusion Criteria**

Patients not willing to give informed consent for ophthalmic examination, known cases of DN and diabetic neuropathy, were excluded. Patients suffering from established nephropathy and neuropathy from any other cause including diabetes at the time of presentation were excluded from the study. Media opacities that preclude fundus examination, known case of HTN, urinary tract infection, and patients with a history of ocular inflammation or ocular trauma were excluded.

#### Methods

Patients with underlying etiology other than diabetes and hypertension were rejected. Patients with concomitant eye disease were also rejected. Patients underwent regular hemodialysis of once a week. The type of dialysis is bicarbonate, and few patients underwent acetone dialysis. Where acidosis is present only bicarbonate dialysis is done.

#### **OPTHALMOLOGICAL EXAMINATION**

Ophthalmological examination is made twice and whenever the patient reports with diminished vision. Complete ophthalmological evaluation included:

- Best corrected visual acuity.
- Slit lamp examination of both eyes.
- Direct ophthalmoscopy.
- Fundus examination with 90D lens and slit lamp.
- Fundus photographs and FFA in suspicion of neovascularization.
- Diabetic retinopathy is classified as per ETDRS classification.
- Hypertensive retinopathy classified as per Keith Wagner Barker classification.

Statistical Analysis: Numerical data was analyzed using the Mann–Whitney test, and categorical

variables included Chi-square test. Statistical analyses were performed using primer software (6.0). A P value of less than 0.05 was considered to be statistically significant.

### RESULTS

Majority of the patients in this study were screened within 6 months of the start of symptoms of uremia patients were already undertaking treatment for diabetes mellitus other with oral hypoglycaemic agents or insulin. Majority of the patients were in the age group 55-60 yrs, accounting to about 60%-men 33.33% & women 26.66%. Most of the patients were women, accounting for 56.66% of the total. [Table 1]

Follow up examination of retinopathy was done at the end of 6 months and one year. Majority of the eyes was found to be stable at the end of 6 months and one year. 4 eyes with severe NPDR had progressed to very severe NPDR. No new vitreous haemorrhage, or retinal detachment was noticed. [Table 2]

Combined retinopathy was present in 12 Patients of the total. Grade I & Grade II were the majority [Table 3]

Visual acuity of no PL in two eyes was due to the presence of tractional retinal detachment majority of the visual acuity remained stable at the end of 6months. Few eyes showed progression of cataract. Drop in visual acuity in two eyes was due to hard exudates near the macula. 9 eyes that underwent photocoagulation were found to improve in visual acuity of 1-2 line [Table 4]

Table 1: Distribution of patients according to age & Sex wise						
Age	Male	Percentage	Female	Percentage		
55-60	10	33.33%	8	26.66%		
61-65	1	3.33%	5	16.66%		
66-75	2	6.66%	4	13.33%		
Total	13	43.33%	17	56.66%		

#### Table 2: Severity of diabetic retinopathy at follow up

Severity of Diabetic Retinopathy	No. of eyes (N=60)	%
Mild NPDR	0	0
Moderate NPDR	5	8.33%
Severe NPDR	24	40%
Very Severe NPDR	17	28.33%
Early PDR	11	18.33%
High Risk PDR	3	5%

#### Table 3: Incidence of hypertension retinopathy

	No. of Eyes (N=60)	%
Grade I	5	8.33%
Grade II	5	8.33%
Grade III	3	5%
Grade IV	0	0

#### Table 4: Visual acuity in diabetic ESRD on dialysis (N=60 eyes)

BCVA	Base line	Follow up
6/6	0	0
6/9	2	0
6/12	7	10
6/18	7	7
6/24	12	14
6/36	22	16
1/60 - 6/60	6	6
CfCf – HM	1	1
PL ±PR	1	1
No PL	1	1

### **DISCUSSION**

Diabetes is defined as a major group of metabolic disease characterized by hyperglycemia, with disturbances in carbohydrate, fat and protein metabolism either due to defect in insulin secretion, action or both.15 No distinction is attempted in ESRD treatment outcome between type I and type II diabetes mellitus patients. Today it is generally accepted that the renal replacement therapy should be considered earlier in diabetic than non-diabetic ureamic patients.

The majority of the patients in the study were in the age group 55- 60years accounting for about 60% of the total. In the study conducted by Brenner et al16 found age distribution of ESRD patients of diabetic origin to be higher at 56 years. Robert C Ramsamy et al17 group of patients on an average were 48 years but this study group included both type I type II DM.

Males and females were studied for their distribution in relation to retinopathy and nephropathy. It was found that ESRD of diabetic origin showed a slight female preponderance accounting for about 56.66%.

In the study conducted by Berman et al,<sup>[16]</sup> similar results were noted with females undergoing dialysis in upto 68% of the total. Robert C. Ramsamy et al,<sup>[17]</sup> showed almost equal distribution of males and females in their study. Three suppositions were given by Klein R et al,<sup>[18]</sup> to explain why there are more women among the dialysed diabetic studied (1) women with diabetes mellitus live longer with the disease than men do. (2) women with diabetes may be more metabolically stable (3) More women are willing to accept dialysis and endure stress than are men.

Diabetic Retinopathy was graded under the ETDRS classification with hypertensive retinopathy graded under Keith Wagner Barker Classification. Berman et al,<sup>[16]</sup> followed a classification that combined both Kanski and ETDR classification. The retinopathy was classified as no retinopathy, background macular edema, retinopathy nonproliferative retinopathy + macular edema, proliferative retinopathy, vitreous hemorrhage and tractional retinal detachment. More simpler classification have also been followed like in the Jean-Louis Brenato Fenck study mentioned in Diabetic Renal - retinal syndrome as early, edematous, mixed, ischemic and complicated. People with hypertension were classified in 4 groups as common arteriosclerosis, cross sign, exudates and papilledema.

In this study the distribution of retinopathy was mild NPDR 0% moderate NPDR 8.33%, Severe NPDR 40%, very severe NPDR 28.33%, early PDR 18.33% and high risk PDR 5%. This study was concordant with Berman et al,<sup>[16]</sup> which showed a high percentage of background retinopathy and nonproliferative retinopathy in their study in the range of 52%.

Robert C Ramsamy et al,<sup>[17]</sup> in the study conducted on insulin dependent diabetes ESRD patients found proliferative diabetic retinopathy to be common at 59% at the outset of dialysis. Studies conducted by Nguyen Q, D. et al,<sup>[19]</sup> showed that main risk factor or risk of non-proliferative retinopathy are the duration and degree of compensation of diabetes mellitus and stage of diabetic nephropathy. In this study the underlying nephropathy is severe needing medical and renal replacement therapy hence the presence of very severe, severe and proliferative retinopathy being common. Schwartz et al,<sup>[20]</sup> showed histological evidence of Kimmelstiel Wilson nodules and sever retinopathy. No renal biopsy was however done in any of our cases. Incidence of hypertension and associated retinopathy was 40% in our group of study. Epidemological studies mention hypertension as a risk factor for the development of diabetic retinopathy and may be superimposed on diabetic retinopathy. Yazdani et al,<sup>[21]</sup> study showed out of 64 patients with CRF, 21 had diabetes and hypertension accounting to about 32%. In this study, most common retinopathy graded was group 1& 2 of Keith Wagner Barker classification. Hypertension could be the underlying risk factor for the development of severe retinopathy.

Robert C. Ramsay et al,<sup>[17]</sup> in their study conformed the stabilization of baseline visual acuity in a majority and deterioration in some. Patients on dialysis in this study by Robert C. Ramsamy,<sup>[17]</sup> were both Type I and Type 11DM and followed for a minimum of 2 years on dialysis. As are study had a short follow up the end result could not be compared though similar causes of visual loss were found to be proliferative retinopathy and macular edema. Moreover, where type-I DM is associated with greater incidence of proliferative retinopathy on long term the same does not hold good for Type-II DM who formed the major in this study group.

Berman et al,<sup>[16]</sup> noted 7eyes in background retinopathy and 8 eyes of non-proliferative retinopathy to have macular edema. Both these groups constituted a majority of the total retinopathy. Prompt treatment in the form of focal, panretinal photocoagulation or both resulted in stabilization of vision. Whereas in our study photocoagulation was not included. Deterioration in visual acuity in our study demonstrated coincident with CSME and in some to the appearance of hard exudates on macula. Kline et al,<sup>[18]</sup> has suggested that type II DM is a group prone to macular edema. Baseline visual acuity was noted to be stabilized in a majority but this was just a I year follow up which needs to be further followed up for long time. 9 eyes underwent photocoagulation for macular edema and showed improvement at the end of six months in the form of improved visual activity of 1-2 lines. Other patients with clinically significant macular edema were advised to undergo photocoagulation.

## CONCLUSION

End stage renal disease is a microvascular insult of diabetes where retinopathy is also common. Better understanding of importance of control of hypertension, improvement in hemodynamic monitoring, increased accessibility of dialysis units has improved the quality of life of people on dialysis and provide an opportunity for timely ophthalmological intervention.

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