Ocular evaluation in patients with chronic renal failure - a hospital based study

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ABSTRACT

Chronic renal failure affects every organ system including eye. The aim of this study is to conduct thorough ocular examination in the patients of chronic renal failure and to analyze the findings. 119 cases were collected from Nephrology unit of Tribhuvan University Teaching Hospital between 1st June 2002 to 15th December 2003. This was a cross sectional, descriptive type of study. Sampling technique was consecutive and stratified. Severity of renal disease was classified as mild, moderate, severe and end stage renal disease. Twenty-three percent of total 238 eyes had vision < 6/18. The causes for visual impairment were maculopathy 23 eyes, cataract 14 eyes followed by proliferative diabetic retinopathy, 9 eyes. Twelve percent of total eyes had vision <6/60. Lid edema was present in 63.0%, conjunctival pallor in 75.6% and corneal calcification in 1.6%. Retinopathy was the most important finding. Hypertensive retinopathy was present in 56 out of total 119 cases (47.1%). It was more prevalent and tended to be more severe as renal disease progressed. This was statistically significant. Diabetic retinopathy was present in 38 out of 43 diabetic cases (88.3%). Although statistically not proven, more severe grades of diabetic retinopathy were detected with increasing severity of the renal disease. There was one case of bilateral serous detachment of the retina relating to chronic renal failure. In this study, 47 out of 56 cases of hypertensive retinopathy and 19 out of 38 cases of diabetic retinopathy were detected for the first time, thus showing the importance of ocular evaluation of the patients of renal insufficiency.

Keywords: Chronic renal failure, retinopathy, corneal calcification, hospital, Nepal.

INTRODUCTION

Chronic renal failure (CRF) is irreversible and progressive process that results in end stage renal disease (ESRD) where patient has to be dependent on renal replacement therapy for survival.[1] Richard Bright, in 1836 first associated renal disease with blindness. Later on, it was recognized that uremic retinitis is the manifestation of hypertension (HTN).[2] Deterioration of eyesight is due to worsening of hypertensive or diabetic retinopathy, ischemic optic neuropathy, central retinal vein occlusion and cortical blindness. By the ESRD, 80.0% of patients will have developed secondary HTN.[3] Ocular morbidity may be directly due to HTN, uremia and anemia; some are related to the causes leading to chronic renal failure. Some effects are due to haemodialysis.

Important ocular finding related to renal insufficiency are lid edema, conjunctival pallor; and xanthalasma which is associated with increased serum lipids. Corneal and conjunctival calcification may occur due to secondary hyperparathyroidism. Inflammatory reactions of conjunctiva and episclera can be associated with a sudden, marked rise in serum calcium.[4,5] Conjunctival degenerative changes e.g. pinguecula are frequently seen in CRF.[6] Goblet cell density is decreased.[7] Recurrent subconjuctival hemorrhage can occur due to sclerosed conjunctival vessels secondary to HTN.[2] Rubeosis iridis and neovascular glaucoma occur due the posterior segment pathology. Rising concentrations of intracellular calcium might contribute to early cataractogenesis and calcium deposition in lens.[8]

Hypertensive retinopathic changes are particularly severe in renal failure. This has been attributed to the effects of retained nitrogen products.[8] Accelerated hypertension can result in optic disc edema.[9] The ophthalmic appearance is of value in determining the efficacy of the antihypertensive therapy.[10] The retina is accessible to monitor status of blood pressure control.[8] Blindness due to proliferative retinopathy or maculopathy is approximately five times more common in diabetic patients with nephropathy compared with normoalbuminuric patients.[11] Diabetic retinopathy (DR) tends to deteriorate with falling renal function, poorly controlled blood pressure[12,13] and in patients in whom no retinal treatment has been given before.[14,15] Several cases of bullous retinal detachment have been reported in CRF which could be from deranged metabolism, uncontrolled blood pressure and retinal pigment

epithelium dysfunction.[16,17] Both anterior and posterior optic neuropathy can occur in CRF. When haemoglobin level falls below 5gm%, retinopathic features like retinal haemorrhages, hard and soft exudates, and pallor of optic discs (ischemic optic neuropathy) could be present. The retinal arterioles look pale, the vein distended.

Retinopathy is often asymptomatic in its most treatable stage; delay in diagnosis can result in significant increase in the patient's risk of visual loss.[14] Ocular condition is also an indicator of the 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 and or advice can be given before they become irreversibly visually impaired. To the best of authors' knowledge, this type of study has not been done or published for Nepalese population.

METHODOLOGY

Place of study: Tribhuvan University Teaching Hospital (TUTH) and BP Koirala Lions Centre for Ophthalmic Studies (BPKLCOS). *Sample:* Cases of CRF attending in Nephrology Unit. Consecutive cases were collected and were stratified into different grades of CRF. *Study Period:* 18 and half months (1 June 2002-15 December 2003). *Inclusion Criteria:* All cases diagnosed as CRF. *Exclusion criteria:* 1) Cases of reversible renal failure 2) Those that had not gone through ocular examination as per protocol. *Type of the Study:* Cross sectional, non interventional, descriptive, hospital based.

Cases that had undergone following investigations were collected: (1) hemoglobin, total leukocyte count, differential leukocyte count, erythrocyte sedimentation rate, (2) serum urea, serum creatinine, 24 hour urinary creatinine and urinary volume, (3) serum calcium, (4) serum phosphate, (5) serum electrolytes, (6) USG abdomen, (7) urine routine and microscopic examination and (8) lipid profile. All these were performed in the biochemistry laboratory of TUTH.

Glomerular filtration rate (GFR) calculation: Ux V/P where U=24 hour urinary creatinine, V=24 hour urinary volume and P=serum creatinine. [11,18] Cases were classified [1] as mild, if GFR is between 30 to 50 ml/min; moderate, if between 10 to 29 ml/min; severe if less than 10 ml/min and ESRD if GFR is less than 5ml/min. Systemic history was taken. Vitals recorded. Systemic evaluation was done.

For ocular examination**,** all patients were brought to either BPKLCOS or Eye Ward: (1) history taken, (2) best corrected visual acuity recorded (3) intraocular pressure taken (4) detail examination of anterior and posterior segment was done. Pupil was dilated with tropicamide for (a) Indirect ophthalmoscopy with 20 diopter lens followed by (b) evaluation under slit lamp with 90 diopter lens. Hypertensive retinopathy (HR) was graded on the basis of Keith and Wagener classification.[8] DR and macular edema was classified on the basis of early treatment diabetic retinopathy study.[14] Other investigations done according to need were (i) fundus fluorescein angiography, (ii) visual field (iii) fundus photography (iv) Schirmer test

RESULTS

A total of 119 patients of (CRF) were included. The sample size in each grade of CRF were as follows: mild and moderate, 31 cases (26.1%) each; severe, 28 cases (23.5%); ESRD, 29 cases (24.3 %). Mean age of total patients of CRF was 48.3±14.9 years and M: F ratio in total was 2.3:1. Similar demographic parameters were obtained in each of the subgroups. The commonest cause of CRF was HTN, 43 out of 119 (36.1%), followed by diabetes (27.7%) and glomerulonephritis (20.2%). Other causes were adult polycystic kidney disease and calculus. 80.6 % of patients gave history of CRF for one year or less. This included 34.4% who had been diagnosed for less than one month. Only one patient gave history of CRF for 12 years.

Ocular symptoms in patients of CRF: Blurring of vision was the most important symptom complained by 62.0% of patients. Most of it (46.0%) was of gradual onset. Other problems were irritative symptoms (29.4%), and

Table-1: Best corrected visual acuity in the eyes among different grades of CRF

WHO criteria	Grades of CRF Visual acuity	Mild	Moderate	Severe	ESRD	Total	% of total eyes
Good vision	> 6/18	48	47	40	47	182	76.6
Impaired vision	6/60 to 6/24	9	7	4	8	28	11.7*
Legally blind	< 6/60	5	8	12	3	28	11.7**
	Total eyes	62	62	56	58	238	100.0

* P value = 0.395 ** P value= 0.499 Level of significance: P < 0.05 at 95.0% confidence limit

Table-2: Causes of visual impairment (corrected visual acuity less than 6/18) in CRF

Causes of visual impairment	No of eyes	% of the total eyes (out of 238 eyes)
Maculopathy	23	9.7
Cataract	14	5.9
PDR	9	3.8
Optic neuropathy	5	2.1
Corneal scar	1	0.4
Others	4	1.7
Total	56	23.6

red eyes (12.0 %). In spite of this, 56.3 % of patients have never had eye check up before. Only 25.2% of patients had had detailed eye check up including fundus evaluation in the past.

Ocular Findings in patients of CRF: Table-1 shows the best corrected visual acuity. 76.6% of total patients enrolled were with vision 6/18 or better. According to WHO criteria, 11.7% were visually impaired and another 11.7% were in the category of legally blind (vision, <6/60). P value was not significant for visual loss with the severity of renal failure. Table-2 shows that major causes for vision less than 6/18 were maculopathy and cataract, (together, 15.6% of total eyes) followed by proliferative DR. Tables 3 and 4 respectively show anterior and posterior segment findings related to CRF. Significant finding present along with the higher grades of CRF were lid edema (P=0.002), conjunctival pallor (P=0.000003), corneal conjunctival calcification (P=0.005), HR (P=0.0001) and disc edema (P=0.004). Tables 5 and 6 compare the grades of HR and DR with severity of renal failure respectively. Small sample size had made it difficult to comment on the grading of DR with respect to CRF. 47 out of 56 cases (83.9%) of HR were not known before this study was done. Similarly, 19 out of 38 cases (50%) of the DR were detected for the first time. The distribution of intraocular pressure (IOP) among the patients of CRF was found to be the normal bell shaped curve with skewness to the right. Mean IOP was 12.7$\pm$ 3.3mmHg (Range 6 to 42 mmHg).

DISCUSSIONS

Overall, male: female ratio in CRF was 2.3:1 which was similar to the worldwide data[1]. The reason for this could be due to faster rate of deterioration of kidney function in male with some forms of glomerulonephritis and polycystic kidney disease.[1]

Seventy-seven percent of the total eyes had visual acuity of 6/18 or more. However, visual acuity is not the sole indicator of the ocular status. Even advanced DR and HR, may have good central vision until macula is involved. In this study, 2 out of 4 patients of grade IV HR and 20 out of 25 grades III HR had quite good vision, but they were at risk of visual loss. Reports from different centers show blindness in CRF to be from 5 to 15.0 % in the first year of diagnosis.[11] In our study, it was 11.7%. Other studies show that transplanted patients, when followed beyond 10 years, 38.0% had gone blind.[11] Limitation of our study was that it was not prospective.

Table-3: Comparison of anterior segment findings related to CRF in different grades of the disease.

Grades of CRF Ocular findings	Mild (31 cases)	Moderate (31 cases)	Severe (28 cases)	ESRD (29 cases)	Total (119 cases)	P Value
Lid edema	12 cases	18 cases	21 cases	24 cases	75 cases (63.0%)	0.002*
Conjuctival pallor	15 cases	20 cases	28 cases	27 cases	90 cases (75.6%)	0.000003*
Corneal calcification	----	----	----	4 eyes	4 eyes (1.6%)	0.005*
Pinguecula	13 cases	10 cases	15 cases	9 cases	47 cases (39.4%)	0.267
Red eyes of CRF	1 eyes	2 eyes	2 eyes	-----	5 eyes (2.0%)	0.505
Dry eyes	6 eyes	2 eyes	6 eyes	4 eyes	18 eyes (7.5%)	0.368
Cataractous changes with visual impairment	6 eyes	4 eyes	4 eyes	3 eyes	17 eyes (18.0%)	0.785

*Significant, Level of significance: P < 0.05 at 95.0% confidence limit

Table-4: Comparison of posterior segment findings in different grades of CRF

Grades of CRF Ocular findings	Mild (31 cases)	Moderate (31 cases)	Severe (28 cases)	ESRD (29 cases)	Total (119 cases)	P Value
Vitreous hemorrhage	----	4 eyes	2 eyes	2 eyes	8 eyes (8.3%)	0.248
Diabetic Proliferative vitreoretinopathic changes	----	3 eyes	1 eye	2 eyes	6 eyes (2.5%)	0.512
Hypertensive retinopathy	5 cases	13 cases	19 cases	19 cases	56 cases (47.1 %)	0.0001*
Diabetic retinopathy	13 out of 13 diabetic cases	11 out of 15 diabetic cases	7 out of 8 diabetic cases	7 out of 7 diabetic cases	38 out of 43 diabetic cases (88.3%)**	0.428
Maculopathy (diabetic or HTN)	6 cases	7 cases	8 cases	3 cases	24 (20.2%)	0.378
Bullous retinal detachment	----	-----	-----	2 eyes	2 eyes (0.1%)	0.097
Branch retinal vein occlusion	1 eye	----	1 eye	----	2 eyes (0.1%)	0.556
Pallor of the disc	1 eye	----	2 eyes	4 eyes	7 eyes (3%)	0.128
Disc edema (grade IV HTN retinopathy	----		2 eyes	6 eyes	8 eyes (3.3%)	0.004*
Glaucoma suspect	----	1 case	1 case	----	2 cases (1.6%)	0.556

**Percentage is calculated among total diabetic patients in the study
*Significant Level of significance: $P < 0.05$ at 95% confidence limit

In the study, maculopathy accounts for cause of visual loss in the majority, 23 eyes (9.6%). Cataract was the cause for visual impairment in 14 eyes (3 out of 17 cataractous eyes also had maculopathy and there was no improvement of vision in visometry). P value was not significant for cataract when compared with different grades of CRF.

Most of patients were having complaints of blurring of vision (62.0%). Overall only 43.7 had gone for eye check up. This obviously showed the lack of knowledge about the potential ocular complications. Greater percentage of patients in ESRD (58.6% compared to 29.0% in mild group) had gone for eye check up in the past. This could indicate ocular problems with advancing renal disease.

Lid puffiness and conjunctival pallor were present in 63.0% and 75.6% of total cases respectively. Being statistically significant, they can be regarded as consistent finding in CRF. Corneal calcification (1.6%) was present only in patients of ESRD group. Calcification was near the nasal and temporal limbus with a lucid zone and did not affect vision. Different studies[19, 20] show that calcification occurs in 60.0 to 80.0%. Another study[21] reported 36.0% corneal conjunctival calcification. There has been positive

Table- 5: Comparison of grades of hypertensive retinopathy (HR) with CRF

Grades of CRF Grades of HR	Mild (31 cases)	Moderate (31 cases)	Severe (28 cases)	ESRD (29 cases)	Total (119 cases)
I	3	6	4	5	18
II	1	2	1	5	9
III	1	5	13	6	25
IV	0	0	1	3	4
Total cases with HR	5	13	19	19	56

Table-6: Comparison of grades of diabetic retinopathy (DR) among subgroups of CRF

Grades of CRF Grades of DR	Mild 13* cases	Moderate 15* cases	Severe 8* cases	ESRD 7* cases	Total 43 cases
Mild	6	2	1	1	10
Moderate	1	4	2	3	10
Severe	3	1	2	1	7
Very severe	3	1	0	0	4
PDR**	0	1	1	1	3
HR PDR#	0	2	1	1	4
Total cases with DR	13	11	7	7	38

*numbers represents patients with diabetes mellitus in each subgroup of CRF

** PDR: Proliferative Diabetic Retinopathy

HR PDR: High Risk Proliferative Diabetic Retinopathy

correlation of the soft tissue calcification with the duration of hemodialysis.[21,22] Most of the patients (80.6%) in our study had CRF diagnosed for one year or less which could explain our result. Mean intra ocular pressure in patients of CRF was 12.7 $\pm$ 3.3 mmHg. One case in the study had neovascular glaucoma with IOP of 42 mmHg. In a study done in Italy[23], average IOP of CRF patients was slightly less than the control group (14.9$\pm$2mmHg versus 15.6$\pm$1.9mmHg with P=0.07). Our study did not have control group.

The most important and vision threatening findings were in the posterior segment. Forty-eight percent of total patients had HR. It was more prevalent as the renal disease progressed. The findings correlated well with other studies.[24,25] Grade IV HR with optic disc edema was present only in severe CRF and ESRD. Similarly, 19 out of 25 Grade III HR was detected in severe and ESRD together. 88.3% of total diabetics in the study had DR. Mild DR was mostly seen in mild CRF group but moderate, severe and PDR (proliferate diabetic retinopathy) were seen in higher grades of CRF. Although not statistically proven because of small sample size, these data supports previous studies[15,26-28] that DR is invariably present in cases of diabetic nephropathy and that more severe forms of retinopathy are detected as renal disease progresses. Overall, 48 eyes had clinically significant macular edema, most of which (38 eyes) were related to DR and only 5 cases (10 eyes) were associated with HR. All types of maculopathy – focal (16 eyes), diffuse (14 eyes) and chronic (18 eyes) were detected. There was one case of bilateral bullous, exudative type of retinal detachment in a patient with severe grade of renal disease, which was managed with metabolic and blood pressure control. Findings and management were similar with other case reports. [29-33]

Ninety-two percent of grade III HR and all 4 cases of grade IV HR were detected for the first time during this study. Grade III and IV HR have bad prognosis and this may alert the physician for more aggressive management of the blood pressure. Among newly diagnosed DR, there was one PDR, 3 severe and one very severe DR, all never treated before.

Several patients from the study received urgent laser treatment in the retina. Three eyes underwent successful cataract surgery.

In conclusion, detail ocular examination should be undertaken in patients of CRF. If the patient has positive history of abnormal renal status, he should undergo close follow up because they are at an increased risk of visual loss. Awareness is needed of the potential ocular complications of the disease process.

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