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CORNEO-CONJUNCTIVAL CHANGES IN CHRONIC RENAL FAILURE

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INDEXING WORDS

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SYNOPSIS

Seventy patients of chronic renal failure were studied. Slit lamp examination was done in 30 patients which showed conjunctival deposition of calcium in 28 (93.33%) and over the cornea in 26 (86.7%) of cases at 3 and 9 o'clock position on bulbar conjunctiva. Ratio of unilateral and bilateral deposition of calcium crystal over the conjunctiva and cornea were 1:27 & 3:23 respectively. The urinary excretion of calcium and phosphorus were less in comparison to control group.

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INTRODUCTION

The corneo-conjunctival changes encountered in patients of chronic renal failure (CRF) often disturbs patients as well as the treating physicians. Though few reports describing metastatic calcification in vessels and other structural changes in renal failure had been present about 4 decades ago¹³⁾ but unfortunately corneo-conjunctival changes in CRF was not precisely recognized untill 1966 when Abraham noticed a patient of CRF with irritated red eye at first. Subsequently he described corneal changes in 13 out of his 20 patients of CRF treated by intermittent hemodialysis program. The changes ranged from the white limbus girdle of Vogt to that of pronounced corneal calcification specially in the area of palpebral fissure. Since then number of reports have appeared with varying incidences of ocular changes, ranging from 14 to 60% for red eye, 60 to 100% for conjunctival and 65 to 95% for corneal involvement in patients of CRF.^{2, 9, 10, 15, 16, 18)}

The present consensus of opinion regarding the etiopathogenesis of red eye and corneo-conjunctival changes in these patients is that it is because of distant metastatic calcification leading to micro-crystal formation over the corneo-conjunctival surface.^{1, 9, 12, 15)} Though the precise mechanism of this deposition is not clear, number of supporting factors have been recognized in increased Ca and P products leading to increased precipitation¹⁸⁾ and crystal formation. Furthermore, the increased pH level of the corneo-conjunctival surface on account of natural exposed area causing precipitation of calcium salts¹⁴⁾ or decreased production of tears.¹⁶⁾ Further a few reports^{12, 14)} have shown that the patients had marked recovery in the eye problems after kidney transplantation and not by local treatment of the eye or simple haemodialytic correction of the abnormal blood biochemistry.

Fascinating with the above points the present study was undertaken in order to study the incidence of corneo-conjunctival changes in patients of CRF in addition to evaluate the biochemical parameters responsible for distant calcification or presence of micro-crystals over the exposed part of the eye.

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MATERIALS AND METHODS

The present study includes 70 patients of chronic renal failure and twenty controls admitted in the Nephrology Unit of the University hospital of Banaras Hindu University during a period of 2.5 years. Established clinical and biochemical parameters^{5, 6} were taken for selection of patients of chronic renal failure. After a detailed clinical evaluation on preformed form, patients were subjected for detailed investigations which included urinalysis, estimation of urinary proteins, blood urea, serum creatinine, serum calcium, serum phosphorus, alkaline phosphatase, haematological investigations such as determination of haemoglobin, total and differential leucocyte count, ESR and Plain X-ray abdomen or intravenous pyelography for assessing the kidney size. Detailed ocular examination of these patients were performed which included external examination of eye, corneal loops, slit lamp examination in selected patients and tonometry.

OBSERVATION

Amongst the total of 70 cases M:F ratio was 4.5 to 1 and majority of the patients belonged to 4th to 6th decades of their life (Table 1). Chronic pyelonephritis (34.29%) was the commonest followed by chronic glomerulonephritis (GN) (25.56%), diabetic nephropathy (22.23%), renal tuberculosis (5.72%), obstructive uropathy (5.72%) and other unspecified renal diseases (5.72%) were the etiological causes of CRF on clinical grounds.

Table 2 gives mean and standard deviation of biochemical parameters of the patients. Serum calcium was lower than normal in 55 patients, normal and high in 12 and 3 patients respectively. Mean serum phosphorus level was significantly higher than the control group. The product of calcium and phosphorus was above 39.19 (mean $\pm$ 25 S.D.) in 64 out of 70 patients. Mean alkaline phosphatase was significantly high in patients of CRF. The urinary calcium and phosphorus excretion was less than control group. However, the estimation of parathyroid hormone and Vitamin-D was not done in these cases.

In 30 patients slit lamp examination was done. In 93.3% of situation conjunctival calcification was seen which was mostly at 3 and 9 o'clock position on bulbar conjunctiva. As shown in Table

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Table 1 Age and sex distribution of cases of chronic renal failure

Age Group (in years)	Male		Female		Total No. of Case	
	No.	%	No.	%	No.	%
Up to 19	5	7.14%	2	2.86%	7	10.00%
20 - 29	7	10.00%	2	2.86%	9	12.86%
30 - 39	10	14.29%	4	5.71%	14	20.00%
40 - 49	13	18.57%	3	4.29%	16	22.86%
50 - 59	16	22.86%	1	1.43%	17	24.29%
60 and above	6	8.57%	1	1.43%	7	10.00%
Total	57	81.42%	13	18.57%	70	100.00%

Table 2 Biochemical values of the patients

Parameter	Control	C.R.F.	Stat. significance
Blood Urea (mg%) M ± SD	28.46 ± 3.64	199.65 ± 46.976	<0.001
Range	21 - 38	99 - 286	
S. Creat. (mg%) M ± SD	1.02 ± 0.363	5.9 ± 3.654	<0.01
Range	0.6 - 1.4	1.5 - 13.5	
S. Sodium (mEq/L) M ± SD	138.6 ± 6.43	127.05 ± 11.44	NS
Range	133 - 146	100 - 145	
S. Potassium (mEq/L) M ± SD	4.57 ± 0.234	4.43 ± 0.78	NS
Range	3.8 - 5.4	2.2 - 5.5	
S. Calcium (mg%) M ± SD	10.16 ± 0.534	8.69 ± 1.093	NS
Range	9.4 - 11	6.9 - 10	
S. Phosphorus (mg%) M ± SD	2.73 ± 0.662	7.43 ± 2.876	<0.01
Range	2 - 4	4.6 - 16	
S. Protein (Total Gm%) M ± SD	7.43 ± 0.925	5.12 ± 0.66	<0.05
Range	6.2 - 8.2	3.5 - 6.2	
S. Cholesterol (mg%) M ± SD	148.64 ± 13.62	156.05 ± 45.12	NS
Range	140 - 260	81 - 260	
S. Alk. Phosphate (KA Unit) M ± SD	6.73 ± 2.05	10.19 ± 7.77	NS
Range	4 - 12.2	3 - 30	

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3 in 90.0% of cases conjunctival involvement was bilateral and in only one case it was unilateral. The corneal calcification (86.7%) were seen, being bilateral in 76.7% of patients.

Table 3 Serum levels and corneo-conjunctival changes

	Control	Corneal	Conjunctiva
Unilateral	-	3 (10%)	1 (3.33%)
Bilateral	-	23 (76.7%)	27 (90%)
Serum Cal (mg%)	10.16 $\pm$ 0.534	-	-
Mean $\pm$ SD		8.69 $\pm$ 1.095	
Range	9.4 - 11	6.9 - 10	
Stat. Significance	'p'	N.S.	
Serum Phosp. (mg%)			
Mean $\pm$ SD	2.73 $\pm$ 0.662	7.43 $\pm$ 2.876	
Range	2 - 4	4.6 - 16	
Stat. Significance	'p'	<0.01	
Serum Ca x P Product			
Mean $\pm$ SD	27.74	62.81 $\pm$ 10.106	
Range	19 - 44	37.44 - 120	
Stat. Significance	'p'	<0.001	

DISCUSSION

Our majority of the patients belonged to 5th and 6th decade of their lives which has been observed similarly by other also in their series.^{10, 18, 20)}

The biochemical abnormalities as seen in our study, has been earlier reported in literature in patients of CRF. These various changes include hypocalcemia in majority of cases,^{4, 11, 17, 19)} occasional hypercalcemia,¹⁹⁾ hyperphosphatemia in majority or normal serum phosphorus in few cases of CRF,^{7, 19)} significantly raised serum calcium and phosphorus product in these patients,¹⁹⁾ increased level of alkaline phosphatase in majority of situations specially in patients with osteodystrophic changes.^{7, 19)} Similarly reduced urinary excretion of calcium and phosphorus as seen in our patients has been earlier reported.^{3, 7, 8)}

One striking feature as seen on slit lamp examination was deposition of microcrystals of calcium phosphate over the cornea and conjunctiva which are ordinarily missed by naked eye examination. They may cause irritation of the eye leading to "red eye" syndrome of the renal failure.²⁾ We also performed ocular tension in 30 instances only since most of the patients were serious and moribund hence could not be subjected for this examination. Only 30% of our patients had red eye syndrome whereas Abraham et al.¹⁾ found this in 65% of his patients of CRF. Calcium deposition was noted in conjunctiva in 93.33% of cases, mostly in bulbar conjunctiva in interpalpebral area which is quite higher record in comparison to Abraham et al.¹⁾ who got in only 65% of his patients. Schumacher¹⁸⁾ (60%), Easterbrook⁹⁾ are also had varying incidences. However, Porter et al.¹⁶⁾ got the conjunctival changes in all his patients of CRF. We noticed corneal changes in 86.7% of cases which is quite alarming in comparison to Schumacher,¹⁸⁾ 1969 and Abraham,¹⁾ 1966 who reported in 60-65% of their cases whereas Porter, 1973¹⁶⁾ got changes in cornea in 90% of his subjects.

Mechanism of deposition of calcium crystals are still obscure but number of etiological factors have been suggested. The most important factor is elevated calcium and plus phosphorus product as seen in patients of CRF. Usual site of calcium crystal deposition over the conjunctiva is in the interpalpebral region of the bulbar conjunctiva because of loss of CO₂ due to exposure lead to increased (pH towards alkaline side), making calcium salt insoluble in the terms and its final precipitation. Porter and Crembie¹⁶⁾ had noted abnormally low levels of tear production in the patients of chronic renal failure with red eye syndromes. The level of calcium is usually raised in patient of renal failure which causes hypercalcemia but due to associated deficiency of Vitamin-D (1, 25 (OH) D₃), the levels of calcium is usually low. However, the serum phosphate levels are usually raised due to decreased elimination in the urine in patients of CRF. The estimation of PTH and Vitamin D₃ in these patients may give some clues towards the understanding of etiology. Another possibility of regional or geographical factors might be playing some role which needs detailed study and further confirmation.

The corneo-conjunctival crystals remain unaffected by treatment with regular maintenance haemodialysis program which has been reported to regress dramatically after renal transplantation.

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12, 14) Thus the adequate treatment of these corneo-conjunctival changes includes various maneuver for correction of the etiological factors either by kidney transplantation or any other one manoeuver and not only local treatment of eye.

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