



# Analytical Study of Ocular Surface Changes in Patients of Chronic Kidney Disease undergoing Hemodialysis and Peritoneal Dialysis

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## Abstract

**Objectives** The idiopathic group is a significant cause of chronic kidney disease (CKD) in developing countries. Literature available on ocular surface changes has predominantly been reported in patients undergoing hemodialysis. Little is known about the changes in patients undergoing peritoneal dialysis. The present study aimed to identify ocular surface changes in an idiopathic group of CKD undergoing dialysis.

**Aim** To compare tear film disorders and the severity of ocular surface changes (goblet cell density, squamous metaplasia, and corneoconjunctival calcification) in patients of idiopathic etiology with CKD undergoing hemodialysis and peritoneal dialysis. This is an analytical study.

**Materials and Methods** Asymptomatic adult patients of idiopathic CKD, on treatment with dialysis underwent comprehensive ophthalmic examination, including best-corrected visual acuity, slit-lamp examination, and a dilated fundus examination. Dry eye assessment was done by ocular surface staining score, Schirmer test, and tear breakup time (TBUT). Conjunctival impression cytology was studied to assess changes on ocular surface. Chest X-rays for aortic calcification were reviewed and data analyzed.

**Results** Both eyes of 76 patients of hemodialysis and 32 patients of peritoneal dialysis were studied. Ocular surface staining (OSS) scores were low. Impression cytology showed a drop in goblet cell density, presence of squamous metaplasia, and conjunctival keratinization significantly more in the hemodialysis group. No correlation was seen between the presence of conjunctival calcification and aortic calcification.

## Keywords

- ▶ chronic kidney disease
- ▶ renal dialysis
- ▶ impression cytology
- ▶ conjunctival keratinization
- ▶ squamous metaplasia
- ▶ calcification

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**Conclusion** The hemodialysis group had mild subclinical dry eye but keratinization of conjunctiva was seen. Similarly, advanced squamous metaplasia was seen in the peritoneal dialysis group. These changes were positively correlated to decrease in goblet cell density.

## Introduction

Chronic kidney disease (CKD) has an estimated prevalence of ~8 to 16% worldwide. It is usually due to type 2 diabetes mellitus and hypertension in developed countries. In contrast, it is a more prevalent disease in low- and middle-income countries. Besides these causes, glomerulonephritis, infection, and environmental factors such as pollution, pesticides, and herbal remedies play a significant role in its etiology, especially in Asia.<sup>1</sup> Management of end-stage renal disease calls for dialysis, which may be hemodialysis and peritoneal dialysis. Hemodialysis uses a machine to filter the blood. Peritoneal dialysis uses the lining of the abdomen and peritoneal membrane to filter the blood. Wastes are taken out by dialysate in cycles. Peritoneal dialysis is self-administered by the patient at home.<sup>2</sup>

CKD patients develop a dry eye for various reasons such as uremia, hypertension, secondary hyperparathyroidism, vitamin D deficiency, osteomalacia, and electrolyte imbalance.<sup>3</sup>

The exact mechanism regarding the effects of hemodialysis on the eye remains unknown, though Mvogo et al propose that hyposecretion of lacrimal fluid occurs due to comorbidities.<sup>4</sup> Charlton et al state that tears are hyperosmolar and are the pathogenic mechanism for dry eyes in patients with end-stage renal disease undergoing hemodialysis.<sup>5</sup> Chen et al claim that ocular surface changes occur during hemodialysis. The authors report that a change in oncotic plasma pressure in patients with chronic renal failure leads to increased matrix metalloproteinases (MMP-9,-1,-13,-3), responsible for the ocular surface disease of dry eye.<sup>6</sup>

Dry eye causes huge optical aberrations. This ultimately reduces the quality of vision and hinders self-care, and is unacceptable. Measures to correct dry eye improve the quality of vision.<sup>7</sup>

In low- and middle-income countries, the idiopathic group of CKD remains a significant cause for patients needing dialysis. These patients are remarkably different as environmental factors play an important role in etiology. Early diagnosis and intervention by an ophthalmologist will go a long way in maintaining good visual outcomes.<sup>1</sup>

Various reports are available regarding eye changes in patients mainly on hemodialysis. They include dry eyes, decreased anterior chamber depth, increased lens thickness, increased retinal and choroidal thickness after hemodialysis.<sup>3,8,9</sup>

A few isolated reports are beginning to appear regarding the squamous metaplasia, keratinization, and calcification of conjunctiva in patients undergoing hemodialysis. The relation of these conditions may be due to the comorbidities in these reports.<sup>10</sup> Not much has been reported about the effects of peritoneal dialysis on the eyes.

Therefore, the present study was designed to answer these scientific curiosities and find if these conditions are related to the type of dialysis.

## Objectives

The primary objective was to find the incidence of tear film disorders (high ocular surface staining score, abnormal Schirmer's test, tear film breakup time) and the severity of ocular surface changes (decrease in goblet cell density, presence of squamous metaplasia, keratinization of the CKD chronic kidney disease undergoing hemodialysis and peritoneal dialysis).

Secondary objectives included to look for an association between the altered tear function and the type of dialysis; compare the changes in impression cytology of conjunctiva (squamous metaplasia, keratinization, and calcification) with the changes in the conjunctiva (goblet cell density); and to correlate the presence of conjunctival calcification with aortic arch calcification, the latter being a high-risk factor for patient mortality.

## Materials and Methods

The study was approved by the Institutional Ethics Committee. The study adheres to the tenets of the declaration of Helsinki. Written informed consent was taken from all participants.

Inclusion criteria were adult patients with CKD of idiopathic etiology attending dialysis clinics under the Department of Nephrology in a tertiary care hospital in south India. Exclusion criteria were patients with other known causes of altered ocular surface including, diabetes mellitus, Sjogren's syndrome, cicatricial pemphigoid, rheumatoid arthritis, active ocular infection, blepharitis, those who underwent ocular surgery in the last 3 months, using any topical medication, known patients of dry eyes and those using contact lenses. Patients developing CKD after transplant were also excluded from the study. Demographic data collection included the patient's name, age, gender, hospital number and, type of dialysis. The duration of treatment was taken as per the hospital records.

Any history of eye complaints was recorded. Best-corrected visual acuity was recorded. Detailed ophthalmic examination included anterior segment examination for gross calcification of conjunctiva, Meibomian gland assessment, and observation of ocular surface after fluorescein staining was done by a hand-held slit lamp.

Alterations in the tear film were checked by the history of foreign body sensation, fluctuation of vision quality, or errors in shades of colors. Dry eye questionnaire was offered only to those whose symptoms were suggestive of dry eyes. The examination included performing Schirmer I test (Schirmer II test was done if required) and recording tear breakup time (TBUT) as per the standard protocol. All observations were recorded using standard units. Both eyes were tested, and an

average of the 2 eyes in a patient was considered for analysis. For obtaining samples of conjunctival impression cytology, supero-temporal bulbar conjunctiva was chosen as the site in all patients. The sample collection procedure was followed as described by Singh et al.<sup>11</sup> Samples from both eyes were taken. The average value of the eyes was taken for analysis. All patients underwent a dilated fundus examination.

Millipore 22 Micron Mixed Esters of Cellulose Filter Paper (Merck Life Sciences Pvt. Ltd. Bengaluru, India) was used. Samples were collected for conjunctival impression cytology. The paper was placed in the superotemporal quadrant of the conjunctiva, removed in a peeling motion, and placed in a jar with a fixative solution containing 95% ethanol. Care was taken to put the cell-containing surface of the strip facing upward. The paper was kept in a fixative solution for at least 10 minutes. After reaching the cytology laboratory, the sample was subjected to periodic acid–Schiff (PAS) staining.

The strips were mounted with distyrene, a plasticizer, and xylene (DPX) and reported. All slides were examined by a single blinded observer and graded according to impression cytology grading (► **Table 1**) as proposed by Haller–Schober.<sup>12</sup>

Another single blinded observer in the department of radiology reviewed chest X-rays of all patients to look for aortic calcification.

## Statistical Analysis

**Sample size:** Assuming the incidence of calcification among patients undergoing hemodialysis and peritoneal dialysis as 60% to 79% and 60% to 71%, respectively, an  $\alpha$  error of 5% and power of the study to be taken as 80%, the calculated sample size was estimated to be 142.<sup>13,14</sup>

Considering a nonresponse rate of 10%, the final sample size was 155. Software “N Master” was used. However, previous data showed that about 40 patients per annum undergo peritoneal dialysis, so about 80 patients were recruited. Patients undergoing peritoneal dialysis were converted to hemodialysis whenever they could not maintain their blood parameters. Therefore, patients recruited under the PD group were comparatively fewer than in the HD group.<sup>4</sup>

Variables studied were independent variables such as age, gender, etiology of CKD, and duration of dialysis. Dependent variables such as the length of wetting (mm) on the Schirmer

test, time (seconds) as measured through tear film break-up time, goblet cell density (cells/mm<sup>2</sup>), grades of squamous metaplasia, presence of corneconjunctival calcification, and grades of aortic calcification.

Statistical analysis was done using Stata version 14.0. Independent variables such as age and duration of illness are expressed as mean with standard deviation. Dependent variables such as the results of the Schirmer test, TBUT, and goblet cell density are expressed as median with an interquartile range.

Analytical statistics, including changes in impression cytology, grades of changes, and tear film parameters, were done using Fisher exact test.

## Results

A total of 108 patients with idiopathic etiology for CKD were studied. Participants *n* (%) were 76 (70.37) in the hemodialysis group and 32 (29.63) in the peritoneal dialysis group. There were 69 (63.89%) males and 39 (36.11%) females. The mean (SD) age of participants was 38.2 years (12.9) in the hemodialysis group and 41.3 years (12.8) in the peritoneal dialysis group, the difference not being statistically significant ( $t = -1.14294$ ,  $df = 106$ ,  $p = 0.25$ ).

### Dry Eye Parameters

The median (IQR) of dry eye parameters was assessed as an average of values for both eyes. Using the Schirmer test, the average value was found to be 18 mm (9–25) in the hemodialysis group and 20 mm (15–30) in the peritoneal dialysis group. The difference was not statistically significant ( $p$ -value = 0.07). Overall, the Schirmer test showed some form of dry eyes (wetting of the strip of less than 10 mm after 5 minutes) in 39.5% of patients in the hemodialysis group and 12.5% in peritoneal dialysis. This difference was found to be statistically highly significant ( $\chi^2 = 7.596$ ,  $df = 1$ ,  $p$ -value < 0.001) (► **Table 2**).

The median (IQR) of average values for TBUT in both eyes was 8 seconds (5–10) for the hemodialysis group and also 8 seconds (6–10) for the peritoneal dialysis group. A value of less than 10 seconds was taken as suggestive of dry eyes. Decreased TBUT was seen in 20 (26.3%) hemodialysis and 14 (43.7%) peritoneal dialysis group patients. The difference in

**Table 1** Impression cytology grading

Grade	Epithelial cells	Squamous metaplasia (N:C ratio)	Degree of keratinization	Goblet cell density	Goblet cell morphology	Calcification
0	Intact, dense	None (1:1–1:3)	None	Normal >500 cells/mm <sup>2</sup>	Normal	Present/Absent
1	Slightly loosened, low	Low graded (1:4–1:6)	Low graded	Slightly reduced 100–500 cells	–	
2	Loosened	Distinct (1:6–1:10)	Distinct	Distinctly reduced 100–500 cells	–	
3	Single cells	Massive >1:10	Massive	Sporadic or no goblet cell seen	Pathological	

**Table 2** Comparison of dry eye parameters in patients undergoing hemodialysis and peritoneal dialysis as compared with the normative data (N = 108)

Dry eye parameters	Hemodialysis (N = 76) n (%)	Peritoneal dialysis (N = 32) n (%)	p-Value
Schirmer 1 (<10 mm)			
Right eye median (IQR)	18 (9–25)	20 (15–30)	0.07 <sup>a</sup>
Left eye median (IQR)	18 (9.5–25)	20 (15–30)	0.06 <sup>a</sup>
Tear breakup time (<10 s)			
Right eye median (IQR)	8 (5–10)	8 (6–10)	0.69 <sup>a</sup>
Left eye median (IQR)	8 (5–10)	8 (5–10)	0.83 <sup>a</sup>
Schirmer			
Dry eye present	30 (39.5)	4 (12.5)	< 0.001 <sup>b</sup>
Dry eye absent	46 (60.5)	28 (87.5)	
Tear breakup time			
Normal	56 (73.7)	18 (56.3)	0.07 <sup>b</sup>
Decreased	20 (26.3)	14 (43.7)	

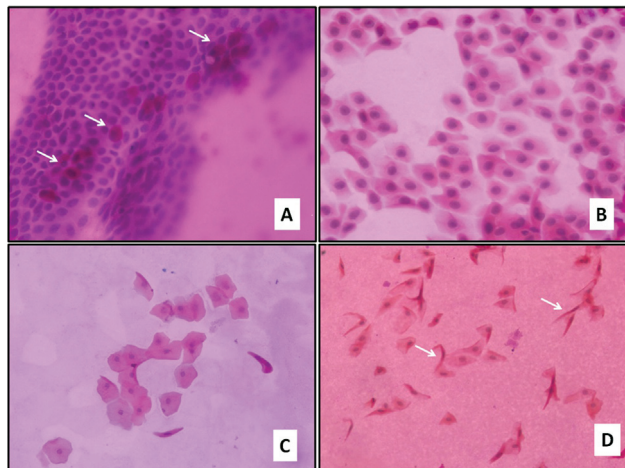
<sup>a</sup>Mann-Whitney U test.<sup>b</sup>Chi-square test.

the proportion of patients with lesser TBUT values in our study was not statistically significant (chi-square = 3.173, df = 1, p-value 0.07).

### Impression Cytology Study

#### Squamous metaplasia:

Significantly higher grade of squamous metaplasia (N:C ratio of 1:10) was seen in 25% of patients treated with hemodialysis. In comparison, it was seen in 68.75% of patients treated on peritoneal dialysis. This difference was statistically significant (p-value = 0.001). This finding indicates that patients undergoing peritoneal dialysis develop advanced grades of squamous metaplasia (► Fig. 1).



**Fig. 1** Conjunctival impression cytology (200X, PAS-PAP stain) (A) shows normal epithelial cells, high N:C ratio, mucin cells (white arrows) classified as Grade 0 squamous metaplasia. (B–D) (PAS-PAP, 300X) gradual loss of epithelial cell cohesion, decrease in the N:C ratio and mucin cells classified as grades 1, 2, and 3 squamous metaplasia. D-spindling of cells (arrows) indicate severe keratinization/squamous metaplasia.

On analyzing, goblet cell density of more than 100 cells, i.e., Grade 0–2 density, the distribution, was equal (75% of patients) in both groups. On analyzing, severe loss of goblet cell density (<100 cells; grade 3), the distribution was equal (25% of patients). This indicates that the goblet cell density does not vary with the type of dialysis.

#### Keratinization

Minimum keratinization (Grade 0–1) was seen in 56.8% of hemodialysis patients. This was seen in 73.3% of patients undergoing peritoneal dialysis. An advanced degree of keratinization (grade 2–3) was seen in 43.2% of patients undergoing hemodialysis and 35.7% of patients undergoing peritoneal dialysis. A statistically significant (p = 0.03) difference was found between the groups. It is inferred that hemodialysis patients have a higher risk of developing keratinization.

#### Calcification of Conjunctiva

No patient undergoing hemodialysis developed conjunctival calcification, while it was seen in 6.3% of patients undergoing peritoneal dialysis. This difference was not found to be statistically significant. The type of dialysis does not seem to influence the risk for conjunctival calcification (► Table 3).

On comparing squamous metaplasia with grades of goblet cell density amongst the study participants, grade 0–2 squamous metaplasia was seen in 89.1% of patients with a goblet cell density of more than 100 (grade 0–2). Also, 10.9% of those with goblet cell density less than 100 (grade 3) had low grades (Grade 0–2) of squamous metaplasia. About 42.1% of grade 3 squamous metaplasia did not have a significant loss of goblet cells (grade 0–2). In total, 57.9% of patients with grade 3 squamous metaplasia had grade 3 goblet cells (<100 cells/mm<sup>2</sup>). The difference between the grade 3 squamous metaplasia with grade 3 goblet cell density was significant

**Table 3** Comparison of changes seen on conjunctival impression cytology in patients undergoing hemodialysis and peritoneal dialysis

Conjunctival changes	Hemodiaysis n (%)	Peritoneal dialysis n (%)	Chi-square, p-Value
Squamous metaplasia (N = 108)			
Grade 0,1 and 2	57 (75%)	10 (31.25%)	0.001 <sup>a</sup>
Grade 3	19 (25%)	22 (68.75%)	
Goblet cell density (N = 108)			
Grade 0	21 (27.64)	3 (9.3)	0.061 <sup>a</sup>
Grade 1	26 (34.21)	11 (34.4)	
Grade 2	10 (13.15)	10 (31.3)	
Grade 3	19 (25)	8 (25)	
Degree of keratinization (N = 102)			
Grade 0	21 (28.4)	3 (10.7)	0.03 <sup>a</sup>
Grade 1	21 (28.4)	15 (53.6)	
Grade 2	25 (33.8)	10 (35.7)	
Grade 3	7 (9.4)	0	
Conjunctival calcification (N = 108)			
Yes	0	2 (6.3)	0.09 <sup>a</sup>
No	76 (100)	30 (93.7)	

<sup>a</sup>Chi-square-test.

( $p$ -value = 0.001). There is a high risk of developing squamous metaplasia if the goblet cell density is < 100 cells/mm<sup>2</sup>.

The association between the goblet cell density and degree of keratinization was analyzed. About 14.7% of patients with grade 3 goblet cell density had low degrees of keratinization (grade 0–2). In contrast, those with grade 3 keratinization had grade 3 goblet cell density (absent goblet cells). No patient had grade 3 keratinization with lower grades of goblet cell density (grade 0–2). The difference between the two groups was statistically significant ( $p < 0.01$ ). Therefore, it can be inferred that if the goblet cell density goes low, there is a risk of developing conjunctival keratinization.

All patients with conjunctival calcification had (grades 0–2 ) normal goblet cell density. No patient with grade 3

goblet cell density had conjunctival calcification. The difference was not statistically significant ( $p$ -value = 0.410). It implies that conjunctival calcification is not associated with goblet cell density (→ **Table 4**).

Patients with conjunctival calcification did not show aortic calcification on their chest X-ray films. It is concluded that there is no relation between conjunctival calcification and aortic calcification.

## Discussion

### Ocular Surface Disorder

The study included 76 patients in HD and 32 in the PD group. These patients were asymptomatic for ocular complaints. In

**Table 4** Comparison of goblet cell density with the presence of squamous metaplasia, keratinization, and conjunctival calcification amongst the participants (N = 108)

Variables	Goblet cell density Grade 0,1,2	Goblet cell density Grade 3	Chi Square Value	Degree of freedom	p-Value
Squamous metaplasia (Grade) (n = 74)					
0,1,2	49 (89.1)	6 (10.9)	17.618	1	< 0.001
3	8 (42.1)	11 (57.9)			
Keratinization (Grade) (n = 102)					
0,1,2	81 (85.3)	14 (14.7)	28.989	1	< 0.01
3	0	7 (100)			
Conjunctival calcification (n = 108)					
Absent	79 (74.5)	27 (25.5)	0.679	1	0.410
Present	2 (100)	0			

Note: Significant  $p$ -Value are marked in bold letters.



our study, the mean age was middle age and comparable in both HD and PD groups. So, various causes of dry eyes in the elderly age group did not influence the study results. The mean duration of dialysis was 1.35 years amongst the study participants. The ocular surface staining score was low ruling out severe dry eyes. Though the Schirmer test showed a significant difference between the two types of dialysis groups, TBUT did not show the same. The variability can account for the difference in the accuracy of the Schirmer test. Some feel that it is a reasonably accurate test,<sup>15</sup> while others think that its accuracy is low and has a weak link to the symptoms of dry eyes.<sup>16</sup> The Schirmer test reflects the tear production of an eye. TBUT reflects the tear evaporation from the surface. A surface irregularity may induce rapid TBUT, which does not necessarily mean an abnormal tear film. TBUT is known to vary in an individual. Also, TBUT is not a closely reproducible phenomenon in an individual eye.<sup>17</sup>

Taskapili states that hemodialysis alters tear osmolality and volume transiently. These alterations are correlated to body weight, ultrafiltration, and creatinine alterations.<sup>18</sup>

Charlton et al studied renal dialysis patients. The authors reported that all subjects had hyperosmolar tears, and serum and tear osmolality was positive for dry eyes. Authors state that despite having hyperosmolar tears, renal dialysis patients are a particular group of the population that remains asymptomatic for dry eye.<sup>5</sup>

Aktas et al. reported changes in tear functions of patients undergoing hemodialysis. They found that 62.7% had dry eyes by TBUT method, while 21.3% had dry eyes according to Schirmer test.<sup>19</sup>

Chen et al correlated ocular changes in hemodialysis patients to the etiology of chronic renal failure (CRF). Tear breakup time and Schirmer's test decreased significantly and showed the same trend independent of the etiology of CRF.<sup>8</sup>

## Impression Cytology

### Squamous Metaplasia

Singh et al described the relevance of impression cytology. The procedure removes superficial (1–3) layers of conjunctival cells, and the same can be used for histological, immunohistological, and molecular studies. The accuracy has been found to be correlated with histological samples in 80% of cases. Therefore, it is well accepted, non-invasive procedure to study ocular surface disorders.<sup>11</sup> Doughty reported the development of squamous metaplasia in contact lens wearers.<sup>20</sup> Chen et al claim that squamous metaplasia in severe Sjogren's syndrome is due to an immune regulator-deficient dry eye.<sup>21</sup> Demir et al proposed that the duration of renal failure is a risk factor for squamous metaplasia.<sup>22</sup>

Murine et al established a correlation between squamous metaplasia and dry eyes. The authors proposed a grading system for the changes seen.<sup>23</sup> Bakari et al studied changes in impression cytology in patients undergoing hemodialysis and graded them. Authors found the changes to be grade 0 in 9%, grade 1 in 51%, grade 2 in 31%, and grade 3 in 9% of patients. The authors concluded that the changes in patients with CRF on regular hemodialysis are due to chronic inflam-

mation of the conjunctiva.<sup>9</sup> Various attempts have been made as mechanism for squamous metaplasia in patients undergoing dialysis, which is usually hemodialysis. De Palva et al did an experimental study on C57BL/6 and IFN- $\gamma$ -knockout mice to find the pathogenesis of squamous metaplasia. Authors found migration of CD4+ T-cells and an increase in interferon levels, especially, IFN- $\gamma$  linking immune mechanism to squamous metaplasia.<sup>24</sup> Cobo et al discussed the role of chronic inflammation in patients with CKD. These patients are believed to be having uncontrolled, persistent, and maladaptive inflammation. These patients have an accelerated aging process due to inflammation. Inflammation leads to uremic toxin accumulation, especially large and middle molecules. Middle molecules are protein-bound and difficult to remove in dialysis. These middle molecules, including cytokines and other pro-inflammatory products, are ~23% uremic toxins generated endogenously. This maladaptive inflammation causes squamous metaplasia in addition to other effects.<sup>25</sup>

The present study included all patients with idiopathic kidney disorders; it allowed us to compare the groups based on the type of dialysis. Our study is the first with a moderate number of patients, even in the peritoneal dialysis group. So, a comparison has been done to study if the type of dialysis influences the findings on the ocular surface. Our study found that higher grades of squamous metaplasia were seen in patients undergoing peritoneal dialysis, and the difference between the two groups was statistically significant.

Destefanis et al conducted an experimental study on canine keratoconjunctivitis sicca and hypothesized that metabolic changes could affect immune response orchestration in a model of immune-mediated ocular disease.<sup>26</sup> There may be a similar process in humans and remains unexplored to date.

Tseng et al state that acute inflammation causes loss of goblet cells leading to squamous metaplasia.<sup>27</sup> Our study showed that the difference between the grade 3 squamous metaplasia with advanced (grade 3) goblet cell density loss is significant ( $p$ -value, 0.001). We found that the risk of squamous metaplasia increased if the goblet cell count was less than 100 cells/mm<sup>2</sup>.

### Conjunctival Keratinization

Maumenee studied conjunctival keratinization under various conditions. The author concluded that bulbar conjunctiva undergoes keratinization in vitamin A deficiency. The author mentions that the conjunctival and corneal epithelium can develop keratinization, similar to skin under suitable tissue culture.<sup>28</sup>

Nelson et al stated that normal eyes have normal epithelium and goblet cell density in the palpebral and bulbar conjunctiva. Eyes with the primary ocular surface disease have abnormal epithelium and goblet cells in the bulbar and palpebral conjunctiva. When such abnormalities occur only on the bulbar conjunctiva, environmental factors play an essential role.<sup>29</sup>

Nakamura studied the molecular mechanism and found that various keratinization-related proteins are involved in a severely cicatrizing ocular surface disease.<sup>30</sup>

Our study has shown an advanced grade of keratinization in both groups of patients undergoing dialysis. A statistically significant difference in conjunctival keratinization between the groups was seen. The tendency seemed to be higher in patients in the hemodialysis group. We believe that low-grade chronic inflammation plays a role in ocular surface changes in these patients. Also, the patients are usually on antihypertensive medications and diuretics, known to cause inflammation.

### Calcification

Aktas et al reported changes in the eyes of the patients undergoing hemodialysis. The most common finding was conjunctival calcification in 81.3%. This correlated to the serum calcium and phosphate levels.<sup>19</sup>

Bakari et al reported that conjunctival calcification was more common and extensive in CRF patients than in the controls. The severity of conjunctival changes was not related to the calcium deposition elsewhere. No correlation was found between impression cytology grading and calcium deposition.<sup>9</sup>

Stibor et al examined regular dialysis patients and compared them with the control group. The authors found that pathological changes, including calcification, are due to premature aging in patients of CRF undergoing regular hemodialysis.<sup>31</sup>

Kiani et al found that 32.2% of patients with HD developed conjunctival calcification. The study had patients with diabetes mellitus (39.6%) and hypertension (38.8%). The authors reported a significant relation between conjunctival calcification and the etiology of HD.<sup>10</sup>

Ozdemir et al tried to correlate the ocular surface changes of the conjunctiva (alteration in tear functions) and corneoconjunctival calcification in patients of CRF undergoing hemodialysis. They did not find any correlation between corneoconjunctival calcification and altered tear functions.<sup>32</sup>

In our study, gross conjunctival calcification was seen only in two patients of peritoneal dialysis and none in the HD group. No patient showed corneal calcification. The patients were asymptomatic. No calcification features were seen on impression cytology, as the specimen was taken from the superotemporal conjunctiva of both eyes. Long-term influences cannot be commented at present.

Vignelli and Stucchi studied conjunctival calcification with various laboratory parameters in chronic patients of hemodialysis. They found that lesions usually occur in the paralimbal area in the exposed bulbar conjunctiva. It was believed to be due to high alkalinity here as CO<sub>2</sub> diffuses from this area leading to calcium deposition.<sup>33</sup>

Our study did not support this hypothesis as we did not find a low goblet cell density in these patients. The grade of aortic arch calcification was high in both groups though there was no significant difference between the groups. No significant correlation was seen between conjunctival calcification and aortic calcification in our patients.

### Conclusion

The present study highlights the need for regular ophthalmic examination in apparently asymptomatic patients undergo-

ing dialysis. The risks vary between the type of dialysis being used. The treating physician needs to be aware of the various eye changes, especially squamous metaplasia, conjunctival keratinization, and calcification, especially with the idiopathic group of CKD.

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### Conflict of Interest

None declared.

### Ethical Approval

The study was approved by the Institutional Ethics Committee (Human Studies).

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