ORIGINAL ARTICLE

To Study Changes in Corneal Endothelium in Patients of Chronic Kidney Disease at GMC Jammu

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Abstract

Background: Chronic Kidney disease is a global health concern and patients with Chronic kidney disease (CKD) have an accelerated atherosclerosis and increased risk of thrombotic- ischemic complications as compared to general population. In addition, there is evidence of endothelial damage that may be attributed to proinflammatory state and toxin buildup due to reduced renal clearance. The aim of this study is to evaluate the effect of CKD on corneal endothelium and correlate with severity of disease. **Methods:** It is a prospective, cross-sectional study conducted in Department of Ophthalmology, GMC, Jammu for a period of 6 months from October 2023 to March 2024. The study included 3 categories of patients each with 30 patients of either sex and between 15 and 80 years of age. **Results:** A total of 90 patients were included in the study. Majority of the patients belonged to age group 61-70 years and the most common cause of CKD was found to be Diabetes. We found decreased endothelial cell count with a mean of 2240 ± 396.22 cells/mm^2 in dialysis group. We also found significant increase in coefficient of variation and decreased hexagonality which shows polymegathism and pleomorphism in corneal endothelial cells in CKD cases. However, no correlation was found between blood urea or serum creatinine with endothelial parameters in any group. **Conclusion:** Due to morphological abnormalities in corneal endothelium caused by CKD, patients with CKD are more susceptible to endothelial decompensation and hence special care should be taken before undergoing intraocular surgery.

Key Words

Chronic Kidney Disease, Corneal Endothelium

Introduction

Chronic kidney disease, also known as Chronic kidney failure, is associated with the gradual decrease of kidney function leading to metabolic imbalances, decrease in the GFR (glomerular filtration rate) and retention of harmful waste products in the body. About 10% individuals suffer from chronic kidney disease worldwide and it is a rapidly expanding global health concern[1]. Diabetes and hypertension account for about two-thirds of cases worldwide[2]. It is progressive and irreparable condition that can result in end-stage renal disease which needs renal replacement therapy for survival.

Numerous ocular problems associated with chronic kidney disease have been documented, such as conjunctival calcium deposits[3], band-shaped keratopathy[3], cataract[4], retinal detachment and retinopathy[5].

There has been speculation that the aforementioned issues could be related to body fluids, such as the aqueous

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Manuscript Received: 29.05.2024; **Revision Accepted**: 30.07.2024;

Published Online First: 10 Jan, 2025

Open Access at: https://journal.jkscience.org

Cite this article as: Gupta S, Kour C, Gupta V. To Study Changes in Corneal Endothelium in Patients of Chronic Kidney Disease at GMC Jammu. JK Science 2025; 27(1):9-13

humor, losing their homeostasis. This leads to the accumulation of urea and other undesirable chemicals in the aqueous humor. The aim of the study was to demonstrate that patients with CKD may have corneal endothelial abnormalities, as the aqueous humor is primarily responsible for maintaining the corneal endothelium.

Material and Methods

It is a prospective, cross-sectional study conducted in Department of Ophthalmology, GMC, Jammu for a period of 6 months from October 2023 to March 2024. Prior approval of the institutional ethical committee has been taken. The study comprised of three groups of patients, each with thirty patients of either sex and between 15 and 80 years of age. Group A comprised stage 5 CKD cases who were on dialysis, group B comprised of stage 3 and 4 CKD cases, whereas group C comprised the age-matched controls. These 3 groups were examined by noncontact specular microscopy (Topcon SP 1P), and their endothelial parameters [central corneal thickness (CCT) in micrometers, endothelial cell density (ECD) in cells per square millimeter, coefficient of variation (CV) in percentage, and hexagonality (Hex) in percentage] were analyzed.

Study participants having a background of ocular surgery or laser treatment of cornea, any corneal abnormality, a history of trauma, on any topical medication, and any active or old ocular disease history were excluded from this study.

Every participant provided their informed consent. Complete medical history with dialysis history was obtained. They were also investigated for complete blood profile, serum creatinine, blood urea and blood sugar levels. Blood investigations were obtained prior to dialysis in dialysis instances.

Complete ophthalmic examination of both eyes was done and then measurement of important parameters like endothelial cell density, measurement of coefficient of variation, measurement of hexagonality, measurement of central corneal thickness, and measurement of average cell size was carried out using Non-contact Topcon SP 1P specular microscope. Average reading from three images was taken for all parameters and the eye with worst reading was selected.

Statistical Analysis

Data analysis was done by using SPSS (Statistical Package for Social Sciences) version 26.0. Analysis of variance (ANOVA) test was used to compare the CCT, CV, CD, and % Hex in control, dialyzed, and non-dialyzed groups. Pairwise comparison of CCT, CV, CD, and % Hex was done by using the Tukey test. Pearson correlation coefficient, linear regression line equation, and R2 were calculated with respect to serum urea, serum creatinine, serum calcium, and serum phosphorus to assess the influence on endothelial parameters. P value < 0.05 was considered as significant.

Results

Most of the study participants in Group A were in the age group of 61 to 70 years (11.1%) followed by age group of 41-60 years (13.2%). On the other hand, percentage of study participants in Group B belonging to age group of 61 to 70 years was 13.3% followed by age group of 41 to 50 years in which the percentage of study participants of category B was 8.8 %. In Group C also, maximum participants were in the age group of 61 to 70 years (16.6%) followed by age group of 51-60 years (7.7%). Overall, the maximum percentage of study participants was in the age group of 61-70 years (41.1%) followed by 51-60 years (22.2%) and 41-50 years (17.7%) ***(Table 1).***

Table 1: Age Distribution of the Study Population

Age	Group A N (%)	Group B N (%)	Group C N (%)	Total
<20 years	3 (3.3)	0	2 (2.2)	5 (5.5)
21-30	2 (2.2)	1 (1.1)	2 (2.2)	5 (5.5)
41-50	6 (6.6)	8 (8.8)	2 (2.2)	16 (17.7)
51-60	6 (6.6)	7 (7.7)	7 (7.7)	20 (22.2)
61-70	10 (11.1)	12 (13.3)	15 (16.6)	37 (41.1)
>70	3 (3.3)	2 (2.2)	2 (2.2)	7 (7.7)

Table 2 shows data regarding the comparison between the three groups in context of corneal alterations. The mean endothelial cell density was 2240 ± 396.22 cells/mm^2 in group A, 2490 ± 351.81 cells/mm^2 in group B and 2560 ± 249.61 cells/mm^2 in group C. The difference between the three groups was statistically significant ($p<0.01$). The value of coefficient of variance was 38 ± 5.6% in group A, 39 ± 4.6% in group B and 27 ± 0.6% in group C. The difference among the three groups was statistically significant ($p<0.001$). The percentage of hexagonality was 52 ± 7.1% in group A, 46 ± 5.7% in group B, 50 ± 6.1 in group C. The difference in values of percentage of hexagonality was statistically significant ($p<0.0015$). The difference in values of the average size of cells in group A (490 ± 77.46 um^2), group B (400 ±

Table 2: Comparison of Endothelial Parameters Among Various Groups

Parameter	Dialysis (Group A)		Non-dialysis (Group B)		Control (Group C)		P
	Mean SD		Mean SD		Mean SD		
ECD, cells/mm^2	2240	396.22	2490	351.81	2560	249.61	<0.001
CV, %	38	5.6	39	4.6	27	0.6	<0.001
Hx, %	52	7.1	46	5.7	50	6.1	0.0015
Avg, µm^2	490	77.46	400	77.11	357	20.11	<0.001
CCT, µm	510	37.44	513	46.57	518	26.73	0.711

77.11 um^2), and group C (357 ± 20.11um^2) was substantially significant statistically (p<0.001). The mean CCT value in group A was 510 ±37.44 µm, in group B 513 ± 46.57µm and in group C 518 ± 26.73µm. The difference in CCT values between the three groups was statistically insignificant (p=0.711).

The mean concentration of blood urea among the study participants in the dialysis group was found out to be 140 mg/dL, while in the non-dialysis group it was 80 mg/dL. Blood Urea showed no relationship with any corneal endothelium parameter ***(Table 3).***

Table 3: Linear Correlation Between Mean Blood Urea and Endothelial Parameters in Both Dialysis and Non-dialysis Group

Pearson correlation coefficient (r) values for different parameters	Blood urea	
	Group A	Group B
ECD (cells/mm^2)	0.25	0.26
CV (%)	0.086	-0.27
Hx (%)	0.36	-0.269
Avg (µm^2)	-0.28	-0.18
CCT (µm)	-0.09	0.38

When compared to nondiabetic CKD cases, diabetic CKD exhibited a significant reduction in endothelial cell density. Hexagonality values and CCT values were substantially lower in diabetics, although CV was significantly greater in CKD in diabetes patients, indicating a more pleomorphic propensity in Diabetes ***(Table 4).***

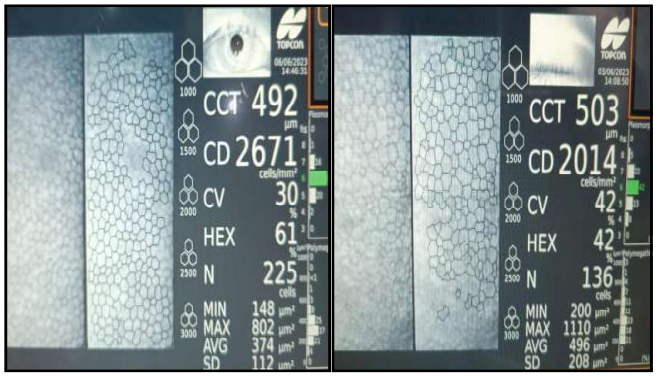

Fig 1: Specular Photograph of Non-CKD and CKD Patient, Respectively.

Discussion

Chronic kidney disease (CKD), also known as chronic renal failure, is a progressive loss of kidney function over

Table 4: Endothelial Parameters in Diabetic and Other CKD Cases in Dialysis and Non-Dialysis Group

Parameters evaluated	Type 2 Diabetes Mellitus		Other causes	
	Group A	Group B	Group A	Group B
ECD,cells/mm^2	2249.86	2340	2470.47	2577
CV, %	42	40	39	36
Hx, %	43	46	51	49
Avg, µm^2	460.44	440.80	438.80	383.50
CCT, µm	499.26	521.34	521.60	523.44

months or years. The embryogenic relationship between the eye and kidney was found in the mid-nineteenth century, revealing several shared characteristics. Research has linked it to several eye diseases, including age-related macular degeneration, diabetes-related retinopathy, glaucoma, and cataracts. These diseases can cause problems with vision and calcification of the cornea and conjunctiva[6,7]. In this study examined changes in corneal endothelial cells in patients with CKD. The ECD ranged between 1844 to 2636 mm^2 in the dialysis group and 2139 to 2841mm^2 in the non-dialysis group and 2311 to 2809 mm^2 in the study participants in control group. Sati *et al,.*[8] and Diaz *et al,.*[9] also reported lower cell density in individuals with chronic kidney disease compared to non-dialysis subjects in their studies.

Our study found significant differences in CV, hexagonality, and mean cell size across the three groups, suggesting polymegathism and pleomorphism in these cells. Dube *et al*. reported considerable polymegathism and pleomorphism in the corneal endothelium of CKD patients, even after controlling for age.[10]

Accumulated toxins in aqueous humour might damage corneal endothelial cells, leading to morphological changes in response to the insult. Patients with CKD may have morphological alterations due to elevated aqueous urea and oxidised glutathione levels, which can induce cell stress. Gundus *et al*. found that chronic osmotic stress, such as diabetes and ageing, generates abnormal F-actin fibres in endothelial cells, resulting in polymegathism to regulate cell volume.[11]

We found increased central corneal thickness in patients who were recently diagnosed and started on dialysis since long time. Patients with long-term disease had thinner corneas, suggesting adaptive modifications. Elbay *et al*. and Chen *et al*. reported no significant difference in CCT following hemodialysis[12,13]. The mean CCT in CKD patients was 509.2 ± 39.47 µm, while in controls it was 511.8 ± 24.77 µm. These findings are consistent with a study conducted in Chennai on 6574 healthy participants, which found a mean CCT of 511.4 ± 33.5 µm.[14] This observation indicates that the Indian population has propensity towards thinner corneas.

We found no significant relationship between blood urea levels and endothelial measures. Sati *et al*. observed a positive association between blood urea and corneal endothelium parameters, which contradicts our findings.[8] While no association was found between blood urea and serum creatinine, it is important to consider the potential harmful effect on the corneal endothelium. In CKD, inflammatory markers and hyperuricemia increase, leading to oxidative stress and reduced nitric oxide release. This can contribute to endothelial dysfunction.[15]

Diabetes was the leading cause of CKD in 17 of 50 (34%) patients, while Dahal *et al*. [16] identified HTN in 123 (41%), and diabetes in 98 (32.6%) of 300 cases. Diabetic CKD patients had lower ECD and hexagonality compared to non-diabetics, whereas CV was higher. Diabetes, a recognised risk factor for endothelial cell death and renal failure, has been shown to have a more damaging effect on corneal endothelial cells. However, studies by Parekh *et al.* [17] and Inoue *et al*.[18] found no correlation between these alterations and systemic variables.

Conclusion

CKD significantly impacts corneal endothelial health, leading to decreased cell density and increased cellular irregularities. These changes are more pronounced in patients undergoing dialysis. These findings underscore the importance of careful ocular monitoring and management in CKD patients, particularly before any intraocular surgeries.

Acknowledgements

Department of Ophthalmology, GMC Jammu.

Declarations

Funding: Nil
Conflict of interest: None
Ethical approval: Taken

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