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Research article

Evaluation of changes in corneal endothelium in chronic kidney disease a cross sectional study

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ABSTRACT

Chronic kidney disease is a growing global health concern that affects approximately 10 percent of overall worldwide people. High blood pressure and diabetes account for around two-thirds of all cases of chronic kidney disease worldwide. Because the kidneys and eye grow at about the same embryonic period, around the 4th week to 6th week of pregnancy, there is a strong link connecting kidney problems and eye problems. Hence the aim of the study was to carry out evaluation of changes in corneal endothelium in chronic kidney disease. The study included three categories of patients, each with twenty five patients. Stage 5 CKD patients on dialysis were placed in Category A, non-dialyzed stage three and four CKD patients were placed in category B, and healthy controls of matching age were placed in category C. They had their whole blood composition evaluation, concentration of blood urea, concentration of serum creatinine, and concentration of blood sugar levels checked as well. Both eyes were inspected and measurement of important parameters like endothelial cell density in cornea, measurement of coefficient of variation (CV percent), measurement of percentage of hexagonally (Hx percent), measurement of central corneal thickness (CCT), and measurement of average size of cells was carried out using a non-contact variant of specular microscope (TOPCON SP 300P) utilizing. Topcon Cell Count Software. Endothelial cell density changed significantly in kidney disease patients compared to controls. In our study, we discovered a substantial difference in CV, hexagonality, and mean cell size across the three groups, indicating polymegathism and pleomorphism in these cells. It was observed that participants who were recently diagnosed with CKD and dialysis commenced recently had a higher central corneal thicknesses than those who had been on hemodialysis for a long time. Patients with long-term illness, on the other hand, had thinner corneas, indicating adaptive alterations. Due to morphological abnormalities in the corneal endothelium caused by CKD, such as pleomorphism and polymegathism, patients with CKD may be more susceptible to endothelial damage. This necessitates extra precaution in patients having CKD undergoing intraocular surgery.

Keywords: Chronic kidney disease, corneal epithelium, Endothelium

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INTRODUCTION

Chronic kidney disease considered as CKD is a growing global health concern that affects approximately 10 percent of overall worldwide people. High blood pressure and diabetes account for around two-thirds of all occurrences of CKD worldwide. CKD is an irreparable and progressive condition that leads to occurrence of end-stage kidney disease, in which patients must rely on kidney replacement treatment to live. Approximately 1, 30,000 people are on dialysis, with the number rising to around 232 per million people. Because the kidneys and eye grow at about the same embryonic period, around the 4th week to 6th week of pregnancy, there is a strong link connecting kidney problems and eye problems. According to studies, persons with CKD have a higher incidence of eye illnesses and impaired vision [1,2].

Starting from the anterior segment to posterior segment numerous ocular findings are present in the patients with CKD including refractive changes, dry eye, corneal, and conjunctival epithelial erosions, perilimbal calcium deposits, band keratopathy, intraocular pressure (IOP) fluctuations, posterior subcapsular cataract, ischemic optic neuropathy, choroidal perfusion delay, corneal endothelium alterations, and thickness changes in the central cornea, retinal nerve fiber layer, and choroid [3,4].

According to data from the ICMR, the number of people with diabetes in the among the adult population of India has climbed to 7.1 percent with a prevalence of twenty eight percent in the urban

area population having age over forty years). Meanwhile, today's overall population of adults in India has a documented disease burden of hypertension of seventeen percent. (14.8 percent from rural area and 21.4 percent from urban area. Panesar et al found a similar frequency of 17.4 percent even in a Delhi slum-resettlement colony. With the increased incidence of chronic diseases in India, the frequency of CKD is projected to climb, and this is, without a doubt, the most important demographic to target [5,6].

Vascular remodeling, inflammatory condition, per oxidation, vascular dysfunction, and dyslipidemia are all major contributors to CKD as well as eye disorders. Early alterations can be noticed in these cases with the use of early ocular screening [7,8]. The focus of this research was to use the approach of specular photography to estimate the impact of CKD upon corneal endothelial changes and link the findings with disease severity. We also wanted to see if there was a difference in corneal alterations between diabetic and non-diabetic CKD.

MATERIALS AND METHODS

A cross-sectional investigation was carried out at a tertiary level healthcare center. The ethics committee of the institution had given its prior consent. The study included three categories of patients, each with twenty five patients of either sex or ranging in age from fifteen to eighty years old. Stage 5 CKD patients on dialysis were placed in Category A, no dialyzed stage three and four CKD patients were placed in category B, and healthy controls of matching age were placed in category C. Hemodialysis undergoing patients were those who had been on bicarbonate dialysate dialysis for minimum duration of three months, 3 times in a week, for three to five hours per session.

Study participants having a background of ocular operation or laser treatment of cornea, any corneal abnormality, a history of trauma, a history of tropical medicine, or a history of present or old eye disease were all excluded from further analysis. GFR is used to classify CKD into five stages, with G3 category and G4 category being nondialyzed (GFR values between fifty nine ml/min to fifteen mL/min per 1.73 m2) and G5 being dialyzed (GFR values below fifteen mL/min per 1.73 m2).

Each subject gave their informed consent. A complete medical history was acquired; including a history of dialysis. They had their whole blood composition, concentration of blood urea, concentration of serum creatinine, and concentration of blood sugar levels checked as well. Blood investigations were obtained prior to dialysis in dialysis instances.

Following registration, both eyes were inspected and measurement of important parameters like Endothelial cell density in cornea, measurement of coefficient of variation (CV percent), measurement of percentage of hexagonality (Hx percent), measurement of central corneal thickness (CCT), and measurement of average size of cells was carried out using a non-contact variant of specular microscope (TOPCON SP 300P) utilizing Topcon Cell Count Software. The ocular examination was performed 30 minutes before the process of dialysis in the study participants belonging to dialysis group. For all of the criteria, the output response from three photos was collected, as well as the eyes with one of the worst findings was chosen.

Statistical analysis

The SPSS software (Statistical Package for Social Sciences) 21.0 version was used to analyse the data. Each group needed at least 25 people, according with power analysis. The CCT, CV, ECD, and percent Hx in the category of controls, dialyzed category, and nondialyzed category were compared using an ANOVA statistical examination. To analyze the impact affecting endothelial parameters, the Pearson correlation coefficient method and R2method were determined with respect to concentration of blood urea and concentration of serum creatinine. A statistically significant value of $P < 0.05$ was used.

RESULTS AND DISCUSSION

Table no 1shows that most of the study participants in category A were in the age group of 61 to 70 years (26.3%) followed by age group of 51-60 years (21.8%). On the other hand, percentage of study participants in category B belonging to age group of 61 to 70 years was 32.1%. It was followed by age group of 41 to 50 years in which the percentage of study participants of category B was 23.2%. In category C also, maximum participants were in the age group of 61 to 70 years (40.9%) followed by age group of 51-60 years (19.1%). Overall, the maximum percentage of study participants was in the age group of 61-70 years (34.8%) followed by 51-60 years (28.4%) and 41-50 years (25.7%).

Table 1: Distribution of study participants according to age

Age of study participants	Category A (%)	Category B (%)	Category C (%)	Total
< Twenty years	8.1	-	3.7	5.1
21-30 years	3.9	-	-	2.4
41-50 years	14.2	23.2	4.3	25.7
51-60 years	21.8	12.8	19.1	28.4
61-70 years	26.3	32.1	40.9	34.8
>70 years	9.7	3.9	5.1	6.4

Table no 2 shows data regarding the comparison between the three categories in context of changes in cornea. The median value of endothelial cell density was 2276 ± 386.63 cells/mm^2 in category A, 2421±353.99 cells/mm^2 in category B and 2492±261.74 cells/mm^2. The difference between the three categories was substantially not important statistically (p =0.46). There was analysis of coefficient of variance among different categories. The value of coefficient of variance was 37±6.9 % in category A, 38±5.6% in

category B and 32±0.9% in category C. The variation among the three categories was substantially important statistically. (p=0.001). The percentage of hexagonality was 51±8.4 in category A, 51±5.9 in category B, 53±5.9 in category C. The difference in values of percentage of hexagonality was non- significant statistically. The difference in values of the average size of cells in category A (536±77.57 um^2), category B (441±74.72 um^2), and category C (468± 21.07 um^2) in three categories was substantially significant statistically. (p=0.004).

Table 2: Analysis of comparison among endothelial parameters in different parameters

Parameter	Category A		Category B		Category C		p
	Median value	SD	Median value	SD	Median value	SD	
Endothelial cell density, cells/mm2	2276	386.63	2421	353.99	2492	261.74	0.46
Coefficient of variance %	37	6.9	38	5.6	32	0.9	0.002**
Percentage of hexagonality	51	8.4	51	5.9	53	7.9	0.042
Average size of cells(, um^2)	536	77.57	441	74.72	468	21.07	0.004**
Central corneal thickness, um	524	37.48	526	47.68	576	27.81	0.643

Table no 3 shows that the variation in values of central corneal thickness among three categories was statistically non significant (p= 0.643). Data regarding the impact of duration of procedure in dialysis over endothelial parameters has been presented in table 3. The variation in the median values of endothelial cell density, coefficient of variation, percentage of hexagonality and average size of cells when the duration of process of dialysis was less than one year, one to three years and more than three years was statistically non significant (p= 0.394, 0.977, 0.782,0.557). It was observed that value of central corneal thickness was 527±35.67 um when the duration of process of dialysis was less than one year, 491± 41.68 um when the duration was between one year and three years, 485.31±17.68 when the duration of procedure was more than three years. The variation among the values was substantially important statistically. (p=0.026).

Table 3: Data regarding impact of duration of dialysis upon endothelial parameters

Parameters evaluated	Less than one year		One to three years		More than three years	p	
	Median values	SD values	Median values	SD values	Median values	SD values	
Endothelial cell density, cells/mm2	2381.4	421.67	2289.8	291.61	2412.8	456.42	0.394
Coefficient of variance %	38%	0.08	39%	0.067	39%	0.077	0.977
Percentage of hexagonality	51%	0.091	49%	0.081	42%	0.086	0.782
Average size of cells (, um^2)	434.5	87.37	458.7	74.81	457	21.61	0.557
Central corneal thickness, um	527	35.67	491	41.68	485.31	17.68	0.026*

Table no 4 shows that the mean concentration of blood urea among the study participants in the dialysis category was found out to be 137 mg/dL, while in the nondialysis group it was 75 mg/dL. Blood Urea, on the other hand, did not appear to have a substantial relationship with any corneal endothelium measure.

Table 4: 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	
	Category A	Category B
Endothelial cell density cells/mm^2	0.26	0.25
Co-efficient of Variance (%)	0.087	-0.26
Hexagonality (%)	0.35	-0.267
Average size of cells (um^2)	-0.27	-0.19
Central corneal thickness (um)	-0.08	0.39

A weak connection among concentration of serum creatinine and changes in corneal endothelial indicators was also reported in table no 5. Anatomical alterations in the corneal endothelium in diabetes patients have already been demonstrated in numerous studies. We wanted to see if renal disease has any remarkable effects on endothelial cell indicators of cornea in diabetic and non - diabetic CKD patients. 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 diabetic instances, although CV was significantly greater in CKD in diabetes patients, indicating a more pleomorphic propensity in Diabetes.

Table 5: Endothelial parameters in diabetic cases and other CKD cases in dialysis and non dialysis group

Parameters evaluated	Type II diabetes mellitus		Other factors	
	Category A	Category B	Category A	Category B
Endothelial cell density, cells/mm2	2251.96	2348	2471.47	2576
Coefficient of variance %	41%	40%	39%	36%
Percentage of hexagonality	44%	47%	51%	49%
Average size of cells (, um^2)	461.44	447.84	438.49	383.54
Central corneal thickness, um	499.28	521.29	521.64	523.46

Chronic kidney disease (CKD), commonly referred to as chronic renal failure, is a gradual deterioration of kidney function spanning months or years. The embryogenic association between the eye and the kidney began in the mid-nineteenth century, and many parallels were discovered. Many studies have linked it to major eye illnesses such as age-related macular damage, diabetes related retinopathy, glaucoma eye disease, and cataract eye disease, all of which cause significant vision problems as well as calcification accumulation on the cornea and conjunctiva [9,10]. In this work, we looked at the alterations in corneal endothelial cells in people with CKD. The ECD varied from 1533 to 3191 mm2 in the study participants in dialysis group, 1502 to 3035 mm2 in the study participants in nondialysis group, and 2108 to 3188 mm2 in the study participants in control group.

Despite the fact that these measures were found to be non-significant, they revealed that cell density changed significantly in kidney disease patients compared to controls. However, Sati et al. as well as Diaz et al. observed reduced cell density in patients with chronic kidney disease than in non-dialysis patients in their research. In our study, we discovered a substantial difference in CV, hexagonality, and mean cell size across the three groups, indicating polymegathism and pleomorphism in these cells [11,12]. The findings matched those of Ohguro et al., who found significant polymegathism as well as pleomorphism in the endothelium of cornea of CKD patients after adjusting for age. These findings revealed that, despite normal values of endothelial cell density, the corneal endothelium is subjected to a persistent assault.

Elevated toxin concentrations in the aqueous hum our may have a deleterious effect on corneal endothelial cells, leading them to morphologically alter in response to the insult. Elevated aqueous urea concentrations and considerably increased oxidized glutathione concentrations in the aqueous hum our in individuals with CKD may create stress to the cells, resulting in these morphological alterations [13,14]. Endothelial cells undergo change involving irregular F actin fibers as a result of persistent osmotic stress, such as in diabetes and old age, according to Kim et al., which leads to polymegathism to sustain cell volume homeostasis. For CKD, a similar phenomenon can be proposed, as there is a disordered equilibrium that leads to these alterations. There's also a messed-up equilibrium that's causing these shifts [15,16] .

We concluded that participants who were recently diagnosed with CKD and dialysis commenced recently had a higher central corneal thicknesses than those who had been on hemodialysis for a long time. Patients with long-term illness, on the other hand, had thinner corneas, indicating adaptive alterations. Elbay et al. as well as Chen et al. found no significant variation in CCT following hemodialysis in another trial. We found that the mean values of CCT in CKD individuals was 510.3±40.58 um while in controls it was found to be 523.9±35.88μm, which was comparable to a research of 6574 healthy participants conducted in Chennai, which found that the mean CCT for the community was 511.4 33.5μm[17.18].

This finding demonstrates the Indian population's proclivity for thinner corneas. We found no strong association among concentration of blood urea and endothelial factors in consideration of endothelial parameters. Our findings contradict those of Sati et al., who discovered a favorable relationship among concentration of blood urea and corneal endothelium characteristics. That although we found no link between blood urea and serum creatinine, we can't rule out the possibility of a detrimental impact on the endothelium of cornea. There is an increase in markers of inflammation in CKD, as well as hyperuricemia, that is known to cause oxidative stress and inflammation, lowering nitric oxide generation and so leading to endothelial dysfunction [19].

We also discovered a significant prevalence of diabetes(35%) causing CKD, while Dahal et al. showed HTN to be the most frequent cause of CKD in 41% of total cases and diabetes to be the most common cause of CKD in 32.6% patients. We also observed that diabetic CKD study participants had lower ECD and Hexagonality than nondiabetic CKD study participants, whereas their CV was higher than nondiabetic CKD study participants. These findings reveal that diabetes, which is a well-known contributing factor for endothelial cell destruction in patients with renal failure, has a damaging effect on ocular endothelial cells. However studies by, Parekh et al & Inoue et al. were unable to demonstrate a link between such changes and systemic variables [20].

We postulate that the endothelium of cornea is constantly stressed in CKD patients, resulting in pathological changes such as polymegathism and pleomorphism as a result of the toxic exogenous exposure. These are delicate cases, and extra caution should be exercised before undergoing any intraocular surgery. When comparing dialysis patients to nondialyzed patients, we found that dialysis patients had more significant endothelial changes. Cases of CKD caused by diabetes must be given even more attention. Patients with CKD should also have a proper ocular examination protocol created because they have several ocular morbidities [21]. However; further research is needed to determine specific chemicals are responsible for these alterations. Because our research is a cross-sectional one, more investigation in bigger patient groups is required.

CONCLUSION

Due to morphological abnormalities in the corneal endothelium caused by CKD, such as pleomorphism and polymegathism, patients with CKD may be more susceptible to

endothelial decompensation. This necessitates extra caution in patients having CKD who are undergoing intraocular surgery.

REFERENCES

1. Mack HG, Savige J, 2017. Chronic kidney disease and cataract: Seeing the light. American Journal of Nephrology. 45, Pages: 522-523. Doi: 10.1159/000475556
2. Varma PP, 2015. Prevalence of chronic kidney disease in India-Where are we heading? Indian Journal of Nephrology. 25(3), Pages-133-135. Doi: 26060360
3. Varughese S, Abraham G, 2018. Chronic kidney disease in India: A clarion call for change. Clinical Journal of American Society of Nephrology. 13(5), Pages: 802- 804. Doi: https://doi.org/10.2215/CJN.09180817
4. Bodaghi B, Massamba N, Izzedine H, 2014. The eye: A window on kidney disease. Clinical Kidney Journal. 7(4), Pages-337-338. Doi: 10.1093/ckj/sfu073
5. Caglayan M, Kosekahya P, Takmaz T, et al, 2017. Effects of haemodialysis on corneal and anterior chamber morphometry and intraocular pressure in patients with end stage renal disease. Arquivos Brasileiros de Oftalmologia. 80(3), Pages- 176-80. Doi: 10.5935/0004-2749.20170043.
6. Wong CW, Wong TY, Cheng CY, et al, 2013. Kidney and eye diseases: Common risk factors, etiological mechanisms, and pathways. Kidney International. 85(6), Pages-1290-1302. Doi: 10.1038/ki.2013.491.
7. Bargman JM, 2015. Chronic kidney disease. In: Fauci AS, editor. Harrison's Principle of Internal Medicine. New York: Mc Graw Hill Proessions. p. 1811.
8. Porter R, Crombie AL, 1973. Corneal and conjunctival calcification in chronic renal failure. British Journal of Ophthalmology. 57(5), Pages- 339-343. Doi: 10.1136/bjo.57.5.339.
9. Easterbrook M, Mortimer CB, I970. Ocular signs in chronic renal failure. British Journal of Ophthalmology. 54(11), Pages-724-730. Doi: 10.1136/bjo.54.11.724.
10. Klaassen-Broekema N, van Bijsterveld OP, 1993. Limbal and corneal calcification in patients with chronic renal failure. British Journal of Ophthalmology. 77(9), Pages-569-571. Doi: 10.1136/bjo.77.9.569.
11. Sati A, Jha A, Moulick PS, et al, 2016. Corneal endothelial alterations in chronic renal failure. Cornea. 35(10), Pages-1320-1325. Doi: 10.1097/ICO.0000000000000922
12. Diaz Couchoud P, Bordas FD, Garcia JR, et al, 2001. Corneal disease in patients with chronic renal insufficiency undergoing hemodialysis. Cornea. 20(7), Pages-695-702.
13. Ohguro N, Matsuda M, Fukuda M, 1999. Corneal endothelial changes in patients with chronic renal failure. American Journal of Ophthalmology. 128(1), Pages-234-236.
14. Kim EK, Geroski DH, Holly GP, et al 1992. Corneal endothelial cytoskeletal changes in F-actin with aging, diabetes, and after cytochalasin exposure. American Journal of Ophthalmology. 114(3), Pages- 329-335. Doi: 10.1016/S0002-9394(14)71800-8.
15. Elbay A, Altinisik M, Dincyildiz A, et al, 2017. Are the effects of hemodialysis on ocular parameters similar during and after a hemodialysis session. Arquivos Brasileiros de Oftalmologia. 80(5), Pages-290-295. Doi: 10.5935/0004-2749.20170071.
16. Chen H, Zhang X, Shen X, 2018. Ocular changes during hemodialysis in patients with end-stage renal disease. BMC Ophthalmology. 18(1), Pages- 208. Doi: 10.1186/s12886-018-0885-0.
17. Vijaya L, George R, Arvind H, et al, 2010. Central corneal thickness in adult South Indians: The Chennai Glaucoma Study. Ophthalmology. 117(4), Pages-700-704. Doi: 10.1016/j.ophtha.2009.09.025.
18. Cai W, Duan XM, Liu Y, et al, 2017. Uric acid induces endothelial dysfunction by activating the HMGB1/RAGE signaling pathway. Biomed Research Interntional. 4391920. Doi: 10.1155/2017/4391920.
19. Dahal P, Gouli S, 2015. Ocular findings in the chronic renal failure. Journal Of College Of Medical Science Nepal. 10(2), Pages- 18-26. Doi: 10.3126/jcmsn.v10i2.12949.
20. Parekh R, Ranagnath KN, Suresh KP, et al, 2006. Corneal end othelium count and thickness in diabetes mellitus. International Journal of Diabetes in Developing Countries. 26(1), Pages-24-26.
21. Inoue K, Kato S, Inoue Y, et al, 2002. The corneal endothelium and thickness in type II diabetes mellitus. Japanese Journal of Ophthalmology. 46(1), Pages- 65-69.

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