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Original Research Article

Study of retinal nerve fiber layer thickness in chronic kidney disease patients

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ABSTRACT

Aims: To compare the RNFL thickness between CKD patients and age matched healthy controls and to correlate RNFL thickness with duration of CKD. RNFL thickness was also assessed in CKD patients with and without haemodialysis.

Materials and Methods: One hundred and fifty eyes were included in the study and were labeled as group A. Equal number of age matched controls were included in group B. RNFL thickness was measured using optical coherence tomography for optic nerve head (ONH) scan.

Results: Mean of average RNFL thickness was studied to be thinner in group A in comparison to group B. Statistically significant thinning was also noted in superior and inferior quadrant of group A. Increase in average RNFL thickness and increase in superior and temporal quadrant RNFL thickness was noted in HD group as compared to non- HD group. A negative correlation was noted between RNFL thickness and duration of CKD.

Conclusion: This study concluded that RNFL thickness was found to be thinner in CKD patients as compared to healthy individuals. However RNFL thickness was found to be thicker in HD group as compared to non- HD group.

1. Introduction

Retinal nerve fibre layer (RNFL) thickness varies at different stages of neuropathy and the variation in thickness is strongly co-related with visual defects. Decrease in RNFL thickness maybe suggestive of early stages of optic neuropathy and this change can be observed even before the detection of any visual disturbances. Hence, it is of clinical significance.[1–3] The pathophysiological model that explains changes in RNFL thickness in patients of CKD includes, vascular ischemia due to anaemia, generalized atherosclerosis and hypotension, retinal ischemia due to transient imbalance in fluid and electrolytes in patients on haemodialysis (HD).[4] Due to ischemia, retinal microvasculature is affected, resulting in decrease blood supply to nerve fibre layer and a consequent decrease in RNFL thickness.[1] During HD osmotically active substances are diffused out, as a result body fluid is lost and the blood osmolarity also decreases.[5,6]

OCT has the maximum sensitivity to measure RNFL thickness and can detect even very small changes.[7] Spectral domain OCT (SD-OCT) is a better device as compared to conventional time domain OCT (TD-OCT), as it provides three-dimensional reconstruction of the scanned area with better resolution.[8]

Very few studies have been conducted to evaluate relationship between RNFL thickness and CKD in the Indian subcontinent. This study was conducted to analyse

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variation in RNFL thickness changes in CKD patients in comparison to healthy age matched controls by OCT, establishing mean total RNFL thickness and also mean RNFL thickness in nasal, inferior, temporal and superior quadrants. Aim of this study was to assess the RNFL thickness "in CKD patients and in healthy subjects and to compare RNFL thickness in CKD patients with and without haemodialysis. We also compare the RNLF thickness with duration.

2. Materials and Methods

One hundred and fifty eyes of 75 patients attending the Medicine OPD having CKD and fulfilling the inclusion criteria and willing to give informed consent were included in the study. Equal number of controls, who were age matched and those who were ready to participate were selected for comparison from the healthy patients attending the Ophthalmology OPD. Study was done over a period of 12 months. Patients of CKD with age >18 years were included in group A and age matched healthy individuals were included in group B. Exclusion criteria for both the groups consisted of patients with any ocular pathology (Glaucoma, age-related macular degeneration, diabetic retinopathy, optic nerve pathology, retinal artery/vein occlusion, vitreous haemorrhage). History of any retinal laser or retinal surgery, cataract surgery less than 3 months, poor media clarity, extremes of ages (< 18 years and > 80 years), any ocular inflammation (uveitis, vasculitis), refractive error of >3diopters hypermetropics or < 3 diopter myopics and uncooperative patients.

All patients underwent a detailed ocular examination including visual acuity, intraocular pressure measurement, anterior segment and posterior segment examination. RNFL thickness was measured using Optovue RTVue 100 3D SD-OCT system. Optic Nerve Head (ONH) scan was obtained of all subjects which utilizes the 3.45mm diameter circle centred around the ONH. The circle is aligned automatically around the ONH which prevents measurement error. The ONH scan comprises of 13 circular scans measuring diameter ranging from 1.30 - 4.90mm and 12 radial lines with 3.70mm length. RNFL examination was carried out in "8 sectors namely superonasal (SN), superotemporal (ST), nasal upper (NU), nasal lower (NL), inferotemporal (IT), inferonasal (IN), temporal upper (TU), and temporal lower (TL).

The data was compiled in MS Excel 2010. SPSS software version 22 was used to perform the statistical analysis. Categorical data was expressed as frequency and continuous data as mean ± standard deviation. General linear model analysis of variance (ANOVA) was used to analyse the normally distributed data for more than two groups. For the comparison of continuous data t test was employed amid two groups (group A and group B). The p value of <0.05 was taken as statistical significant.

3. Result

A total of 150 subjects (300 eyes) were enrolled in the study. These subjects were equally distributed into two groups. Group A included 75 subjects (50%) with CKD and group B included rest 75 subjects (50%), who did not have CKD. These subjects were age matched. It was found that maximum patients, 23 (30.67%) belonged to age group (41-50 years) in both the groups. The mean age was 47.72 ± 13.18 in group A and 47.36 ± 12.48 in group B. The study involved total of 104 males and 46 females. Fifty two males and 23 females were included in each group having male to female ratio of (2 : 1). Both the groups comprised mainly of males.

On measuring RNFL thickness with the help of OCT, mean of average RNFL thickness" was studied to be thinner in "group A" (108.99 ± 17.55 μm) in comparison to "group B" (114.32 ± 14.04 μm) (Table 1 & Figures 1 and 2). The variance between the two groups was statistically significant (p value of 0.004), on using the unpaired t-test.

Mean RNFL thickness was also measured in all 4 quadrants. On comparison statistically significant thinning was noted in superior and inferior quadrant of group A as compared to group B (p value= 0.002 and 0.000 respectively), using unpaired t-test (Figure 3). Other quadrants, temporal and nasal, also showed decrease in mean RNFL two thickness in group A, but it was statistically not significant.

On comparison of mean of average RNFL thickness between HD and non- HD patients, statistically significant increase in thickness was seen in HD group (p-value = 0.000) (Table 2). Statistically significant thickening was seen in superior and temporal quadrant in HD group (p-value= 0.000 and 0.042 respectively). With increase in duration of CKD there is statistically significant decrease in "mean of average RNFL thickness.

A linear correlation was noted between the mean of average "RNFL thickness" and duration of CKD (Figure 4). Spearman correlation was used to find the relationship between duration of CKD and RNFL thickness. With increase in duration of CKD there was statistically significant decrease in "mean of average RNFL thickness (p value= 0.007).

Table 1: Comparison of mean of average "RNFL thickness between group A and group B"(n= 300 eyes)

Group	Average RNFL thickness (Mean ± SD) μm
Group A	108.99 ± 17.55
Group B	114.32 ± 14.04

4. Discussion

In the present study, mean of average "RNFL thickness" was compared among group A and group B. RNFL thickness

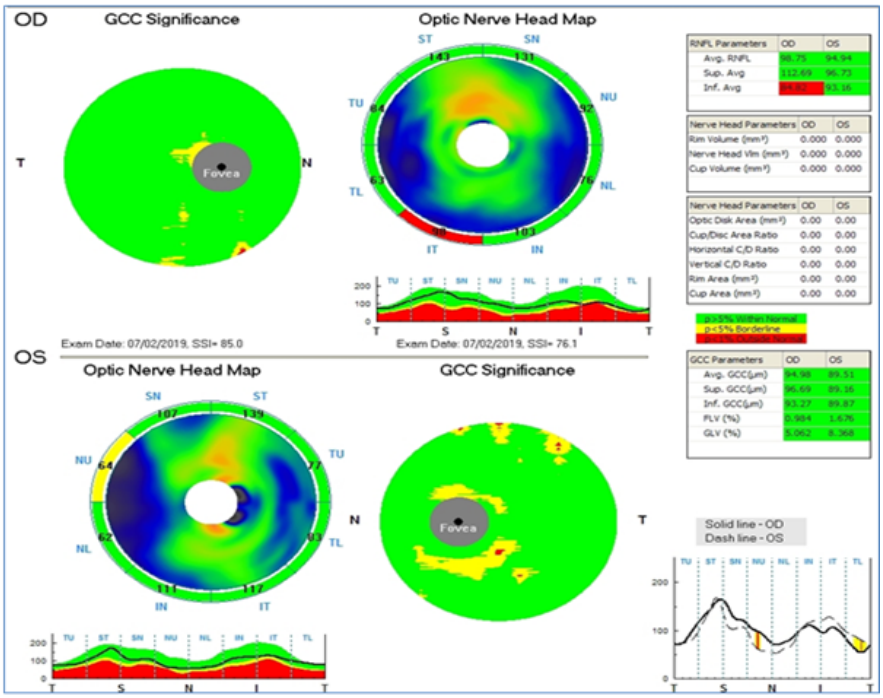

Fig. 1: Group A: Optic nerve head mapping in two groups through OCT

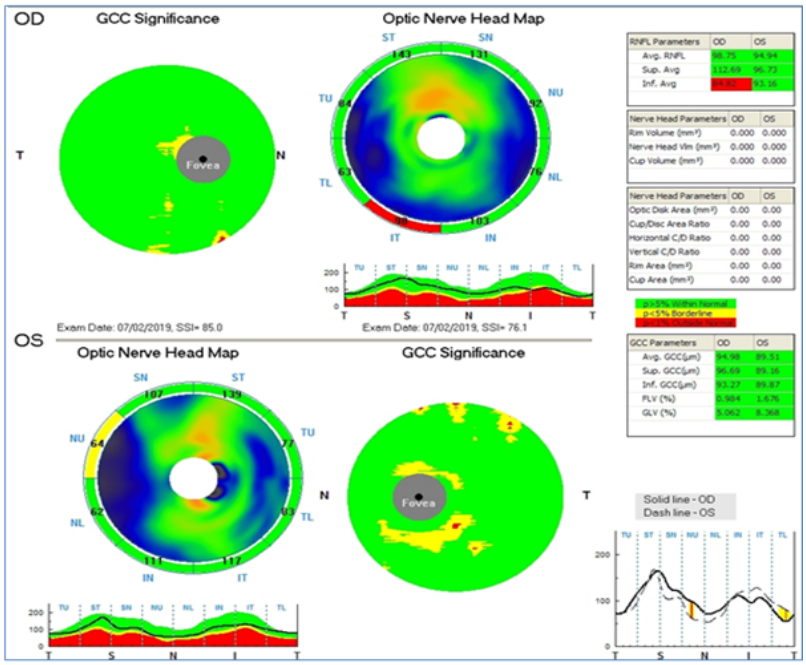

Fig. 2: Group B: Optic nerve head mapping in two groups through OCT

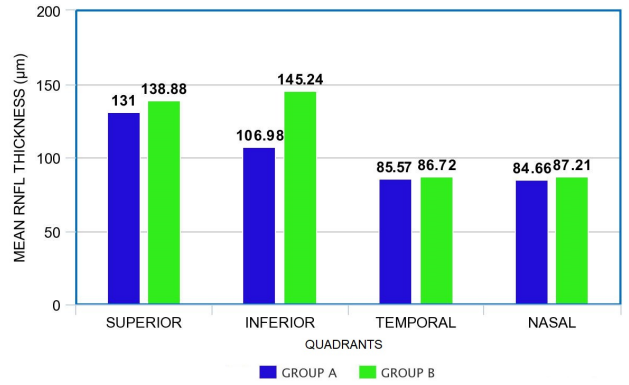

Fig. 3: Comparison of mean of RNFL thickness in 4 quadrants (n= 300 eyes)

Table 2: Comparison of mean of average RNFL thickness between HD and non- HD patients in group A (n= 150 eyes)

	Average RNFL thickness (Mean ± SD) μm
HD (n= 45)	113.18 ± 18.09
Non- HD (n= 30)	102.71 ± 14.75

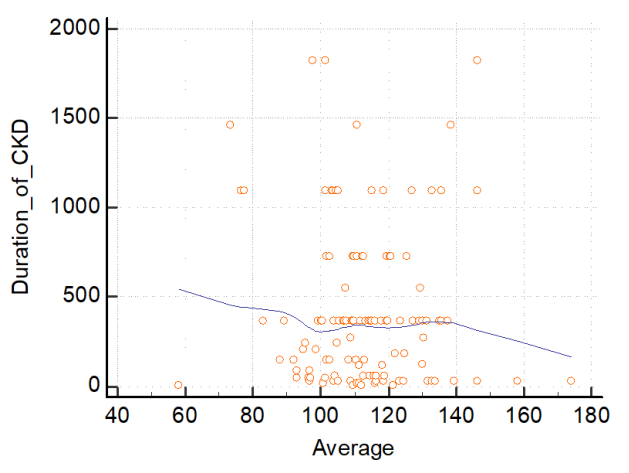

Fig. 4: Linear correlation between the mean of average RNFL thickness and duration of CKD (n= 150 eyes)

was observed to be thinner in group A and was statistically significant (p value 0.004). Thinning was also statistically significant in superior and inferior quadrant of group A as compared to group B. Demir MN et al. also reported similar results with statistically significant (p <0.01) thinning of mean RNFL thickness in chronic renal failure patients in all four quadrant as compared to normal subjects.[9] Change in RNFL thickness in CKD patients may be attributed to vascular ischemia, which results in poor blood supply to retinal layers, subsequently disturbing the retinal vasculature. As a consequence, thinning of RNFL occurs. Thinning is also associated with other factors like HD or systemic condition causing microangiopathy like diabetes mellitus and hypertension.[10]

RNFL thickness was also compared between the HD and non- HD group. On analysing RNFL thickness mean of "average RNFL thickness" was noted to be thicker in HD group and was statistically significant (p-value 0.000). Similar results were noted by Atilgan CU et al.[11] Demir MN et al. also reported similar results with increase in mean of "average RNFL thickness" post-HD, but it was statistically not significant.[12]

We also analysed quadrant wise RNFL thickness in "HD and non- HD group". Results showed increase in RNFL thickness in superior and temporal quadrant in "HD group" as compared to non- HD group and it was statistically significant (p value of 0.000 and 0.042 respectively). Other two quadrants also showed RNFL thickness more in the HD group but it was statistically not significant. These results can be attributed to vasodilation following HD. In renal failure, there is accumulation of inhibitors of Nitrous oxide synthase. With HD these substances are removed, thereby leading to accumulation of Nitric oxide and adrenomedullin. These are the vasoactive substances which eventually leads to vasodilation of retinal vessels. On the contrary, Demir et al. in their study noted mean "RNFL thickness" to be thinner in post HD group as compared to control group, but statistically significant difference was observed only in the inferior quadrant.[12] These changes maybe owing to transient fluid loss that may occur during dialysis, which leads to imbalance of fluid and electrolytes and as a consequence retinal ischemia and RNFL thinning occurs.[10]

5. Limitations

The current study was a cross-sectional study, therefore comparison of RNFL thickness pre and post HD could not be assessed. Another limitation of the study was interpersonal variability while taking the OCT reading. Small sample size was also one of the limitation of the study. Further randomized trials with larger group of patients and additional parameters could further enhance the knowledge.

6. Conclusion

The present study concluded that the mean of average RNFL thickness was significantly thinner in CKD patients as compared to non- CKD patients. Decrease in RNFL thickness maybe suggestive of early stages of optic neuropathy and this change can be observed even before the detection of any visual disturbances with the help of OCT. OCT has the maximum sensitivity to measure RNFL thickness and can detect even very small changes. Hence, it is of clinical significance.

7. Source of Funding

None.

8. Conflict of Interest

None.

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