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# Effect of hemodialysis on Intraocular Pressure

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## ABSTRACT

**Background:** Hemodialysis (HD) is an important and by far the commonest treatment for end stage renal failure (ESRF). Changes in intraocular pressure (IOP) are one of the eye problems among hemodialysis patients.

**Objective:** To evaluate changes in intraocular pressure (IOP) before, during and after single dialysis session. To detect changes in retinal fiber thickness measured by Optical Coherence Tomography (OCT) 6 months after basic examination.

**Patients and methods:** This prospective study was carried out on 80 eyes of 80 patients undergoing regular hemodialysis (HD), both males and females**.** The study was conducted in Aswan University Hospital.

**Results:** There was statically significant (but clinically not significant) decrease in IOP during HD, but there was no significant decrease when measured six month later. No significant difference in the mean IOP as regarding group's age, sex and duration of dialysis was found. Significant decrease in mean average RNFL thickness during the six months was noted as well as between age groups. There was no significance decrease in retinal nerve fiber layer (RNFL) thickness regarding sex and duration.

**Conclusion:** As there was loss of RNFL thickness in hemodialysis patients, visual field changes is recommended to be investigated on such patients. Also the effect of hemodialysis on patients with high IOP or glaucoma should be investigated as well.

**Keywords:** Hemodialysis, Chronic Kidney Disease, OCT, Intraocular Pressure.

## INTRODUCTION

Patients with chronic kidney disease (CKD) are generally treated using a blood-filtration mechanism, such as hemodialysis (HD). During HD, numerous metabolic parameters can change, including blood urea, sodium, potassium, and glucose levels. These fluctuations result in osmotic changes in blood, aqueous and vitreous humor, and other extracellular fluids. Visual acuity, intraocular pressure (IOP) and retinal thickness can also be affected [(1)]**.** Patients with chronic renal failure and renal replacement therapy can have vision loss either due to primary disease as diabetic retinopathy and hypertension or secondary to complications associated with dialysis [(2)]**.**

Ocular complications include reduced corneal endothelium cell density [(3)], ischaemic optic neuropathy [(4)], occipital lobe blindness and endogenous endophthalmitis [(5)]**.** Changes in IOP during or after HD have also been widely reported in the literature [(6)]**.** Elevated IOP and decreased ocular perfusion pressure (OPP) are risk factors for glaucoma development and progression. Unrecognized significant IOP elevation or OPP reduction during HD could lead to glaucomatous optic nerve damage and subsequent visual loss [(7)]**.** The relationship between IOP changes and HD has been evaluated for almost 50 years**.** Reported findings, theories, and conclusions are very different and in some cases, even when a new mechanism for HD influence on IOP was proposed, a critical revision of the previous reports was not performed [(8)]**.**

## AIM OF THE WORK

- The aim of our study is to evaluate changes in intraocular pressure (IOP) before, during and after single dialysis session.
- To detect changes in retinal fiber thickness measured by Optical Coherence Tomography (OCT) 6 months after basic examination.

## PATIENTS AND METHODS

**Study design:** This prospective study was carried out on 80 eyes of 80 patients undergoing regular hemodialysis (HD), both males and females**.** The study was conducted in Aswan University Hospital. All patients underwent measurement of intraocular pressure (IOP), before, during and after single session of dialysis, and followed up by Optical Coherence Tomography (OCT) 6 month after basic examination.

**Inclusion criteria:** Patients were included in the study if they were on regular hemodialysis and were willing and able to undergo a complete ophthalmologic examination.

**Exclusion criteria:** Patients having any ocular disease that would interfere with retinal examination and/or IOP measurement as irregularities or opacity of the cornea, any previous corneal surgeries, dense media opacity, and current eye infection, were excluded.

**Ethical considerations:** Confidentiality of all data was ensured. The steps of the study, the aims, the



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potential benefits all was discussed with the included patients. An informed written consent was obtained from each patient involved in the study.

**The study was approved by the Ethical Committee of Aswan University.**

**All patients in this study underwent comprehensive ophthalmic examination including:**

1. Medical and ocular history.
2. Complete ophthalmic examination:

a) Visual acuity (VA).
b) Anterior segment examination of the eye by slit lamp with exclusion of corneal abnormality, corneal surface irregularity or surgery and current eye infection.

3. Measurement of IOP by Perkins tonometer, approximately 15 minutes before starting HD, two hours after starting HD, 15 minutes after ending HD.
4. Retinal nerve fiber layer (RNFL) and optic disc imaging with OCT twice for every patient, at the beginning of the study and six months later.

**Technique of IOP measurement by Perkins tonometer:**

1. Instillation of topical anaesthetic, benoxinate 0.4% (Benox, Eipico, 10th of Ramadan city, Egypt) and fluorescein strip into the conjunctival sac.
2. Patient was seated in a semi sitting position with the head rested backward and looking straight forward.
3. The blue light from the Perkins tonometer was directed onto the prism head.
4. The tonometer head was perpendicular to the eye and moved forward slowly until the prism rests gently on the center of the patient's cornea.
5. With the other hand, the calibrated dial on the tonometer was rotated until the two semi-circles in the prism head are seen to meet and form a horizontal ‘S’ shape (the inner margins of the semicircles images just touch).
6. The reading on the dial, multiplied by ten, equals the IOP.

Data about IOP was collected at 15 minutes before starting HD, two hours after starting HD, 15 minutes after ending HD.
All IOP measurements were done by the same ophthalmologist.

**Optical Coherence Tomography:**

RNFL and optic disc were measured using spectral domain optical coherence tomography (SD-OCT), (Optovue, Fremont, CA, USA). In this study, the 3-dimensional (3D) disc and nerve head map 4-mm diameter (NHM4) RTVue protocols were used. The 3D disc protocol is a 4 × 4-mm scan centered on the optic disc that can be captured in just a few seconds and captures information over the whole of the optic nerve head, allowing not only the RNFL thickness to be calculated, but also the optic nerve topography and shape to be imaged.

OCT disc scans were performed for all patients in order to establish baseline thickness measurements. The resulting scan provides a 3D image of the optic disc and surrounding area. RNFL thickness measurements were obtained for the 3.45-mm radius ring only, and measurements were described as average RNFL and RNFL in the inferior, temporal, superior, and nasal quadrants. The optic cup was defined automatically by RTVue software as the intersection points of the nerve head inner boundary and a parallel line that is 150 µm above the connecting line of the retinal pigmented epithelial (RPE) tips .Optic disc parameters obtained were optic disc area, optic cup area, neuroretinal rim area, nerve head volume, cup volume, rim volume, cup-to-disc area ratio, cup-to-disc horizontal ratio, and cup-to-disc vertical ratio.

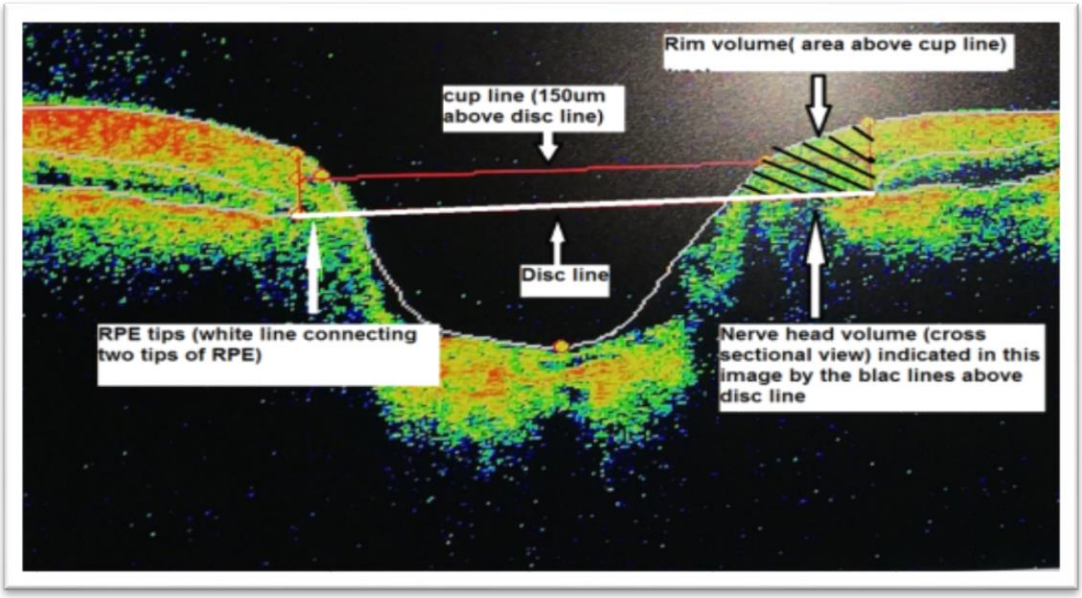


**Fig. (1):** ONH (optic nerve head)

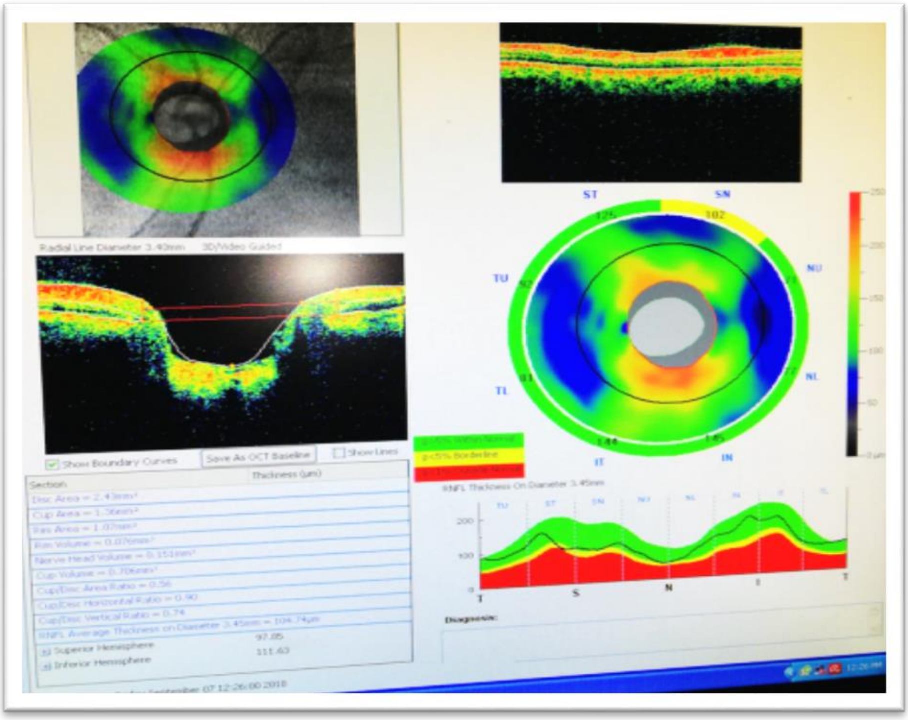

**Fig. (2):** ONH and RNFL thickness of right eye.

***Statistical analysis***

Data were collected, tabulated and statistically analyzed with Statistical Package for Social Science (SPSS) version 16.0 for Windows (Chicago, USA). Qualitative data were described using number and percent (%). The Kolmogorov -Smirnov test was used to verify the normality of distribution of the quantitative data, which were expressed as mean & standard deviation (X±SD) and analyzed by applying T test for independent groups and paired t test for intra-group comparisons of normally distributed variables. Mann Whitney and Wilcoxon signed ranks tests were used for non-normally distributed ones. To compare between more than two groups, ANOVA test was used for normally distributed quantitative variables, Kruskal Wallis and Friedman tests were used for abnormally distributed ones. All these tests were used as tests of significance at probability (P) value < 0.05.

**RESULTS**

Retinal nerve fiber layer (RNFL) were evaluated twice for every patient at the beginning of the study and six months later.

Age of the included patients ranged between 20 and 70 years with a mean of 48 ± 12.51 years. Patients were 50 females (62.5%) and 30 males (37.5%) as show in figure (3).

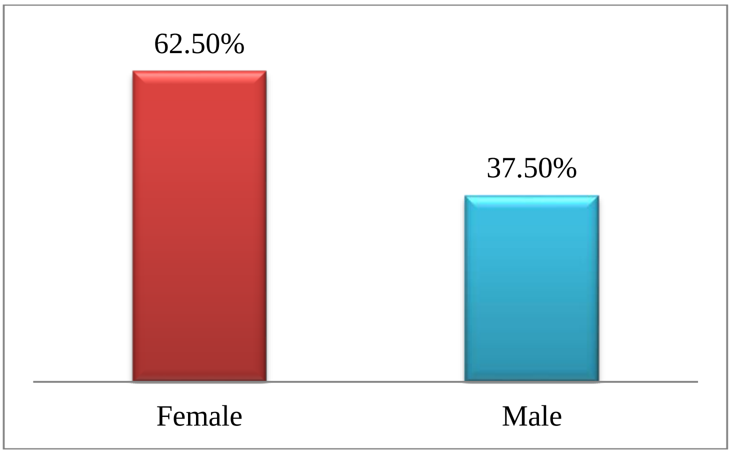


**Figure (3):** Distribution of the included patients as regard sex.

**Effect of gender on IOP:**
There was no significant difference between IOP measures as regarding sex as shown in table (1).

**Table (1):** Comparison of two sex groups regarding their mean basic intra ocular pressure.

| Sex | N (%) | Mean IOP ± SD | z | p-value | Test |
|---|---|---|---|---|---|
| **Male** | **30 (37.5%)** | **10.73 ± 3.26** | **1.593** | **0.111** | **Mann Whitney test (z)** |
| **Female** | **50 (62.5%)** | **11.27 ± 2.85** | | | |

*P-value <0.05 significant IOP= Intraocular pressure.*

**Effect of duration of dialysis on IOP:**
There was no significant difference on IOP regarding duration of dialysis as show in table (2).

**Table (2):** Effect of duration of dialysis on mean intra ocular pressure.

| Duration (year) | N (%) | Mean IOP ± SD | p-value | Test |
|---|---|---|---|---|
| <5 | 52 (65%) | 11.17 ± 2.81 | 0.174 | Kruskal Wallis H test |
| 5 – <10 | 14 (17.5%) | 11.23 ± 3.17 | | |
| ≥10 | 14 (17.5%) | 10.52 ± 3.54 | | |

*P-value <0.05 significant IOP= intraocular pressure.*

**Effect of hemodialysis on IOP:**
Significant decrease in mean IOP was found as show in table (3).

**Table (3):** Effect of hemodialysis on intra ocular pressure.

| IOP | Mean IOP ± SD | p-value | Test |
|---|---|---|---|
| **Pre-HD** | **11.54 ± 2.77** | **0.000** | **Friedman test** |
| **During-HD** | **11.04 ± 2.92** | | |
| **Post-HD** | **10.64 ± 3.30** | | |

*P-value <0.05 significant HD= Hemodialysis IOP= Intraocular pressure Pre-HD= IOP before hemodialysis During-HD=IOP During hemodialysis Post-HD=IOP after hemodialysis.*

**Comparison between three different mean of IOP:**
There was significant decrease in IOP before, during and after single session of dialysis as show in tables (4), (5) and (6).

**Table (4):** Comparison between intra ocular pressure before and during hemodialysis.

| IOP | Mean IOP ± SD | z | p-value | Tet |
|---|---|---|---|---|
| **Pre-HD** | **11.54 ± 2.77** | **-3.429** | **0.001** | **Wilcoxon signed ranks test** |
| **During-HD** | **11.04 ± 2.92** | | | |

**Table (5):** Comparison between intra ocular pressure before and after hemodialysis.

| IOP | Mean IOP ± SD | z | p-value | Test |
|---|---|---|---|---|
| **Pre-HD** | **11.54 ± 2.77** | | | **Wilcoxon signed ranks test** |
| **Post-HD** | **10.64 ± 3.30** | **-3.763** | **0.000** | |

**Table (6):** Comparison between intra ocular pressure during and after hemodialysis.

| IOP | Mean IOP ± SD | z | p-value | Test |
|---|---|---|---|---|
| **During-HD** | **11.04 ± 2.92** | | | **Wilcoxon signed ranks test** |
| **Post-HD** | **10.64 ± 3.30** | **-3.380** | **0.001** | |

*P-value <0.05 significant IOP= Intraocular pressure HD= hemodialysis During-HD=IOP During hemodialysis Post-HD=IOP after hemodialysis*

**Comparison between IOP before hemodialysis in the start of the study and IOP before hemodialysis six month later:**

There was no significant difference between IOP before the session of dialysis in the start of the study and IOP before another session of dialysis six months later, as shown in table (7).

**Table (7):** Comparison between intra ocular pressure before and six months later of hemodialysis.

| IOP | Mean IOP ± SD | t | p-value | Test |
|---|---|---|---|---|
| **Pre-HD** | **11.54 ± 2.77** | | | |
| **6month later-HD** | **11.65 ± 2.62** | **-0.299** | **0.765** | **Paired samples t-test** |

*P-value <0.05 significant IOP= Intraocular pressure HD= Hemodialysis Pre-HD= IOP before hemodialysis 6month later-HD = IOP before hemodialysis six month later.*

**Comparison between RNFL thickness of basic examination and six month later:**

There was significant decrease in average RNFL, average of the superior hemisphere of RNFL, and average of the inferior hemisphere of RNFL thickness of basic examination and six months later as show in tables (8), (9) and (10).

**Table (8):** Comparison between average retinal nerve fiber layer (RNFL) thickness of basic examination and six months later.

| RNFL | Mean ± SD | T | p-value | Test |
|---|---|---|---|---|
| **Pre avg.** | **102.62 ±14.19** | | | **Paired samples t-test** |
| **Post avg.** | **99.88 ± 13.73** | **7.64** | **0.000** | |

*P-value <0.05 significant RNFL= retinal nerve fiber layer pre avg= average of RNFL thickness of basic examination post avg= average of RNFL thickness six month later.*

**Table (9):** Comparison between average of the superior hemisphere of retinal nerve fiber layer thickness of basic examination and six months later.

| RNFL | Mean SD | T | p-value | Test |
|---|---|---|---|---|
| **Pre sup.** | **103.52 ± 13.53** | **5.70** | **0.000** | **Paired samples t-test** |
| **Post sup.** | **100.58 ± 13.33** | | | |

*P-value <0.05 significant RNFL= retinal nerve fiber layer pre sup= average of the superior hemisphere of RNFL thickness of basic examination post sup= average of the superior hemisphere of RNFL thickness six month later.*

**Table (10):** Comparison between average of the inferior hemisphere of retinal nerve fiber layer thickness of basic examination and six months later.

| RNFL | Mean ± SD | T | p-value | Test |
|---|---|---|---|---|
| **Pre inf.** | **101.72 ± 18.02** | | | |
| **Post inf.** | **99.18 ±17.13** | **5.68** | **0.000** | **Paired samples t-test** |

*P-value <0.05 significant RNFL= retinal nerve fiber layer pre inf= average of the inferior hemisphere of RNFL thickness of basic examination , post inf= average of the inferior hemisphere of RNFL thickness six month later.*

## DISCUSSION

Ocular problems such as macular edema, ischemic optic neuropathy, retinal detachment, retinal hemorrhage, and elevated intraocular pressure have been reported to exist in patients with end-stage renal disease (ESRD) [(9)].

Hemodialysis (HD) was mainly used to treat the disorder of water-electrolyte balance of patients with ESRD, exclude excessive small molecule hazardous substances and decrease plasma osmotic pressure at the same time [(10)].

In the present study, Change in IOP before, during and after single dialysis session. Also, six month later was evaluated. Retinal nerve fiber layer (RNFL) thickness was measured by Optical Coherence Tomography (OCT) twice, on the starting of the study and six months later.

Although clinically not significant, statistically significant decrease in IOP during HD was found in the current study (from 11.54 ± 2.77 before HD to 10.64 ± 3.30 after HD). There was no significant change when measuring is repeated six month later from 11.54 ± 2.77 before the session of HD to 11.65 ± 2.62 before another session of HD six months later from the start of the study. Other studies have shown similar results, with reductions in IOP varying between 0.8 and 1.3 mmHg [(11)].

Recent studies showed no change or a decrease in IOP, with no change in ocular perfusion pressure (OPP) during HD [(12)].

Moreover, **Doshiro *et al.*** [(13)] reported a significant IOP decrease during HD in the general study group. Also, **Tokuyama *et al.*** [(14)] related IOP reduction to ultrafiltration rate by the mean of albumin level. Ultrafiltration leads to increase in the oncotic pressure, so there will be a colloid gradient between plasma and interstitial fluid and water moves from the interstitial and aqueous humor to plasma fluid.

All these observations contrast with an earlier study, which showed an increase in IOP during HD, and reported that increase is due to a decrease in plasma osmolarity. Accordingly, a rapid decrease in plasma osmolarity during HD results in an osmotic gradient and causes fluid shift from blood to the eyes, causing an increase in IOP [(15)]. **Tovbin *et al.*** [(16)] also reported an increase in IOP and correlated it with rapid solute removal and high post dialysis urea rebound in dialysis patients.

On the other hand, other studies reported no correlation between serum osmolarity and IOP [(17)]. This is consistent with **Tokuyama *et al.*** [(18)] who found a correlation between change in IOP and colloid osmotic pressure (r = -0.510, p = 0.0012), but not serum osmolarity.

**Caliskan *et al.*** [(19)] reported that it is difficult to compare findings from various studies because of the differences in IOP measurement techniques and the ocular and non-ocular parameters investigated. Findings obtained using the Goldman tonometer tended to find reductions; the use of non-contact tonometer (NCT) resulted in opposite findings in that increased IOP is more likely to take place in a narrow and obstructive anterior chamber angle and tends to decline at an opposite angle.

Regarding sex, most studies reported that women had a higher IOP than men [(20)], this agree with the current study, as the mean IOP in females was (11.27 ± 2.85) higher than males (10.73 ± 3.26) but this difference was not statically significant.

In the current study, there was a decrease in mean IOP for each age group from 11.35 ± 3.42 in age ranged between 20 - < 40 years, to 11.05 ± 2.65 in age ranged between 40 – 60 < years, and then to 10.73 ± 3.18 in age ≥ 60 years. However, this decrease was not statistically significant. This is consistent with other study which reported that the mean IOP is decreased by 0.50 mmHg for each decade increase in age [(21)].

In ESRD patients treated with dialysis, optic neuropathy is a well-defined complication. It is probably caused by significant intra-dialytic hypotension, severe anemia and ischemia due to diffuse atherosclerosis, toxicity and also concomitant systemic diseases such as diabetes mellitus (DM) and hypertension (HTN). All of these are to blame for the development of this condition [(22)].

Also, chronic renal failure (CRF) is responsible for vascular ischemia that affects the retinal microvasculature and may result in a blood supply deficit for the nerve fiber layer and a consequent decrease in its thickness [(23)].

Thinning of the RNFL as an indicator of optic neuropathy may be determined by OCT successfully, OCT is a high-resolution non-contact and non-invasive technique that can analyze the structure of the retina and the optic disc [(24)]. In the present study. there was a statistically significant thinning at the superior and the inferior hemisphere of the RNFL thickness with average of 102.62 ±14.19 on the start of the study to average 99.88 ± 13.73 six month later. This is consistent with **Atilgan *et al.*** [(25)] who reported a significant thinning of the mean RNFL thickness as well as decreased in macular thickness in ESRF patients on HD when compared with normal controls.

On the other hand, **Chen *et al.*** [(26)] reported that during HD, retinal thickness tended to increase in different locations and different layers of the retina, including the RNFL. However, previous research found no statistically significant differences before and after HD in terms of the macular thickness [(27)], the thickness of the surrounding macular areas [(28)], and the macular volume or the layer of retinal ganglion cells [(29)].

This difference in results between these studies and the current study, might be due to timing of the repeated measuring of the RNFL thickness, as they did it before and after single dialysis session, but in the current study measuring of the RNFL thickness was done on starting of the study and 6 months later.

This thinning of RNFL that observed in the current study, did not correlate with the patient's sex and the period of HD, but correlated with the patient's age. This is consistent with **Blumberg *et al.*** **[30]**, who found that while RNFL became thinner with the increasing age, axial length and decreasing of optic disc diameter and gender had no effect. Other study showed a marked decrease in the retinal thickness of patients on HD, which was not correlated with the period of HD, but with the age **[31]**. **Hirasawa *et al.*** **[32]** also determined that a significant thinning occurred at the RNFL with increasing patient's age, but patient's gender and axial length had no any effect.

The present study had some limitations. ESRD patients often have chronic diseases that require the use of systemic medications. Little is known about the effects of systemic medications on IOP **[33]**. Additionally, plasma colloid osmotic pressure was not measured. Another limitation of the present study was the lack of evaluation of central corneal thickness, as measured IOP has been proven to vary depending on central corneal thickness. Underestimating IOP values after HD sessions can happen because of decreases in central corneal thickness induced by fluid loss. **Jung *et al.*** **[34]** showed a significant decrease in central corneal thickness during HD. Lack of normal control age matched group in assessing the RNFL thickness could be another limitation.

## CONCLUSIONS

Intra ocular pressure (IOP) was decreased significantly during hemodialysis in this study, but there was no significant decrease when measuring was repeated six months later. Also, there was significant decrease in average of retinal nerve fiber layer (RNFL) thickness after six months of the follow up.

As there was loss of RNFL thickness in hemodialysis patients, visual field changes is recommended to be investigated on such patients. Also the effect of hemodialysis on patients with high IOP or glaucoma should be investigated as well.

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