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Evaluation of Retinal Nerve Fiber Layer Thickness in Patients with Age-Related Hearing Loss

Yaşa Bağlı İşitme Kaybı Olan Hastalarda Retina Sinir Lifi Kalınlığının Değerlendirilmesi

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ABSTRACT

Introduction: To perform retinal nerve fibre layer (RNFL) analysis in patients with age-related hearing loss (ARHL) using optical coherence tomography (OCT).
Materials and Methods: Sixty-five patients with ARHL and 36 healthy controls were included in this prospective study. Patients with ARHL were divided into two groups—one with mild (33 patients) and one with moderate (32 patients) impairment. A complete ophthalmological examination was applied to all subjects and included best-corrected visual acuity, slit lamp examination, Goldmann applanation tonometer, visual field testing and dilated fundus examination. The RNFL thickness of all participants was measured using an OCT device. Pure tone audiometry tests were performed on the patients using headphones and AC40 audiometry in a silent cabin.
Results: The mean age was 70.39, 70.55 and 71.22 in the control, mild and moderate hearing loss groups, respectively. A statistically significant difference was observed between the control group and patients with moderate ARHL, between inferior quadrant thicknesses(p=0.011) and between mean RNFL thicknesses(p=0.025). The superior, nasal and temporal quadrant RNFL thicknesses were similar across the whole study group, with no statistically significant difference (p values: 0.104, 0.650, 0.470, respectively).
Conclusion: The average RNFL was significantly thinner in the patients with moderate ARHL compared to the controls. As age and the degree of hearing loss increases, RNFL thicknesses decreases.

Key Words: Age-related hearing loss, aging, optical coherence tomography, retinal nerve fibre layer thickness

ÖZET

Amaç: Yaşa bağlı işitme kaybı (YBİK) olan hastalarda optik koherens tomografi (OKT) kullanarak retina sinir lifi tabakası (RSLT) kalınlığı analizi yapmak.
Gereçler ve Yöntem: Bu prospektif çalışmada YBİK olan 65 hasta ve 36 sağlıklı kontrol vardı. YBİK olan hastalar hafif (33 hasta) ve orta (32 hasta) olarak iki gruba ayrıldı. Her hastaya en iyi düzeltilmiş görme keskinliği, yarıklı lamba muayenesi, Goldmann aplanasyon tonometresi, görme alanı testi ve dilate fundus muayenesi dahil olmak üzere tam bir oftalmolojik muayene yapıldı. Tüm katılımcıların RSLT kalınlığı OKT cihazı kullanılarak ölçüldü. Hastaların saf ses odyometri testleri sessiz bir kabinde kulaklık ve AC40 odyometri kullanılarak yapıldı.
Bulgular: Kontrol, hafif ve orta işitme kaybı gruplarında ortalama yaş sırasıyla 70.39, 70.55 ve 71.22 idi. Kontrol grubu ve orta derecede YBİK olan hastalarda inferior kadran kalınlıkları arasında(p = 0.011) ve ortalama RSLT kalınlıkları arasında(p = 0.025) istatistiksel olarak anlamlı bir fark vardı. Üst, nazal ve temporal kadran RSLT kalınlıkları tüm çalışma gruplarında benzer bulundu ve istatistiksel olarak anlamlı bir fark yoktu (sırasıyla p =0.104, 0.650, 0.470).
Sonuç: Orta derecede YBİK olan hastalarda kontrollere kıyasla ortalama RSLT kalınlıkları anlamlı derecede daha ince bulundu. Yaş ve işitme kaybı derecesi arttıkça RSLT kalınlıkları azalır.

Anahtar Kelimeler: Yaşa bağlı işitme kaybı, Yaşlanma, Optik koherens tomografi, Retina sinir lifi tabakası kalınlığı

Introduction

Age-related hearing loss (ARHL), also called presbycusis, is a widespread deficiency among the geriatric population that affects a number of functions, such as cognition, emotion and social function (1). ARHL begins in the high frequency region of the hearing spectrum and can be defined as bilateral, symmetrical and progressive (2). Current research suggests that ARHL is a multifactorial condition with multiple pathways and underlying conditions, such as genetic and

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environmental factors and an individual's lifestyle, contributing to the biological mechanisms (3). Histological, electrophysiological and molecular changes in the hearing system are caused by ageing (2). Possible pathological mechanisms contributing to ARHL include hypoxia and ischemia, the formation of reactive oxygen species and oxidative stress accompanied by the apoptotic and necrotic death of hair cells and spiral ganglion cells, and inherited and acquired mutations of mitochondrial DNA (4).

Factors such as the interaction of numerous genes, cellular pathways, and environmental risks are significant age-related causes of changes in the optic nerve head that cause an increase in oxidative stress. This situation is associated with the gradual degradation of the structure and function of the optic nerve (5). It has been reported in the literature that alterations in the laminar extracellular matrix around the optic nerve head related to age include raised collagen deposition, thickening of the astrocyte basement membranes and increased rigidity (6, 7). This age-related connective tissue stiffening diminishes nutrient diffusion from the laminar capillaries to the centre of the axon bundles. In a recent study, stiffer connective tissue around the optic nerve head was associated with increased ganglion cell loss (8).

The aging process affects both the vision and hearing systems and possibly shares similar pathophysiological mechanisms, such as oxidative stress, apoptotic cell death and ischemia. Both hearing and vision impairments are common issues experienced by the geriatric population, and their prevalence increases with the age (9). Combined vision and hearing disabilities are associated with difficulties in performing daily activities, home injuries, depression, communication impairment and social isolation (9).

Optical coherence tomography (OCT) is a non-invasive technique used for cross-sectional tomographic imaging of the eye. Retinal nerve fibre layer (RNFL) thickness measurements are conducted using OCT and provide significant clinical data to understand disorders of the optic nerve. Technological developments have made it possible to acquire images of the retina and retinal nerve fibre layer at high quality (10).

This study was designed to evaluate RNFL changes by performing RNFL analysis with OCT in patients with ARHL.

Materials and Methods

This prospective study included 65 patients with age-related hearing loss and 36 healthy controls. Patients with age-related hearing loss were divided into two groups—one with mild (33 patients) and one with moderate (32 patients) impairment.

This study was conducted in compliance with the Declaration of Helsinki and with approval of the protocol by the local ethics committee. All subjects were informed about the study prior to obtaining informed consent.

Each subject underwent a complete ophthalmological examination, including best-corrected visual acuity (BCVA) (using a Snellen chart), slit lamp examination, Goldmann applanation tonometry, visual field testing and dilated fundus examination. The central corneal thickness of subjects was measured by the Pentacam Scheimpflug (Oculus, Inc., Wetzlar, Germany) before dilation of the pupil. Ehlers formula was used for the corrected intraocular pressure (IOP) (11).

Exclusion criteria included diseases that potentially affect RNFL thickness, such as diabetes mellitus, obstructive sleep apnoea syndrome, multiple sclerosis and Parkinson's disease, myopia or hyperopia >2 dioptres, any history of intraocular surgery, glaucoma, uveitis or ocular trauma and IOP exceeding 21 mmHg in both eyes. We also excluded patients with cataract and age related macular degeneration.

The RNFL thickness of all participants was measured using an OCT device (Carl Zeiss Meditec, Dublin, CA, USA). Measurement was performed according to the 'Fast RNFL protocol early in the morning (between 8–9 a.m.) by the same masked physician (HF).The peripapillary RNFL thickness of the temporal, nasal, inferior and superior quadrants and the average thickness of the RNFL were obtained with the optic disc 200×200 cube scan protocol along a circle with a diameter of 3.45 mm around the centre of the disc. Signal strengths >8 were included in the study.

Pure tone audiometry (PTA) tests were performed using supraauricular headphones (TDH 39) and AC40 (Interacoustics, Assens, Denmark) audiometry in a silent cabin. The airway thresholds of the patients at the 250, 500, 1000, 2000, 4000, 6000 and 8000 Hertz (Hz)

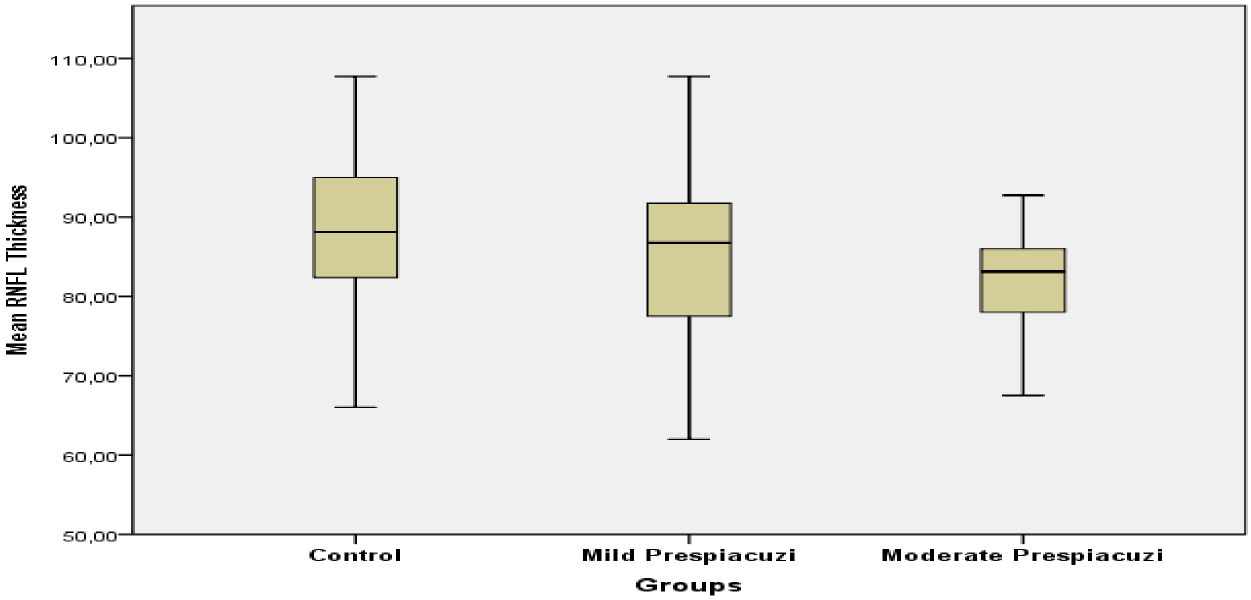

Fig. 1. Distribution of average retinal nerve fiber layer thickness (RNFL) thickness in mild, moderate presbyacusis and control groups

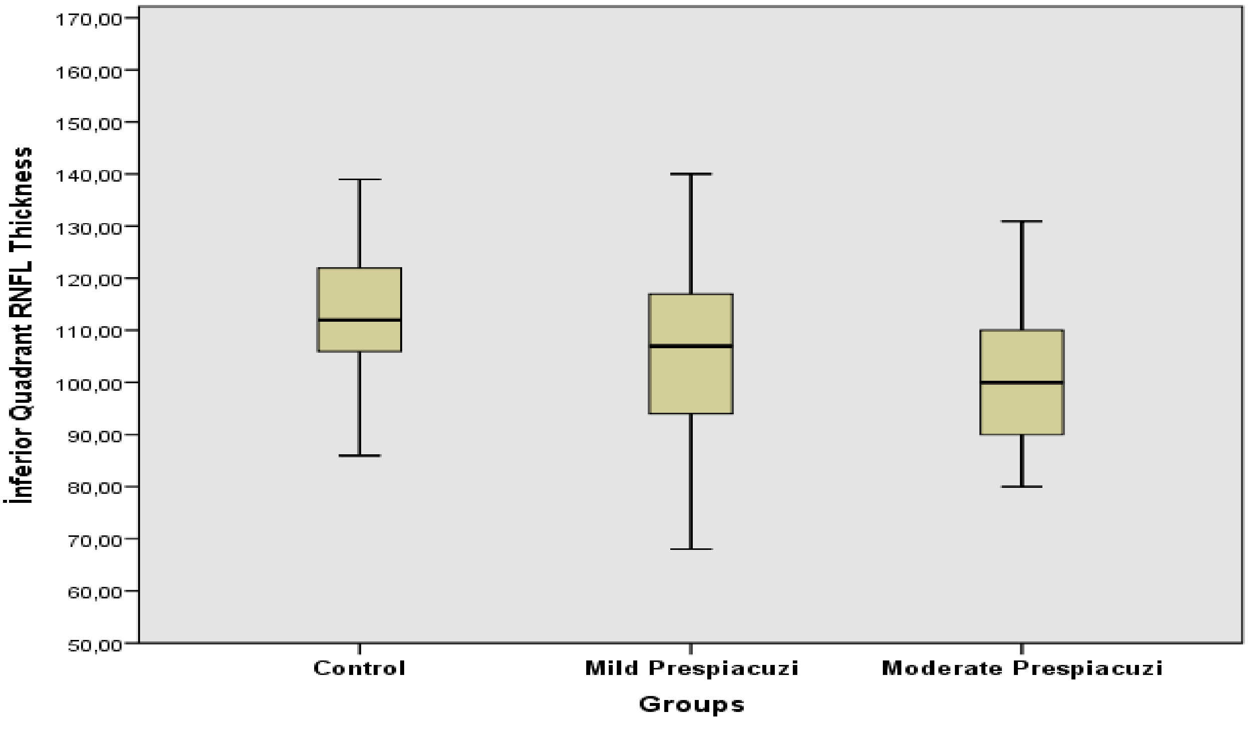

Fig.2. Distribution of inferior retinal nerve fiber layer thickness (RNFL) thickness in mild, moderate presbyacusis and control groups

frequencies, and the bone-conduction thresholds of 500, 1000, 2000 and 4000 Hz were determined. The arithmetic average of the airway thresholds of 500, 1000, 2000 and 4000 Hz was taken as the pure sound threshold average. Air bone gaps greater than 5 decibels (dB) were assessed as conductive hearing loss. A normal hearing threshold greater than 20 dB at any frequency (from 250 Hz to 8000 Hz) was defined as hearing impairment. Hearing levels were classified from N1 to N6. The groups were classified as normal (20 dB or less), mild hearing loss (21–40 dB), moderate hearing loss (41–55 dB), moderate-to-severe hearing loss (56–70 dB), advanced hearing loss (71–90 dB) and very severe hearing loss (>90 dB). Patients with a history of congenital, neonatal, infantile, traumatic or sudden hearing loss, tympanic membrane rupture on otoscopic examination and transmission-type hearing loss were excluded from the study.

Data analysis was performed using the Statistical Package for the Social Sciences (SPSS) program for Windows, version 22.0 (SPSS Inc., Chicago, IL, United States). The Kolmogorov Smirnov test was used to determine whether the distributions of metric discrete and continuous variables were normal. Descriptive findings were shown as mean ± standard deviation (SD). Comparisons between groups were analyzed via the Student's *t* test, while one-way analysis of variance was used for multiple comparisons between groups. The Scheffe post-hoc test was used for comparisons within each group. The chi-square test was used to compare categorical variables. The Pearson's correlation test was used to evaluate the relationship between clinical measurements. A *p* value less than 0.05 was considered statistically significant.

Results

Sixty-five patients with age-related hearing loss (33 mild and 32 moderate) and 36 healthy volunteers were studied. The mean age was 70.39±9,62(52-85), 70.55±9,17(51-86) and 71.22±8,58(51-85) in the control, mild and moderate hearing loss groups, respectively. No significant differences were observed in age, gender, BCVA, IOP or central corneal thickness between the groups (Table 1).

The mean RNFL thicknesses in the groups are presented in Table 2 and Figure 1,2. A statistically significant difference was observed in the control group and patients with moderate ARHL in terms of inferior quadrant thicknesses (p=0.011) and mean RNFL thicknesses (p=0.025). The superior, nasal and temporal quadrant RNFL thicknesses were similar in the sum of the study group, without any statistically significant difference (p values: 0.104, 0.650, 0.470 , respectively).

When the study groups were compared within themselves, no significant difference was found between the control group and the mild hearing loss group (p=0.177). In contrast, there was a statistically significant difference between the control group and the moderate hearing loss group (p=0.032). No significant difference between the mild and moderate hearing loss group was observed (p=0.725).

A significant positive correlation between age and the degree of hearing loss was observed using Pearson's correlation analysis (r=0.396; p=0.001). A negative correlation was observed between age and mean RNFL thickness(r=-0.072; p=0.472). A significant negative correlation between the severity of hearing loss and the mean RNFL thickness was observed (r=-0.225, p=0.024) (Table 3).

Discussion

Combined vision and hearing impairment related to ageing is a significant issue among the elderly population. Compared to hearing or vision impairment alone, dual sensory impairment (DSI), defined as the combination of hearing and vision impairment, may limit daily activities and restrict the social interactions of an individual(9). Studies showed that individuals with DSI experience much greater difficulty in walking, performing daily and social activities and continuing their medical follow-up visits, and they are under greater risk of depression and hip fractures (12, 13).

In the present study, a significant thinning in the average and inferior quadrant RNFL was observed in the moderate ARHL group in comparison with the healthy controls. No significant difference was observed between mild ARHL group and the control group as well as between mild and moderate ARHL groups. Additionally, there was no statistically significant difference between these three groups in terms of superior, nasal and temporal quadrant RNFL thickness values. It has been postulated that both vision and hearing impairment in the elderly may share common risk factors, such as genetics, environmental exposure and lifestyle changes—for example, being exposed to oxidative stress, having atherosclerosis and high cholesterol levels, or having a history of heavy drinking and smoking, which contribute to the normal biological aging process (14). After considering and detailing the effect of age, Chia et al. reported that cataracts and age-related maculopathy are significantly associated with hearing loss in elderly adults (14). According to the findings of Bozkurt et al., age-related macular degeneration, as an important risk factor, might develop hearing loss associated with age (15).

According to Bozkurt et al. defined hearing impairment in which the Pure tone audiometry test on each ear was greater than 25 dBHL (15). In our study, we also defined this threshold value for hearing impairment as 20 dBHL. Pure tone audiometry testing in patients may help us estimate the occurrence of sensorineural hearing impairment in the coming years. Ghasemi et al. reported that hearing impairment was significantly

Table 1. Demographic and baseline characteristics

		Control	Mild	Moderate	P value
Gender (n, %)	Male	12 (33.3)	14 (42.4)	18 (56.3)	0.162[a]
	Female	24 (66.7)	19 (57.6)	14 (43.8)	
Mean Age (year) (SD, min., max)		70.39±9,62 (52-85)	70.55±9,17 (51-86)	71.22±8,58 (51-85)	0,926[b]
CCT (µicron)		537.94	536.73	530.28	0.352[b]
IOP (mmHg)		14.92	16.52	14.63	0.799[b]
Visual Acuity (Snellen)		1.00	0.95	0.97	0.320[b]

IOP: Intraocular pressure, CCT: Central corneal thickness, SD: Standart deviation, a: Chi-Square test, b: One-way ANOVA

Table 2. Mean retinal nerve fiber layer (RNFL) thickness (µ) values in the groups

		Control (n= 36)	Mild (n= 33)	Moderate (n= 32)	P valuea
RNFL thickness (µ) (mean±SD)	Average	88.08±8.95	84.58±10.82	81.47±6.12	0.011*
	Superior	108.08±16.94	103.97±19.39	98.87±16.43	0.104
	Inferior	111.42±18.13	103.70 ±21.71	99.53±13.15	0.025*
	Nasal	71.42±12.04	70.03±10.88	68.66±13.64	0.650
	Temporal	61.42±7.82	60.61±9.53	58.8 ±9.16	0.470

A: one-way ANOVA, RNFL: Retinal Nerve Fiber Layer, µ: micron, SD: standard deviation

Table 3. The correlations between mean RNFL thickness, age and the degree of hearing loss

		Mean average RNFL thickness	Age	The degree of hearing loss
Mean average RNFL thickness	Pearson Correlation	1	-0.072	-0.225*
	P (2-tailed)		0.472	0.024
Age	Pearson Correlation	-0.072	1	0.396**
	P (2-tailed)	0.472		0.001
The degree of hearing loss	Pearson Correlation	-0.225*	0.396**	1
	P (2-tailed)	0.024	0.001	

RNFL: Retinal Nerve Fiber Layer
*Correlation is significant at the 0.05 level (2-tailed)
**Correlation is significant at the 0.01 level (2-tailed)

higher in patients with age-related macular degeneration than the control group at frequencies of 250, 4000 and 8000 Hz (16). In the same study, patients older than 75 years regressed at all frequencies, particularly low and high frequencies, and these findings were not found at low frequencies in age matched controls (16).

Human melanocytes are known to be found in the skin, hair, eyes, inner ears and the meninges (17). The stria vascularis in the cortical structure of the cochlea is the main structure containing melanocytes. It has a less cortical structures and melanocytes at its base compared to the apex of the cochlea. The low concentration of melanin makes the cochlea base predisposed to the accumulation of oxidative stresses and lipofuscin. Age-related deterioration of the stria vascularis is more common at the base and overtime progresses gradually to the apex and then to all parts of the cochlea (16). The anterior segment structures of the eye have similar embryological derivation to those in the tectorial and basilar membranes of the organ of Corti in the inner ear (18). There are numerous studies that investigate the relationship between eye colour as an indicator of inner ear melanin content and hearing loss (17).

Additionally, researchers claimed that darker eye colour is related to cisplatin ototoxicity (17, 19). Papadopoulos et al. reported that exfoliation syndrome is related to sensorineural hearing loss. In their study, they argued that exfoliation syndrome and presbycusis are disorders related to ageing with the same predisposing factors (i.e. genetic, dietary, environmental and socioeconomic factors), and these conditions may be similar in terms of pathologic and biochemical basis (18). Although the relationship between the optic nerve and hearing function is not yet known, research that showed the association between eye and ear structures encouraged us to report this current study.

Age-related macular degeneration, cataract and glaucoma primarily cause vision impairment in old adults (20). In glaucoma patients, RNFL damage occurs with loss of field without vision impairment in the early period. It is accepted that loss of RNFL occurs before measurable optic nerve head and visual field damage. RNFL loss in sixty per cent of the eyes was observed to have occurred six years before visual field defects (21). Therefore, the use of precise and clinical methods to scan the optic disc and RNFL facilitates the diagnosis and follow-up of changes in RNFL thickness due to glaucomatous conditions as well as age-related changes in our study. However, it is crucial to differentiate age-related progressive degeneration of retinal ganglion cells and their axons from the glaucomatous changes of the optic nerve. In a later study by Wu et al., it was reported that a large number of healthy eyes were incorrectly diagnosed as having progressed without counting on normal aging during the average RNFL thickness measurements using OCT imaging (22). Since glaucoma is mostly a disease of the elderly, in our study we exclude all glaucoma susceptible individuals to demonstrate the pure age-related changes in the optic nerve. In the present study, mean RNFL thinning occurred in patients with presbycusis compared with those without presbycusis. The mean RNFL thickness decreased as the presbycusis worsened. We think that the detection of the loss of RNFL in patients without any functional loss in vision or visual field and without any complaints reflected to the clinic may be an objective test for the diagnosis of DSI.

There is a limitation of this work; Although hearing loss is classified in 4 subgroups (23), as there are not enough patients for severe and profound hearing loss groups. That's why our study groups are composed of mild and moderete hearing loss patients. This is the limitation of our work.

In conclusion, the findings of our study demonstrated an association between age-related hearing loss and RNFL thinning. Although the results of the present study are not sufficient to identify the pathologic and biochemical mechanisms, as a hypothesis, we would like to draw attention to the possibility that a similar biological process causes RNFL thinning and hearing impairment. To understand the relationship between changes in the optic nerve, hearing impairment in elderly and the negative effects of these impairment on the quality of life, large-scale epidemiological studies are required with a larger population of subjects.

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References

1. Cruickshanks KJ, Wiley TL, Tweed TS, Klein BE, Klein R, Mares-Perlman JA, et al. Prevalence of hearing loss in older adults in Beaver Dam, Wisconsin. The Epidemiology of Hearing Loss Study. American journal of epidemiology 1998; 148(9): 879-886.
2. Fetoni AR, Picciotti PM, Paludetti G, Troiani D. Pathogenesis of presbycusis in animal models: a review. Experimental gerontology 2011; 46(6): 413-425.
3. Gates GA, Mills JH. Presbycusis. Lancet 2005; 366(9491): 1111-1120.
4. Reiss M, Reiss G. [Presbycusis: pathogenesis and treatment]. Medizinische Monatsschrift fur Pharmazeuten 2009; 32(6): 221-225.
5. El-Sayyad HI, Khalifa SA, El-Sayyad FI, Al-Gebaly AS, El-Mansy AA, Mohammed EA. Aging-related changes of optic nerve of Wistar albino rats. Age (Dordrecht, Netherlands) 2014; 36(2): 519-532.
6. Morrison JC, Dorman-Pease ME, Dunkelberger GR, Quigley HA. Optic nerve head extracellular matrix in primary optic atrophy and experimental glaucoma. Archives of ophthalmology 1990; 108(7): 1020-1024.
7. Downs JC. Optic nerve head biomechanics in aging and disease. Experimental eye research. 2015; 133: 19-29.

8. Steinhart MR, Cone-Kimball E, Nguyen C, Nguyen TD, Pease ME, Chakravarti S, et al. Susceptibility to glaucoma damage related to age and connective tissue mutations in mice. Experimental eye research 2014; 119: 54-60.
9. Davidson JGS, Guthrie DM. Older Adults With a Combination of Vision and Hearing Impairment Experience Higher Rates of Cognitive Impairment, Functional Dependence, and Worse Outcomes Across a Set of Quality Indicators. Journal of aging and health 2017: 898264317723407.
10. Sung KR, Wollstein G, Bilonick RA, Townsend KA, Ishikawa H, Kagemann L, et al. Effects of age on optical coherence tomography measurements of healthy retinal nerve fiber layer, macula, and optic nerve head. Ophthalmology 2009; 116(6): 1119-1124.
11. Ehlers N, Hjortdal J. Corneal thickness: measurement and implications. Experimental eye research 2004; 78(3): 543-548.
12. Lupsakko T, Mantyjarvi M, Kautiainen H, Sulkava R. Combined hearing and visual impairment and depression in a population aged 75 years and older. International journal of geriatric psychiatry 2002; 17(9): 808-813.
13. Campbell VA, Crews JE, Moriarty DG, Zack MM, Blackman DK. Surveillance for sensory impairment, activity limitation, and health-related quality of life among older adults--United States, 1993-1997. MMWR CDC surveillance summaries : Morbidity and mortality weekly report CDC surveillance summaries 1999; 48(8): 131-156.
14. Chia EM, Mitchell P, Rochtchina E, Foran S, Golding M, Wang JJ. Association between vision and hearing impairments and their combined effects on quality of life. Archives of ophthalmology 2006; 124(10): 1465-1470.
15. Bozkurt MK, Ozturk BT, Kerimoglu H, Ersan I, Arbag H, Bozkurt B. Association of age-related macular degeneration with age-related hearing loss. The Journal of laryngology and otology 2011; 125(3): 231-235.
16. Ghasemi H, Pourakbari MS, Entezari M, Yarmohammadi ME. Association of Age Related Macular Degeneration and Age Related Hearing Impairment. Journal of ophthalmic & vision research 2016; 11(1): 54-60.
17. Mujica-Mota MA, Schermbrucker J, Daniel SJ. Eye color as a risk factor for acquired sensorineural hearing loss: a review. Hearing research 2015; 320: 1-10.
18. Papadopoulos TA, Naxakis SS, Charalabopoulou M, Vathylakis I, Goumas PD, Gartaganis SP. Exfoliation syndrome related to sensorineural hearing loss. Clin Exp Ophthalmol 2010; 38(5): 456-461.
19. Todd NW, Alvarado CS, Brewer DB. Cisplatin in children: hearing loss correlates with iris and skin pigmentation. The Journal of laryngology and otology 1995; 109(10): 926-929.
20. Klaver CC, Wolfs RC, Vingerling JR, Hofman A, de Jong PT. Age-specific prevalence and causes of blindness and visual impairment in an older population: the Rotterdam Study. Archives of ophthalmology 1998; 116(5): 653-658.
21. Jeoung JW, Park KH, Kim TW, Khwarg SI, Kim DM. Diagnostic ability of optical coherence tomography with a normative database to detect localized retinal nerve fiber layer defects. Ophthalmology 2005; 112(12): 2157-2163.
22. Wu Z, Saunders LJ, Zangwill LM, Daga FB, Crowston JG, Medeiros FA. Impact of Normal Aging and Progression Definitions on the Specificity of Detecting Retinal Nerve Fiber Layer Thinning. American journal of ophthalmology 2017; 181: 106-113.
23. Jamison DT, Breman JG, Measham AR, et al. Disease Control Priorities in Developing Countries. 2nd ed. New York, NY: Oxford University Press; 2006.