

Serum Electrolyte Concentrations in Primary Glaucoma PatientsAditya Vikram Sharma¹, Aditi Sharma², Sharda Punjabi³, Hem S Desai⁴¹Assistant Professor, Department of Ophthalmology, Geetanjali Medical College & Hospital, Udaipur²Assistant Professor, Department of Ophthalmology, RVRS Medical College, Bhilwara³Professor, Department of Ophthalmology, Geetanjali Medical College & Hospital, Udaipur⁴Senior Resident, Department of Ophthalmology, Geetanjali Medical College & Hospital, Udaipur

Received: 18-03-2023 / Revised: 21-04-2023 / Accepted: 26-05-2023

Corresponding author: Aditya Vikram Sharma

Conflict of interest: Nil

Abstract:

Glaucoma advances covertly, and a late presentation is not uncommon. This study investigated the association between glaucoma and the concentration of tear and serum ions. We evaluated the levels of sodium, potassium, and chloride in the tears and serum of 50 glaucoma patients and 50 controls with similar ages and sexes. Both the test and control groups had a 56.00 ± 14.6 and 56.74 ± 16.74 years old on average, respectively. Their age was not statistically significant. The mean concentrations of sodium, potassium, and chloride in control subjects' tears were 130.22 ± 1.20 , 22.38 ± 5.30 and 121.65 ± 12.20 , respectively, whereas for test subjects (Glaucoma patients), the values were 135.06 ± 9.34 , 16.86 ± 2.3 , and 125.91 ± 10.50 . A paired comparison of means of Control & test was statistically significant. The average levels of sodium, potassium, and chloride ions in the serum of test individuals were 135.82 ± 8.66 , 4.0 ± 0.52 and 101.85 ± 2.77 respectively, while the average levels in the serum of control subjects were 135.00 ± 2.4 , 4.4 ± 0.98 and 101.53 ± 13.6 , respectively. It was not statistically significant if means were compared. Sex did not significantly influence any of the assessed variables. Low potassium ion concentration in glaucoma patients in tears may be a valuable biomarker for the condition. At-risk people can be protected from irreversible glaucoma blindness to a greater extent by an efficient glaucoma screening test.

Keywords: Glaucoma, Sodium potassium, Chlorides, Tear electrolytes.

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

Blinding optic nerve condition called glaucoma characterised by a high rate of retinal ganglion cell (RGC) loss cells die by an apoptotic process. Apoptosis in glaucoma is excessive and dysregulated, and analogous to a faulty physiological mechanism. The Disease exhibits a wonderful deception due to the fact that delayed visual symptoms progresses. As a result, late presentations are typical because glaucoma is the main factor that results in irreversible blindness everywhere [1]. It is anticipated that more than 110 million people will be affected by the illness by the year 2040 [2]. Initial glaucoma appears when no underlying eye disease exists and explains the majority of glaucoma cases seen in clinical practise (92% of all glaucomas). Additional glaucoma is far less frequent (8% of all glaucomas) and is an occasionally occurring side effect of severe eye injuries. The Primary glaucomas are further divided into categories based on to the aqueous humour's anatomical structure a primary open angle glaucoma outflow structure and Glaucoma with primary angle closure. Initial open Up to 70% of

primary eye diseases are caused by angle glaucoma, which is the most common characteristic observed in African descent individuals [3]. The list of potential glaucoma-related genes is reducing and their expression could result in a facility for water humour discharge with an attendant IOP (intraocular pressure) increase [4, 5]. The lens Nerve seems to be delicate as it moves through the stiff sclera in the back. A rise in IOP may result in biomechanical alterations that are currently harming the nerve [5] is the departure point. Additional glaucoma mechanisms involve oxidative stress and ischemia of the eye's tissues influencing both the retinal and trabecular meshwork components [6]. Ultraviolet (UV) light is present in ambient light radiation that the cornea typically absorbs and before it reaches the retina, where it may be, the lens cytotoxic, ultraviolet-B (UVB) radiation traces do finally make it to the retina and anterior chamber, however tissue filtrations. UVB makes the tissue grow apoptosis-related genes are expressed more strongly in a situation where there is a high quantity of reactive

oxygen species (ROS) in a cyclical fashion [7]. The ROS tissue of the retina level is increased much more by mitochondrial energy oxidative phosphorylation, a process that is RGC and other unmyelinated nerves require it very much. Inevitably, oxidative phosphorylation results in the very reactive unpaired electron leaking. Both Mechanisms can interact to increase ROS to unhealthy stages [8]. High concentration of ROS in cells have oxidative stress, which can change the electrolyte flux across the RGC cell membrane in a way that is beneficial. Glaucoma is associated with increased apoptosis [9, 10].

The main intracellular cation is potassium (K⁺). While the main extracellular cation is sodium (Na⁺). Negative anions are connected to these positive ions, mostly bicarbonate (HCO₃⁻) and chloride (Cl⁻) to Ensure that the two compartments are electrically neutral. [11]. this concentration gradient's preservation is mostly through the electrogenic Na⁺/K⁺ pump. These electrolytes are present in blood and tears as ions, are inorganic compounds that have electrical charges, and mediate a variety of physiological processes, such as fluid balance, impulse transmission, and cellular protection performs [12, 13]. A small amount of extracellular when potassium leaves the intracellular space, it can the compartment for extracellular fluid, leading in volume of the cell shrinks. The diffusion of cytochrome c into the mitochondria's cytosol, causing cells to internal mechanism of apoptosis [14–18]. Agents that block K⁺ channels, including high concentrations of barium ions (Ba²⁺) or there is evidence that extracellular K⁺ can stop apoptosis. [19].

Tears' high potassium content aids in preserving the corneal epithelium by lowering the difference in intracellular and extracellular therefore reducing intracellular loss of at extracellular levels reducing corneal epithelial loss with potassium [18, 20, 21] Apoptosis. A cornea epithelium in good health is a more effective UVB absorber, possibly preventing severe injury to the delicate ocular tissues, particularly the Lens, RGC, and trabecular meshwork [7, 22]. To alterations in intracellular sodium levels and, to a lesser extent Chloride levels have also been connected to enhanced apoptosis-induced cell death [23, 24]. Biomarkers are bodily components that can giving unbiased information about the present a live thing's physiological condition [25]. Tear provides a benefit as a bodily fluid for research due to the simplicity of its non-intrusive collection, being an external fluid that is close by electrolyte concentration in tears primarily establishes its osmolarity, which is the foundation in order to identify dry eye disease (DED) [26]. Studies have argued that a certain tear's dimension Electrolytes might be a helpful auxiliary in the

evaluation diabetes mellitus patients [27, 28]. Changes in Currently, proteomics are being used in a frenzied "man-hurt" for glaucoma biomarkers in tear sufferers [29, 30]. Hagan et al. did a fantastic job. Research for tear-related biomarkers in ocular and systemic diseases: overview of proteomic approaches [31]. rom clotted blood and with whole blood, serum is produced. The "guinea pig" in laboratory medicine is blood. Higher levels of immunoglobulin-G, red blood cell count, and chloride have all been observed in glaucoma subjects' blood and sera [32].

In the tear and serum concentrations, the ions in the extracellular fluid sodium, potassium, and chloride levels in glaucoma patients and age- and sex-matched controls were assessed. The results covered in relation to any associations between the observed parameters and the existence or absence of glaucoma phenotype.

Methodology

The study was case –controlled cross-sectional hospital based study of eligible and consenting adult subjects attending in the ophthalmology department, Geetanjali Medical College and Hospital. The current investigation, which was conducted on 50 glaucoma diagnosis as shown by a vertical, faint or nonexistent neuroretinal margin, a visual field linked with a cup to disc ratio of 0.7 irregularities [33. 34]. When compared to control groups, inclusion qualifications were being at least 30 years old and not having any pink neuroretinal rim, a sign of glaucoma intraocular pressure and a vertical cup to disc ratio greater than 0.6 of > 21 mmHg and no known family members with glaucoma. Each eye's visual acuity was evaluated. Snellen's chart is used. The current investigation, which was conducted on 50 glaucoma diagnosis as shown by a vertical, faint or nonexistent neuroretinal margin, a “visual field irregularities corresponding with a 0.7 CDR (cup to disc ratio)” [33. 34]. When compared to control groups, inclusion qualifications were being at least 30 years old and not having any pink neuroretinal rim, a sign of glaucoma intraocular pressure and a vertical cup to disc ratio greater than 0.6 of > 21 mmHg and no known family members with glaucoma.

“Each eye's visual acuity was evaluated using a standard Snellen's chart for distance. Both eyes were looked into detail with slit lamp biomicroscopy done with (Haag) three-mirror Streit BM900R. Both indentation and non-indentation gonioscopy were done using Goldmann R gonioscopy to rule out any secondary glaucoma causes. For every patient Aplanation tonometry was done with the Haag Streit Goldmann R-type and two readings were recorded every time. Fundoscopy (dilated) for background retina & optic nerve head examination was done with a Volk

USA) +78D superfield aspheric lens. Using Central visual fields perimeter was done with Optopol™ 1000 perimeter projection with a single operator and standard settings. Field analysis and visual field testing completed within three months of the study's start was regarded as legitimate. All tests were completed; the primary investigator oversees the project. Representative examinations of a test subject's and a control subject's central visual fields

appear in appendices IV and V. sample gathering and evaluation All samples were collected from 10 a.m. to 12 p.m. to reduce how much the electrolyte content of bodily fluids is affected by diurnal change [35]. The four millilitres of Antecubital vein was sampled for venous blood sterilised 5 mL hypodermic needle and syringe into a vein and then put into a clean, glass plane tube a blood was allowed to clot for 30 minutes while standing, and a centrifuge was used to perform a 5,000 spins per minute at a pace that produces a supernatant serum. An inferior tear sample of 200 µl was taken the ocular surface's lateral tear meniscus has a dry and four batches of sterile 50 µl planar capillary tubes was drained into a sterile test tube made of flat glass [36].

Practical basal tear collection is challenging, especially from corneal numbing agent [37]. Basal and reflex however, protein content appears to be the key difference between tears [38-40]. Tear collecting from the eyes is made easier by tilting the head. The lateral canthal region and the conjunctiva were reduced to reduce reflex tearing, an example of tears obtained from a total of 4 participants (control and test) per weekday taking into account the time required to obtain sufficient tear volume is necessary for a reliable outcome from the a tool for measurement. Within two hours of collection, samples of serum and tears were both by automated equipment to estimate electrolytes (Sodium, Potassium & Chloride). On the

electrolyte analyser, the electrolytes were analyzed using the ISE method. Analysis of Statistics Version 13 of Excel was used for data analysis. The mean and Standard Deviation (SD) values were used to represent the data. The students' t-tests were used to analyse the difference between the groups. The significance level was fixed at 0.05.

Results

The measurement of the amounts of tears and serum concentration in 25 females' sodium, potassium, and chloride ions and 25 males from the control group were examined, while there were 24 men and 26 females in the test (Glaucoma patients) group. The average age of the individuals was older, at 56.00 ± 14.91 years, as opposed to the control group's average age of (Table 1) 56.72 ± 16.74 years. But at this age the difference ($P = 0.81$) was not statistically significant. sodium, potassium, and chloride averages concentrations in test- and control-subject individuals' tears were 135.06 ± 9.34 , 16.86 ± 2.30 and 125.9 ± 10.5 (mEq/L) and 130.89 ± 11.20 , 22.38 ± 5.30 , 121.65 ± 12.2 (mEq/L) in tears accordingly (Table 2). The two groups' respective means compared, and the P-values were 0.025, <0.0001 and 0.044 for sodium, potassium and chloride concentrations, indicating a significant difference. Mean sodium, amounts of potassium and chloride in the serum of test and control participants were 135.82 ± 8.66 , 4.10 ± 0.52 , 101.85 ± 2.77 (mEq/L) and 135.00 ± 2.4 , 4.4 ± 0.98 , 101.53 ± 13.6 , (mEq/L) and so forth. An evaluation of the P-values for the means in the two groups was 0.702, 0.050, and 0.20 for sodium, potassium, and chloride. According to these P-values, there is no statistically significance in the electrolyte concentration in the test serum, and control group but it was statistically significant in tear sodium, potassium and chloride concentrations when compared control group and test group. (Table 2)

Table 1: Serum Electrolytes in Control and Glaucoma patients

Parameters	Control			Test Glaucoma patients			P- Value Control Vs Test
	Male (n=25)	Female (n=25)	Total (n=50)	Male (n=24)	Female (n=26)	Total (n=50)	
Age	57.23	56.25	56.74 16.74	54.35	57.67	56.0 14.6	0.81
Serum Sodium	134.58	135.43	135.00 2.4	136.34	135.30	35.82 8.66	0.702
Serum Potassium	4.14	4.52	4.4 0.98	4.07	4.3	4.10 0.52	0.050
Serum Chloride	101.52	101.54	101.53 13.6	102.3	101.4	101.85 2.77	0.20

Table 2: Tear Electrolytes in Control and Glaucoma patients

Parameters	Control			Test (Glaucoma patients)			P- Value Control Vs Test
	Male (n=25)	Female (n=25)	Total (n=50)	Male (n=24)	Female (n=26)	Total (n=50)	
Age	54.35	55.76	55.05 18.4	54.66	56.43	55.54 14.5	0.882
Tear Sodium	129.56	132.22	130.89 11.20	133.87	136.26	135.06 9.34	0.025
Tear Potassium	21.55	23.21	22.38 5.3	17.22	16.51	16.86 2.3	<0.0001
Tear Chloride	119.66	123.65	121.65 12.2	126.43	125.39	125.91 10.5	0.044

Discussion

Glaucoma is a serious public health concern for eyes importance. It is impossible to overstate the significance of an inexpensive and reliable test that can identify the developing as there is currently no treatment for the condition, its stages and its blindness cannot be reversed. In the current investigation, the concentration of certain large cations and anion sodium [Na⁺], potassium [K⁺], and chloride [Cl⁻] in tears and serum of 50 primary glaucoma patients and 50 healthy controls who were at least 30 years old were examined. Both groups had similar ages and sexes. (Table 1). The typical electrolyte content of tear it was demonstrated that both the test group and the control group substantial increases in [Na⁺] and [Cl⁻] in test than control while [K⁺] is higher in control than test, and were highly significant. There have been claims that there apical K⁺ and Cl⁻ active secretion into tear fluid Lachrymal gland acinar cells [41–42]. Studies have demonstrated the necessity of high tear [K⁺] in keeping the corneal epithelium at a healthy thickness, which, in turn, can lessen RGC death and proximal and distal UVB-induced cell injury [19, 22]. The average [K⁺] in tear of test in the current study was individuals was discovered to be considerably less than the typical values for controls (16.86 mmol/L) respectively.

In literature that can be applied to, a similar study was discovered compare the results to these findings. Although, it is well established that one of the main risk factors for Eye pressure [43]. Possibly a compromised system the corneal epithelium may be impacted by decreased tear [K⁺] due to its capacity to absorb incident UVB, it may expose the RGC to the trabecular meshwork components UVB's harmful effects. It could also signify a defect in potassium channels that is widespread that cause more apoptotic cell death in the afflicted cells.

The importance of increased [Na⁺] in tear of It's uncertain when test individuals are compared to controls (P = 0.025). However, it could be a defence mechanism to counteract the high [K⁺] or

the opposite. The three electrolytes' serum concentrations in the Glaucoma group's scores were comparable to those seen in the control group, and no appreciable difference was noticed (Table When compared to the outcomes of other studies, the values from the current investigation looked to be in a medium position. studies conducted both domestically and abroad [44–47]. Thus, it appears that many devices that use many measurement methods (flame photometry) vs ion selective electrode) provide various outcomes that must be taken into account while interpreting any specified outcome. In one investigation, chloride was significantly higher level in the glaucoma patients' serum contrasted with controls [32]. Despite the fact that greater levels of chloride were found in the test serum. In this study, participants were contrasted with controls and The difference was not statistically significant.

Conclusion

Human cells are modulated by the presence of the primary electrolytes in health and illness. Potassium is the main cation inside cells, but outside them concentration changes the volume of cells, which is a sign of cell death that has been predetermined. The current study did reveal that glaucoma affects the ocular surface individuals have low tear [K⁺] in an aging-related manner. The convenience of collecting must be increased standardising the measurement of a tear sample increase the viability of employing this fluid for glaucoma screening at the population level. Potassium's function and its secretory channels and glaucoma development. Its connection to IOP, favourable family history, and in a follow-up, the disease's severity may be contested. Studies that are prospective and comprehensive are preferred. The epistemological constraints that have prevented advancement in early and efficient glaucoma management. That will be a big step forward in battling the Glaucoma-related ocular morbidity and mortality's misery has come to stand for.

Acknowledgement: We deeply thank Geetanjali Medical College and attached Hospital, Udaipur for providing all the resources needed to carry out the

work. The authors acknowledge the substantial assistance provided by the academics whose publications are cited and listed in the manuscript's references.

Declarations

Ethics clearance: The Institutional Ethics Committee provided the ethical clearance certificate

References

1. Ekweremadu EN, Ezech CO. Tear and serum electrolyte concentrations as a biomarker in primary glaucoma subjects. *Life Res.* 2021;4(1):5.
2. Quigley HA, Broman AT. The number of people with glaucoma worldwide in 2010 and 2020. *Br J Ophthalmol.* 2006;90(3):262–267.
3. Resnikoff S, Pascolini D, Etya'ale D, et al. Global data on visual impairment in the year 2002. *Bull World Health Organ.* 2004;82:844–851
4. Fan BJ, Wang DY, Lam DS, Pang CP. Gene mapping for primary open angle glaucoma. *Clin Biochem.* 2006;39(3):249–258.
5. Wiggs JL. Genetic etiologies of glaucoma. *Arch Ophthalmol.* 2007; 125(1):30–37.
6. Burgoyne CF, Downs JC, Bellezza AJ, et al. The optic nerve head as a biomechanical structure: a new paradigm for understanding the role of IOP related stress and strain in the pathophysiology of glaucomatous optic nerve head damage. *ProgRetin Eye Res.* 2005; 24:39–73.
7. Izzotti A, Saccà SC, Longobardi M, et al. Sensitivity of ocular anterior chamber tissues to oxidative damage and its relevance to the pathogenesis of glaucoma. *Invest Ophthalmol Vis Sci.* 2009; 50:5251–5258.
8. Caricchio R, McPhie L, Cohen PL. Ultraviolet B radiation-induced cell death: critical role of ultraviolet dose in inflammation and lupus auto antigen redistribution. *J Immunol.* 2003; 171(11):5778–5786.
9. Turrens JF. Mitochondrial formation of reactive oxygen species. *J Physiol.* 2003; 552:335–344.
10. Nickells RW, Semaan SJ, Schlamp CL. Involvement of the Bcl2 gene family in the signaling and control of retinal ganglion cell death. *Prog Brain Res.* 2008; 173:423–435.
11. Edlich F, Banerjee S, Suzuki M, et al. Bcl-XL retrotranslocates Bax from the mitochondria into the cytosol. *Cell.* 2011; 145:104–116.
12. Electrical signals of nerve cells. Purves D, Augustine GJ, Fitzpatrick D, et al., ed(s). *Neuroscience.* 2nd ed. Sunderland (MA): Sinauer Associates;2001:Chapter 2.Xiao AY, Wei L, Xia S, et al. Ionic mechanism of ouabain-induced concurrent apoptosis and necrosis in individual cultured cortical neurons. *J Neurosci.* 2002; 22:1350–1362.
13. Hughes FMJ, Cidlowski JA. A primary role for K⁺ and Na⁺ efflux in the activation of apoptosis. *J Biol Chem.* 1997; 272:32436–32442.
14. Maeno E, Ishizaki Y, Kanaseki T, et al. Normotonic cell shrinkage because of disordered volume regulation is an early prerequisite to apoptosis. *Proc Natl Acad Sci U S A.* 2000;97: 9487–9492.
15. Yu SP, Choi DW. Ions, cell volume, and apoptosis. *Proc Natl Acad Sci U S A.* 2000;97: 9360–9362.
16. Cain K, Langlais C, Sun XM, et al. Physiological concentrations of K⁺ inhibit cytochrome c dependent formation of the apoptosome. *J BiolChem.* 2001; 276:41985–41990.
17. Trimarchi JR, Liu L, Smith PJS, et al. Apoptosis recruits two-pore domain potassium channels used for homeostatic volume regulation. *Am J Physiol Cell Physiol.* 2002;282(3):C588–C594.
18. Glupker CD, Boersma PM, Schotanus MP, et al. Apoptosis of corneal epithelial cells caused by ultraviolet B-induced loss of K(+) is inhibited by Ba(2.). *Ocul Surf.* 2016 ;14(3):401–409.
19. Botelho SY, Martinez EV. Electrolytes in lacrimal gland fluid and in tears at various flow rates in the rabbit. *Am J Physiol.* 1973; 225: 606–609.
20. Rismondo V, Osgood TB, Leering P, et al. Electrolyte composition of lacrimal gland fluid and tears of normal and vitamin A-deficient rabbits *CLAO J.* 1989;15:222–229.
21. Green K, MacKeen DL, Slagle T, et al. Tear potassium contributes to maintenance of corneal thickness. *Ophthalmic Res.* 1992; 24(2):99–102.
22. Kunzelmann K. Ion channels and cancer. *J Membr Biol.* 2005; 205:159–173.
23. McCarthy J, Cotter T. Cell shrinkage and apoptosis: a role for potassium and sodium ion efflux. *Cell Death Differ.* 1997; 4: 756–770.
24. Ilyin SE, Belkowski SM, Plata-Salaman CR. Biomarker discovery and validation: technologies and integrative approaches. *Trends Biotechnol.* 2004; 22: 411–416.
25. Harris RL. Tear osmolarity—a new gold standard? *Adv Exp Med Biol.* 1994; 350:495–503.
26. Wang S, Hou X, Liu Y, et al. Serum electrolyte levels in relation to macrovascular complications in Chinese patients with diabetes mellitus. *Cardiovasc Diabetol.* 2013; 12, 146.
27. Okukpon J, Okukpon O. Tear electrolyte assessment of diabetic patients in Southern

- Nigeria. *Afr Health Sci.* 2019; 19(4):2839–2845.
28. Ghaffariyeh A, Honarpisheh N, Shakiba Y, et al. Brain-derived neurotrophic factor in patients with normal-tension glaucoma. *Optometry.* 2009; 80(11):635–638.
 29. Pieragostino D, Agnifili L, Fasanella V, et al. Shotgun proteomics reveals specific modulated protein patterns in tears of patients with primary open angle glaucoma naïve to therapy. *Mol Biosyst.* 2013;9(6):1108–1116.
 30. Hagan S, Martin E, Enríquez-de-Salamanca A. Tear fluid biomarkers in ocular and systemic disease: potential use for predictive, preventive and personalised medicine. *EPMA J.* 2016;7(1):
 31. Cohen LP, Wong J, Jiwani AZ, et al. A survey of preoperative blood tests in primary open-angle glaucoma patients versus cataract surgery patients. *Digit J Ophthalmol.* 2014; 20(2):20–28.
 32. National Population Commission (NPC) Nigeria National Census. Population distribution by sex, state, LGAs and senatorial district: 2006 census priority tables. <http://www.population.gov.ng/index.php/publication/140-popn-distri-by-sexstate-jgas-and-senatorial-distr-2006>. Accessed September 15, 2020.
 33. Ekwerekwu CM, Umeh RE. The prevalence of glaucoma in an onchoendemic community in south - Eastern Nigeria. *West Afr J Med.* 2002; 21: 200–203.
 34. Khan RN, Saba F, Kausar SF, et al. Pattern of electrolyte imbalance in type 2 diabetes patients: experience from a tertiary care hospital. *Pak J Med Sci.* 2019; 35(3):797–801.
 35. Atherton JC, Dark JM, Garland HO, et al. Changes in water and electrolyte balance, plasma volume and composition during pregnancy in the rat. *J Physiol.* 1982; 330, 81–93.
 36. Jordan A, Baum J. Basic tear flow: does it exist? *Ophthalmology.* 1980; 87:920–930.
 37. Abusharha AA, AlShehri TM, Hakami AY, et al. Analysis of basal and reflex human tear osmolarity in normal subjects: assessment of tear osmolarity. *Ther Adv Ophthalmol.* 2018;10:
 38. Thaysen JH, Thorn NA. Excretion of urea, sodium, potassium and chloride in human tears. *Am J Physiol.* 1954; 178:160-164.
 39. Stuchell RN, Feldman JJ, Farris RL, et al. The effect of collection technique on tear composition. *Invest Ophthalmol Vis Sci.* 1984; 25 (3):374–377.
 40. Selvam S, Mircheff AK, Yiu SC. Diverse mediators modulate the chloride ion fluxes that drive lacrimal fluid production. *Invest Ophthalmol Vis Sci.* 2013; 54 (4):2927–2933.
 41. Mircheff AK. Lacrimal fluid and electrolyte secretion: a review. *Curr Eye Res.* 1989; 8(6): 607– 617.
 42. Friedman DS, Wilson MR, Liebmann JM, et al. An evidence-based assessment of risk factors for the progression of ocular hypertension and glaucoma. *Am J Ophthalmol.* 2004; 138(3 suppl): S19–S31.
 43. Isichei UP. Relative hyperelectrolytemia in northern Nigerians. *Int J Trop Med Hyg.* 1978; 27(5):1049–1051.
 44. Olalekan AW, Oluwaseun FA, Oladele HA, et al. Evaluation of electrolyte imbalance among tuberculosis patients receiving treatments in Southwestern Nigeria, Alexandria. *J Med.* 2015; 51(3):255–260.
 45. Ugwu CE. Serum electrolytes and blood pressure of apparently healthy Ngerians. *Glob J Pure Appl Sci.* 2009; 15(2):155–159.
 46. Makun HA, Alaya LA, Gbadebo BJ, et al. Establishment of reference values for serum electrolytes in normal and gastroenteritic subjects in Minna, Nigeria. *Trace Elem Med.* 2001; 18: 147– 151.
 47. Hasan R, Halim A, Serafi S, Javed A, et al. A study to compare serum electrolytes concentrations of normal individuals with valvular heart disease and myocardial infarction patients. *Int J Cardiovasc Dis Diagn.* 2019;4(1):022–027.