AGE AND GENDER VARIATION IN INTRAOCULAR PRESSURE

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Abstract
During the last 7 years, the intraocular pressure (IOP) of 7000 males and females of different age groups were measured by Goldmann applanation tonometer. The results show a statistically significant decrease of IOP with age after the age of 30 years. They also show a higher reading in females than in males after the age of 40 years.

Introduction
In most nations, the average of normal IOP is about 16 mm Hg. The normal range is regarded to be 10-21 mm Hg. The average tends to increase with age. It is also slightly higher in females than in males after the age of 40 years. There is a clinical impression that IOP decreases with age in Iraqi people. Shiose demonstrated that IOP tend to decrease with age in Japanese. The aim of this study is to confirm this clinical impression. No similar study was done in Iraq.

Methods
Intraocular pressure of 3500 males and 3500 females (14000 eyes of 7000 subjects) were measured by Goldmann applanation tonometer attached to Haig-streit slit lamp. Lidocaine 1% solution or oxybuprocainium 0.4% solution were used as local anesthetics. Fluorescein paper or fluorescein 1% solution were used with cobalt blue light.
The people were classified into 7 age groups and as the following:
1- The 1st age group (11-20 years).
2- The 2nd age group (21-30 years).
3- The 3rd age group (31-40 years).
4- The 4th age group (41-50 years).
5- The 5th age group (51-60 years).
6- The 6th age group (61-70 years).
7- Above 70 years.
The study was designed in such away to cover 500 males and 500 females in each group.
Most people in the 1st age group were above the age of 15 years due to difficulty in measuring IOP in children. People in this study were patient who attended a private clinic for some ophthalmic problems. All the measurements were taken between 4-9 PM. Excluded from the study are people with the following conditions in one or both eyes:
1- All types of glaucoma.
2- Ocular hypertension.
3- Pseudoxefoliation.
4- Anterior uveitis.
5- Trauma.
6- Retinal detachment.
7- Topical steroid therapy.
8- Recent consumption of alcohol.
9- Coneal scars.
10- Corneal edema
11- Previous intraocular surgery.
12- Single eye.

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Results
Table I shows the distribution of IOP according to the age groups and gender. In table II, the average, standard deviation, range, median, and mode are shown.
Table III demonstrate a statistically significant higher IOP reading in females than in females after the age of 40 years (student t-test). Table IV demonstrates a statistically significant decrease in IOP in each age group and in both sexes when compared to the preceding and the 1st age group after the age of 30 years (student t-test).
Figure 1 shows schematic representation of the mean IOP in each group and for both sexes.
The curves of distribution of IOP in the 1st, 2nd, 3rd, 4th, and 5th age groups resemble a Gaussian curve skewed to the right (the higher reading) as shown in figures 2 and 3.
Figure 4 demonstrates bimodal curve for females and trimodal curve for both sexes in the 6th age group. It also demonstrates bimodal curve for females and for both sexes in the 7th age group.
The curve of distribution of all age groups resembles a Gaussian curve as shown in figure 5.
Discussion
In 1958, Leydhecker and associates published a population study in which 10000 persons with no known eye disease were examined with SchiÖtz tonometers. These investigators obtained a distribution of pressures that resembled a Gaussian curve, but was skewed toward the higher pressure. The results were interpreted to represent two subpopulations: a large, "normal" group and a smaller group that was felt to represent previously unrecognized glaucoma (these include individuals with and without established glaucomatous optic nerve damage). In the "normal" group, the mean IOP was 15.5 ± 2.57 mm Hg. Two standard deviation above the mean was approximately 20.5 mm Hg, which the authors interpreted as the upper limit of "normal", since approximately 95% of the area under a Gaussian curve lies between the mean ± 2 standard deviations. However, the later principle does not apply when a frequency distribution is skewed, and the concept of "normal" IOP limit must be viewed as a rough approximation.
Subsequent studies, using either indentation or applanation tonometry, have generally agreed with Ledhecker's finding, with small differences probably related to population selection and testing techniques.
In 1965, Armaly tested IOP of 2316 individuals between the age of 20-79 years with Goldmann applanation tonometers. The mean IOP was 15.91 mm Hg. He proposed that if the normal population is divided into several subpopulations based on sex and age, the distribution curve of each of these subpopulations is Gaussian in nature. He found a slight increase of mean IOP in each decade above the age of 40 years. In addition, in people 40 years of age and older, women had slightly higher pressure than men.
In Perkins study with Goldmann applanation tonometers, the mean IOP of 2000 individuals of >40 years old was 15.2 mm Hg.
In 1966, Johnson found a mean IOP of 15.4 mm Hg in 7577 individuals of >41 years old with the use of ShiÖtz tonometers.
Segal & Skwierczynska, in 1967, found a significant higher IOP in women than in men in 15695 individuals of >30 years old with the use of ShiÖtz tonometers.
Loewen, et al, in 1976, found a mean IOP of 17.18 mm Hg in 4661 individuals 9-89 years old with the use of Goldmann applanation tonometers.
The mean IOP of 8899 individuals 5-94 years old was found to be 16.25 mm Hg by Ruprecht, et al\textsuperscript{10} in 1978 with the use of Goldmann tonometers. Shiose & Kawase\textsuperscript{11}, in 1986, found a significant higher IOP in women than in men by testing 75545 men and 18158 women with Goldmann applanation tonometers. David et al\textsuperscript{12}, in 1987, studied 2504 individuals 40-70 years old and found a mean IOP of 14.93 mm Hg. The mean IOP was 15.4 mm Hg in 4856 individuals 43-86 years old as found by Klein, et al\textsuperscript{13}, in 1992.

Results of studies in infants and children have been conflicting. It may be influenced by the level of cooperation of children, if they are awake, the anesthetic or sedating agents, or the type of the tonometer. IOP of the newborn has been reported to be 11.4 ±2.4 mm Hg\textsuperscript{14}. In other study, IOP of infants under 4 month of age was 8.4 ± 0.6 mm Hg\textsuperscript{15}. In a study of 460 children between birth and 16 years, the mean IOP rose from 9.59 ± 2.3 at birth to 13.73 ± 2.05 at 3-4 years, with more stable measurement thereafter\textsuperscript{16}.

Large cross-sectional studies of almost 200,000 Japanese subjects by Shiose\textsuperscript{4} actually show a decrease in IOP with age. Shiose suggested that the Japanese data may be reconciled with Western data by postulating that age normally leads to a reduction in IOP, but this effect is overcome in Western populations by the increases prevalence of systolic hypertension and obesity, both of which are associated with increased IOP.

In most of the above studies, the data are either from a screening program for glaucoma or a survey in which subjects are not selected. In this study, which shows a significant decrease of IOP with age, subjects with normal eyes are selected.

The explanation of Shiose that the decrease in IOP in Japanese is due to decrease prevalence of systolic hypertension and obesity might not explain this decrease in Iraqi people in whom both systolic hypertension and obesity are common.

IOP is determined by the rate of aqueous production (inflow) and the rate of its drainage (outflow). When inflow equals outflow, a steady state exists, and the pressure remains constant.

The aqueous is formed by the non-pigmented epithelia of the ciliary body. It is formed by active secretion that is not affected by the level of IOP, ultrafiltration which is determined by the difference between the pressure in the ciliary body capillaries and the IOP, and diffusion which is determined by the difference between the osmotic pressure of a particular substance in the plasma and the aqueous. Water is added to the aqueous by the corneal endothelial pump.

Using a technique of scanning ocular fluorophotometry in more than 300 normal subjects, 3-83 years of age, the mean rate of aqueous flow between 8 AM and 4 PM was 2.75 ± 0.63 µL/min\textsuperscript{17,18}. The flow in the morning was higher, at 2.86 ± 0.73 µL/min than in noon, which was 2.63 ± 0.57 µL/min\textsuperscript{17,18}. The rates during sleep are approximately one-half of those during the morning\textsuperscript{19,20}.

The concept that aqueous production decrease with age\textsuperscript{21} was supported with fluorophotometric studies, and was found to be 2.4-3.2% per decade after the age of 10 years\textsuperscript{17,22}.

Most of the aqueous humor leaves the eye at the anterior chamber angle through the conventional (canalicular) system which consists of trabecular meshwork, Schlemm's canal, intrascleral channels, and episcleral and conjunctival veins. The conventional
route accounts for 83\%\textsuperscript{23} to 96\%\textsuperscript{24} of aqueous outflow in human. The other 4-17\% is drained by a number of systems that are only partially understood, uveoscleral\textsuperscript{24-26} and uveo-vortex\textsuperscript{27} systems. These alternate pathways are called the unconventional or extracanicular systems\textsuperscript{28}, or secondary pathways\textsuperscript{29}. Pores and giant vacuoles in the inner endothelium of Schlemm’s canal appear to be part of transcellular system for aqueous outflow\textsuperscript{30-34}. Many theories have been assumed for the mechanism of transport of aqueous through the trabecular system. One theory suggests active transport which is supported indirectly by the demonstration of enzymes\textsuperscript{35} and electron microscopical structures\textsuperscript{36}. However, the bulk evidence supports the theory of passive (pressure-dependent) transport since the number of vacuoles has been shown to increase with progressive elevation of IOP\textsuperscript{37-40}. This phenomenon is reversible in the enucleated eye\textsuperscript{37}. Also, hypothermia has no effect on the development of the vacuoles in the enucleated eye\textsuperscript{41}. The resistance to outflow could be at the trabecular meshwork, juxtacanalicular connective tissue, and Schlemm’s canal. Probably, the majority of the resistance to outflow is at the inner wall endothelium of Schlemm’s canal\textsuperscript{30-33}. Tracer studies in human\textsuperscript{23} and animals\textsuperscript{24-28} eyes suggest that aqueous passes through the root of the iris and interstitial spaces of ciliary muscles to reach the suprachoroidal space. From there, it passes to episcleral tissue via the pores surrounding blood vessels or nerves or through the actual collagen substance of the sclera. This is called the uveoscleral outflow. Studies by tracer in primates have demonstrated that tracer can penetrate vessels of the iris, ciliary muscles, and anterior choroids to eventually reach the vortex vein\textsuperscript{26,42}. In conclusion, the level of IOP is affected by two factors, the aqueous production and the resistance of its drainage. The aqueous production decreases with age and probably the resistance to outflow. In people with increase IOP with age, the increase in the resistance outflow is more than the decrease in the aqueous production. The reverse is true. The explanation of decrease in the mean IOP with age in Iraqi people might be that in most people the decrease in aqueous production is more than the increase in resistance to outflow. In people with primary open angle glaucoma and ocular hypertension, the increase in the resistance to outflow is much more than the decrease in aqueous production which result in IOP higher than normal.
Table I: Distribution of IOP according to the age groups and gender. IOP (mm Hg). 1 (11-20 y). 2 (21-30 y). 3 (31-40 y). 4 (41-50 y). 5 (51-60 y). 6 (61-70 y). 7 (over 70 y) M= males F= females B= both T= total

| IOP Group | 9    | 10   | 11   | 12   | 13   | 14   | 15   | 16   | 17   | 18   | 19   | 20   | 21   |
|-----------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| 1         | M -- | --   | --   | --   | 12   | 32   | 120  | 217  | 411  | 208  | --   | --   | --   |
|           | F --  | --   | --   | --   | 14   | 30   | 124  | 214  | 412  | 206  | --   | --   | --   |
|           | B --  | --   | --   | --   | 26   | 62   | 244  | 431  | 823  | 414  | --   | --   | --   |
| 2         | M --  | --   | --   | --   | 2    | 20   | 34   | 148  | 212  | 382  | 202  | --   | --   | --   |
|           | F --  | --   | --   | --   | 2    | 24   | 38   | 142  | 212  | 386  | 196  | --   | --   | --   |
|           | B --  | --   | --   | --   | 4    | 44   | 72   | 290  | 424  | 768  | 398  | --   | --   | --   |
| 3         | M --  | --   | --   | 8    | 62   | 74   | 190  | 342  | 214  | 104  | 6    | --   | --   | --   |
|           | F --  | --   | --   | 24   | 48   | 76   | 192  | 340  | 208  | 106  | 2    | 4    | --   | --   |
|           | B --  | --   | --   | 32   | 110  | 150  | 382  | 682  | 422  | 210  | 8    | 4    | --   | --   |
| 4         | M --  | --   | 2    | 10   | 40   | 40   | 122  | 234  | 282  | 236  | 30   | 4    | --   | --   |
|           | F --  | --   | 2    | 32   | 82   | 108  | 268  | 434  | 552  | 448  | 62   | 12   | --   | --   |
|           | B --  | 16   | 40   | 84   | 114  | 270  | 428  | 572  | 424  | 38   | 11   | 3    | --   | --   |
| 5         | M     | 18   | 32   | 86   | 202  | 200  | 150  | 146  | 86   | 55   | 15   | 9    | 1    | --   |
|           | F     | --   | 29   | 41   | 67   | 104  | 106  | 237  | 154  | 206  | 24   | 21   | 7    | 4    |
|           | B     | 18   | 61   | 127  | 269  | 304  | 256  | 383  | 240  | 261  | 39   | 30   | 8    | 4    |
| 6         | M     | 22   | 60   | 100  | 298  | 196  | 108  | 102  | 65   | 25   | 12   | 6    | 2    | 4    |
|           | F     | --   | 32   | 48   | 88   | 116  | 122  | 216  | 150  | 189  | 17   | 18   | 4    | --   |
|           | B     | 22   | 92   | 148  | 386  | 312  | 230  | 318  | 215  | 214  | 29   | 24   | 6    | 4    |
| T         | M     | 40   | 100  | 228  | 596  | 606  | 668  | 900  | 1293 | 1139 | 976  | 445  | 5    | 4    |
|           | F     | --   | 71   | 119  | 257  | 346  | 576  | 1179 | 1502 | 1485 | 993  | 452  | 16   | 4    |
|           | B     | 40   | 171  | 347  | 853  | 952  | 1244 | 2079 | 2795 | 2624 | 1969 | 897  | 21   | 8    |

Table II: The mean, standard deviation, range, median, and mode (mm Hg) M males F females B both T total

| IOP Group | Mean, standard deviation | Range | Median | Mode |
|-----------|--------------------------|-------|--------|------|
| 1         | M 17.61±1.11             | 14-19 | 16.5   | 18   |
|           | F 17.6±1.12              | 14-19 | 16.5   | 18   |
|           | B 17.6±1.11              | 14-19 | 16.5   | 18   |
| 2         | M 17.5±1.2               | 13-19 | 16     | 18   |
|           | F 17.48±1.22             | 13-19 | 16     | 18   |
|           | B 17.49±1.21             | 13-19 | 16     | 18   |
| 3         | M 15.88±1.36             | 12-19 | 15.5   | 16   |
|           | F 15.86±1.42             | 12-20 | 15.5   | 16   |
|           | B 15.87±1.39             | 12-20 | 15.5   | 16   |
| 4         | M 15.33±1.61             | 11-19 | 15     | 16   |
|           | F 15.49±1.48             | 10-19 | 14.5   | 16   |
|           | B 15.41±1.54             | 10-19 | 14.5   | 16   |
| 5         | M 15.19±1.67             | 10-20 | 15     | 16   |
|           | F 15.41±1.55             | 10-20 | 15     | 16   |
|           | B 15.3±1.61              | 10-20 | 15     | 16   |
| 6         | M 13.51±1.2              | 9-20  | 14.5   | 12   |
|           | F 14.96±2.09             | 10-21 | 15.5   | 15   |
|           | B 14.24±2.17             | 10-21 | 15.5   | 15   |
| 7         | M 12.98±1.99             | 9-21  | 15     | 12   |
|           | F 14.7±2.08              | 10-20 | 15     | 15   |
|           | B 13.84±2.21             | 9-21  | 15     | 12   |
| T         | M 15.43±2.29             | 9-21  | 15     | 16   |
|           | F 15.93±1.93             | 10-21 | 15.5   | 16   |
|           | B 15.68±2.13             | 9-21  | 15     | 16   |
Table III: The significance of difference between the males and females average of IOP in each age group. The table shows a significant higher readings in females than in males after the age of 40 years (student t-test).

| Age group | P value compared with previous age group | P value compared with 1st age group |
|-----------|------------------------------------------|-----------------------------------|
| 1st       | >0.5                                     | >0.5                              |
| 2nd       | >0.5                                     | >0.5                              |
| 3rd       | >0.5                                     | >0.5                              |
| 4th       | <0.05                                    | <0.05                             |
| 5th       | <0.01                                    | <0.01                             |
| 6th       | <0.001                                   | <0.001                            |
| 7th       | <0.001                                   | <0.001                            |
| total     | <0.001                                   |                                   |

Table IV: The significance of decrease of the average of IOP with age. The table shows a significant decrease in the mean of IOP in males and females after the age of 30 years (student t-test).

| Age group | P value compared with previous age group | P value compared with 1st age group |
|-----------|------------------------------------------|-----------------------------------|
| 2nd       | >0.05                                    | >0.05                             |
| 3rd       | <0.01                                    | <0.01                             |
| 4th       | <0.01                                    | <0.01                             |
| 5th       | <0.01                                    | <0.01                             |
| 6th       | <0.001                                   | <0.001                            |
| 7th       | <0.001                                   | <0.001                            |
Age and gender variation in intraocular pressure

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Figure 1: The mean IOP of the different age groups

Figure 2: IOP distribution in the 1\textsuperscript{st}, 2\textsuperscript{nd}, and 3\textsuperscript{rd} age groups. Each curve resembles a Gaussian curve that skewed to the right.
Figure 3: Distribution of IOP in the 4th and 5th age group. Each curve resembles a Gaussian curve skewed to right.

Figure 4: Distribution of IOP in the 6th and 7th age group. In the 6th age group the curve is bimodal for the females and trimodal for both sexes. In the 7th age group the curve is bimodal for the females and for both sexes.

Figure 5: Distribution of IOP in all age groups. The curve resembles a Gaussian curve skewed to right.
References

1. Shiose Y: Intraocular pressure: New perspectives. Surv Ophthalmol 34:413, 1990.
2. Leydhecker, W, Akiyama, K, Neumann, HG: Der intraokulare Druck gesunder menschlicher Augen. Klin Monatsbl Augenheilkd 133:622, 1958.
3. Colton, T, Ederer, F: The distribution of intraocular pressures in the general population. Surv Ophthalmol 25:123, 1980.
4. Annaly, MF: On the distribution of applanation pressure. I. Statistical features and the effect of age, sex, and family history of glaucoma. Arch Ophthalmol 73:11, 1965.
5. Annaly, MF: Age and sex correction of applanation pressure. Arch Ophthalmol 78:480, 1967.
6. Perkins, ES: Glaucoma screening from a public health clinic. Br J Ophthalmol 1:417, 1965.
7. Johnson, LV: Tonographic survey. Am J Ophthalmol 61:680, 1966.
8. Segal, P, Skwierczynska, J: Mass screening of adults for glaucoma. Ophthalmologica 153:336, 1967.
9. Loewen, U, Handrup, B, Redeker, A: Results of glaucoma mass screening program. Klin Monatsbl Augenheilkd 169:754, 1976.
10. Ruprecht, KW, Wulle, KG, Christl, HL: Applanation tonometry within medical diagnostic “check-up” programs. Klin Monatsbl Augenheilkd 172:332, 1978.
11. Shiose, Y, Kawase, Y: A new approach to stratified normal intraocular pressure in a general population. Am J Ophthalmol 101:714, 1986.
12. David, R, Zangwill, L, Stone, D, Yassur, Y: Epidemiology of intraocular pressure in a population screened for glaucoma. Br J Ophthalmol 71:766, 1987.
13. Klein, BEK, Klein, R, Linton, KLP: Intraocular pressure in an American community. The Beaver eye study. Invest Ophthalmol Vis Sci 33:2224, 1992.
14. Radtke, ND, Cohan, BE: Intraocular pressure measurement in the newborn. Am J Ophthalmol 78:501, 1974.
15. Goethals, M, Missotten, L: Intraocular pressure in children up to 5 years of age. J Pediatr Ophthalmol Strabismus 20:49, 1983.
16. Pensiero, S, Dapozzo, S, Perissutti, P, et al: Normal intraocular pressure in children. J Pediatr Ophthalmol Strabismus 20:79, 1992.
17. McLaren, JW, Brubaker, RF: A scanning oculometer. Invest Ophthalmol Vis Sci 29:1285, 1988.
18. Brubaker, RF: Flow of aqueous humor in humans. Invest Ophthalmol Vis Sci 32:3145, 1991.
19. Reises, GR, Lee, DA, Topper, JE, Brubaker, RF: Aqueous humor flow during sleep. Invest Ophthalmol Vis Sci 25:776, 1984.
20. McLaren, JW, Trochner, SD, Reit, S, Brubaker, RF: Rate of aqueous humor determined from measurement of aqueous flare. Invest Ophthalmol Vis Sci 31:339, 1990.
21. Becker, B: The decline in aqueous secretion and outflow facility with age. Am J Ophthalmol 46:731, 1958.
22. Brubaker, RF, Nagtaki, S, Townsend, DJ, et al: The effect of age on aqueous humor formation in man. Ophthalmology 88:283, 1981.
23. Jocson, VL, Sears, ML: Experimental aqueous perfusion in enucleated human eyes. Arch Ophthalmol 86:65, 1971.
24. Bill, A, Phillips, CT: Uveoscleral drainage of aqueous in human eyes. Exp Eye Res 12:275, 1971.
25. Pederson, JE, Gaasterland, DE, MacLellan, HM: Uveoscleral aqueous outflow in the rhesus monkey: importance of uveal re-absorption. Invest Ophthalmol Vis Sci 16:1008, 1977.
26. Inomata, H, Bill, A: Exit site of uveoscleral flow of aqueous humor in cynomolgus monkey eyes. Exp Eye Res 25:113, 1977.
27. Sherman, SH, Green, K, Laties, AM: The rate of anterior chamber fluorescein in the monkey eye. I. The anterior chamber outflow pathways. Exp Eye Res 27:159, 1978.
28. Inomata, H, Bill, A, Smelser, GK: Unconventional routes of aqueous humor outflow in cynomolgus monkey (Macaca irus). Am J Ophthalmol 73:893, 1972.
29. McMaster, PRB, Macri, FJ: Secondary aqueous outflow pathways in the rabbit, cat, and monkey. Arch Ophthalmol 79:297, 1968.
30. Feeley, L, Wissig, S: Outflow studies using an electron dense tracer. Trans Am Acad Ophthalmol Otolaryngol 70:791, 1966.
31. Inomata, H, Bill, A, Smelse, GK: Aqueous humor pathways through the trabecular meshwork and into Schlemm’s canal in the cynomolgus monkey (Macaca irus). Am J Ophthalmol 73:760, 1972.
32. Segawa, K: Pores of the trabecular wall of Schlemm’s canal. Ferritin perfusion in enucleated human eyes. Acta Soc Ophthalmol Jpn 74:1240, 1970.
33. Tripathi, RC: Ultrastructure of the exit pathway of the aqueous in lower mammals (a preliminary report on the “angular aqueous plexus”). Exp Eye Res 12:31, 1971.
34. Tripathi, RC, Tripathi, BJ: The mechanism of aqueous outflow in lower mammals. Exp Eye Res 14:73, 1972.
35. Tarkkanen, A, Niemi, M: Enzyme histochemistry of the angle of the anterior chamber of the human eye. Acta Ophthalmol 45:93, 1987.
36. Vegge, T: Ultrastructure of normal human trabecular endothelium. Acta Ophthalmol 41:193, 1963.
37. Johnstone, MA, Grant, WM: Pressure-dependent changes in structure of the aqueous outflow system of human and monkey eyes. Am J Ophthalmol 75:365, 1973.
38. Grierson, I, Lee, WR: Changes in the monkey outflow apparatus at graded levels of intraocular pressure: a qualitative analysis by light microscopy and scanning electron microscopy. Exp Eye Res 19:21, 1974.
39. Grierson, I, Lee, WR: Pressure-induced changes in the ultrastructure of the endothelium lining Schlemm’s canal. Exp Eye Res 79:549, 1975.
40. Kayes, J: Pressure gradient changes on the trabecular meshwork of monkeys. Am J Ophthalmol 79:549, 1975.
41. Van Buskirk, EM, Grant, WM: Influence of temperature and the question of involvement of cellular metabolism in aqueous outflow. Am J Ophthalmol 77:565, 1974.
42. Ravila, G, Butler, JM: Unidirectional transport mechanism of horse-radish peroxidase in the vessels of the iris. Invest Ophthalmol Vis Sci 25:827.