COMPARISON OF INTRAOCULAR PRESSURE IN SYSTEMIC HYPERTENSIVE PATIENTS AND NON HYPERTENSIVE PATIENTS

By

DR. PRASHANT MAHESH KORANMATH

Dissertation Submitted to the

B.L.D.E UNIVERSITY VIJAYAPURA, KARNATAKA

In partial fulfilment of the requirements for the award of the degree of

MASTER OF SURGERY

In

OPHTHALMOLOGY

Under the guidance of

Dr. M. H. Patil M.S.

PROFESSOR

DEPARTMENT OF OPHTHALMOLOGY

B. L. D. E. UNIVERSITY'S SHRI B. M. PATIL MEDICAL COLLEGE, HOSPITAL & RESEARCH CENTRE

VIJAYAPUR 586103

2018

B.L.D.E UNIVERSITY'S

SHRI B.M.PATIL MEDICAL COLLEGE, HOSPITAL & RESEARCH CENTRE, VIJAYAPUR

DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation/thesis entitled **"COMPARISON OF INTRAOCULAR PRESSURE IN SYSTEMIC HYPERTENSIVE PATIENTS AND NON HYPERTENSIVE PATIENTS"** is a bonafide and genuine research work carried out by me under the guidance of **Dr. M. H. PATIL** M.S, (Ophthalmology) Professor, Department of Ophthalmology, Shri B.M. Patil Medical College, Vijayapur, Karnataka.

Date:

Place: Vijayapur **DR. PRASHANT M KORANMATH**

B.L.D.E UNIVERSITY'S

SHRI B.M.PATIL MEDICAL COLLEGE, HOSPITAL & RESEARCH CENTRE, VIJAYAPUR

CERTIFICATE BY THE GUIDE

This is to certify that the dissertation entitled **"COMPARISON OF INTRAOCULAR PRESSURE IN SYSTEMIC HYPERTENSIVE PATIENTS AND NON HYPERTENSIVE PATIENTS"** is a bonafide and genuine research work carried out by **DR. PRASHANT M KORANMATH** in partial fulfilment of the requirement for the degree of MS in Ophthalmology.

Date:

Place: Vijayapur

Dr. M. H. PATIL M.S,

Professor,
Department of Ophthalmology
BLDEU'S Shri B.M Patil
Medical College Hospital and
Research centre, Vijayapur.

B.L.D.E UNIVERSITY'S

SHRI B.M.PATIL MEDICAL COLLEGE, HOSPITAL & RESEARCH CENTRE, VIJAYAPUR

ENDORSEMENT BY THE HOD

This is to certify that the dissertation entitled **"COMPARISON OF INTRAOCULAR PRESSURE IN SYSTEMIC HYPERTENSIVE PATIENTS AND NON HYPERTENSIVE PATIENTS"** is a bonafide research work done by **DR. PRASHANT M KORANMATH** under the guidance of, **Dr. M. H. PATIL** MS, Professor, Department of Ophthalmology, Shri B.M Patil Medical College, Vijayapur.

Date:

Place: Vijayapur

Dr. VALLABHA K.

M. S., D.O.M.S.(Ophthalmology)
Professor,
BLDEU's Shri B.M. Patil
Medical College, Hospital &
Research Centre, Vijayapur.

B.L.D.E UNIVERSITY'S
SHRI B.M.PATIL MEDICAL COLLEGE, HOSPITAL & RESEARCH CENTRE, VIJAYAPUR

ENDORSEMENT BY THE PRINCIPAL / HEAD OF THE INSTITUTION

This is to certify that the dissertation entitled **"COMPARISON OF INTRAOCULAR PRESSURE IN SYSTEMIC HYPERTENSIVE PATIENTS AND NON HYPERTENSIVE PATIENTS"** is a bonafide research work done by **DR. PRASHANT M KORANMATH** under the guidance of, **Dr. M. H. PATIL** MS, Professor, Department of Ophthalmology, Shri B.M Patil Medical College, Vijayapur.

Date:

Place: Vijayapur

Dr. S. P. GUGGARIGOUDAR

M.S. (ENT)
BLDEU's Shri B.M. Patil
Medical College, Hospital &
Research Centre, Vijayapur.

B.L.D.E UNIVERSITY'S
SHRI B.M.PATIL MEDICAL COLLEGE, HOSPITAL & RESEARCH CENTRE, VIJAYAPUR

COPYRIGHT

DECLARATION BY THE CANDIDATE

I hereby declare that the BLDE University, Karnataka shall have the rights to preserve, use and disseminate this dissertation / thesis in print or electronic format for academic / research purpose.

Date:

Place: Vijayapur **DR. PRASHANT M KORANMATH**

© B.L.D.E UNIVERSITY VIJAYAPUR

ACKNOWLEDGEMENT

On completion of my post-graduation journey and this scientific document I would like to acknowledge the immense help received from my mentors in the department of general surgery.

With privilege and respect, I would like to express my deepest gratitude to my guide **Dr. M.H. Patil** for his constant inspiration, extensive encouragement and support which he rendered in pursuit of my post graduation studies and in preparing this dissertation.

I am forever grateful to professors **Dr Vallabha K, Dr. Sunil Biradar** for their guidance and encouragement provided to me to achieve new heights professionally over my course period.

I am grateful to associate professor **Dr. R.K Ijeri** for his guidance and encouragement.

I am extremely thankful and grateful to **Dr. Jyoti R.C** for her constant support and guidance.

I am extremely thankful to Professor **Dr. S. P. Guggarigoudar**, principal of BLDEU's Shri B. M. Patil Medical College Hospital and Research Centre, Vijayapur for permitting me to utilise resources in completion of my work.

My sincere thanks to our Medical Superintendent **Dr. Vijaykumar Kalyanappagol** for his support and inspiration.

My thanks to all the staff of library, ophthalmology department and the hospital for their cooperation in my work.

I would also like to thank my colleagues and friends **Dr. Vinit S Shah, Dr Dishitha P Rathod** for their constant support, help and cooperation.

I would also like to thank my juniors **Dr. Ashwini** and **Dr. Sowmya** for their cooperation and support.

I am deeply indebted to my parents **Dr. Mahesh Koranmath** and **Vijayalaxmi Koranmath** for their blessings and constant motivation. I would also like to thank **Dr Ruhi Satija** for her constant support, motivation and encouragement. Last but not the least I convey my heartfelt gratitude to my patients without whose cooperation this study would be incomplete.

DR. PRASHANT KORANMATH

ABSTRACT

Background and Aim:

Intraocular pressure is an essential entity in maintaining the structural and functional integrity of the eyeball. The most important factor which regulates the intraocular pressure within physiological limits is the aqueous humour. The intraocular pressure is maintained by the equilibrium between aqueous production from ciliary body and its drainage via trabecular complex. The aqueous humor helps in maintaining the nutrition of the avascular structure of the globe and act as a refractive medium in the eye. An increase in intraocular pressure leads to a clinical complex known as glaucoma. Among the various possible causes, high blood pressure is one of the possible cause of ocular hypertension. There are limited data as to whether the moderate changes in blood pressure that often accompany treatment for hypertension are associated with synchronous changes in IOP.

Aim-

To study the relationship between blood pressure and intraocular pressure in systemic hypertensive and non hypertensive patients.

Methods :

128 subjects with hypertension and 128 nonhypertensive subjects who were age-matched sex matched, were enrolled for the study. Blood pressure was measured with Sphygmomanometer in supine position. IOP measurement was done using Goldman's Applanation Tonometer. Dilated fundouscopy was done for all cases.

Results :

It was observed that IOP increased as Systolic Blood Pressure increases, which are statistically significant. Similarly IOP increases as Diastolic Blood Pressure increases, which is statically significant (p value <0.001*).

The mean IOP in Normotensive patients was 11.21 mmHg, 12.65mmHg in RE and 12.77mmHg in LE in Pre-Hypertensive patients, 14.70mmHg in RE and 14.87mmHg in LE in Grade 1 Hypertensive patients, 17.75mmHg in RE and 17.87mmHg in LE in Grade 2 Hypertensive patients. Mean total IOP 14mmHg in RE and 14.09mmHg in LE, which is statically (P VALUE=<0.001)

Conclusion:

Systemic blood pressure increases Intraocular pressure significantly and advancing age is also associated with elevated intraocular pressure.

Hence, person with systemic hypertension and advancing age need periodic Blood Pressure and Intraocular pressure monitoring and control. This will help in control / reduce progression of glaucoma.

Keywords: Blood pressure, intraocular pressure, systemic blood pressure, glaucoma.

LIST OF ABBREVATIONS

MmHg	– Millimetre of mercury.
IOP	– Intraocular Pressure.
OHT	– Ocular Hypertension.
TM	– Trabecular meshwork.
JCT	– Juxtacanalicular connective tissue.
SC	– Schlemm's canal.
ITS	– Intratrabecular spaces.
AV	– Arterio-venular.
ONH	– Optic nerve head.
CCT	– Central corneal thickness.
OHTS	– Ocular hypertension treatment study.
POAG	– Primary Open Angle Glaucoma.
MAP	– Mean ophthalmic artery pressure.
OPP	– OCULAR PERFUSION PRESSURE
ERG	– Electroretinogram.
ONH	– Optic Nerve Hypoplasia.
eNOS	– Endothelial nitric oxide synthase.
NO	– Nitric oxide.

ET – Endothelin.

cGMP – Cyclic guanosine monophosphate.

NAME – Nitroarginine methyl ester.

ET – Endothelin receptors.

OAG – Open Angle Glaucoma.

BLSA – Baltimore Longitudinal Study of Aging.

SBP – Systolic Blood Pressure.

DBP – Diastolic Blood Pressure.

LALES – Los Angeles Latino Eye Study.

ODH – Optic disc haemorrhage.

GAT – Goldmanns' Applanation Tonometer.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF GRAPHS

LIST OF FIGURES

INTRODUCTION

Intraocular pressure is dynamic balance between aqueous humor production in the ciliary body and its elimination via canal of schelmm, maintaining intraocular pressure within its physiological range (10 – 20mmHg). Formation of aqueous involves secretion, ultrafiltration and diffusion(Secretory process involves 95%).[1] Increase in systolic blood pressure will increase the blood flow to ciliary body of eye which is responsible for production of aqueous by ultrafiltration resulting in increased intraocular pressure. Increased intraocular pressure will have effect on the drainage of aqueous humour via the episcleral veins by affecting the pressure gradient between aqueous in anterior chamber and in the episcleral veins.[2]

21mm of Hg is considered the upper limit of normal IOP and levels above this are viewed with suspicion and need evaluation.

IOP is a dynamic function. Any single measurement of IOP is just a momentary sample and may or may not reflect the average pressure for the patient at that hour, day or week. Normally it varies with the time of the day, heartbeat, blood pressure level, respiration and position. The pattern of diurnal curves varies with a tendency to be higher in the morning and lower in the afternoon and evening.

Different IOP readings at different times of the day have been observed and defined by diurnal variation tests. IOP measurements during different hours of the day have a well-recognized clinical importance, which can directly affect the diagnosis and management of the patient with IOP related conditions. In clinical practice performing diurnal IOP curves has several indications: (1) in patients with ocular hypertension (OHT) it is essential to obtain baseline IOP levels and monitor the

condition, (2) in cases when a suspicious looking optic disc is discovered in patients without apparent IOP elevation and (3) in glaucomatous patients with progressive damage whenever single IOP measurements are within the 'normal' range. But it is very difficult to obtain patient compliance to compare the IOP findings at different times on the same day and many ophthalmologists follow-up their patients on different days to obtain their diurnal variation curve which helps them in their further line of management.

Intraocular pressure is an essential entity in maintaining the structural and functional integrity of the eyeball. Any abnormality in the intraocular pressure of a given eye can result in the dysfunction of the eye. The most important factor which regulates the intraocular pressure within physiological limits is the aqueous humour. The intraocular pressure is maintained by the equilibrium between aqueous production from ciliary body and its drainage via trabecular complex. The aqueous humor helps in maintaining the nutrition of the avascular structure of the globe and act as a refractive medium in the eye. An increase in intraocular pressure leads to a clinical complex known as glaucoma. Among the various possible causes, high blood pressure is one of the possible cause of ocular hypertension.

Intraocular pressure (IOP) has been found to be associated with systemic blood pressure levels in population based studies.[3-12] The relation appears to be reasonably consistent across the range of values of IOP and both systolic and diastolic blood pressures. It has been postulated that treatment of hypertension may place the eye at relatively increased risk of visual field deficits because of an imbalance in the relation of blood pressure to IOP.[13] This thought has been given credence, in part, because of the clinical dictum that sudden lowering of blood pressure is associated

with loss of visual field in some people.[14] Blood pressure increases with age in most populations, and medical intervention has been successful in lowering blood pressure and the subsequent risk of the systemic sequelae of high blood pressure. There are limited data as to whether the moderate changes in blood pressure that often accompany treatment for hypertension are associated with synchronous changes in IOP.

Hence, the present study was done at our tertiary care center to compare intraocular pressure in systemic hypertensive and non-hypertensive subjects and to find the relationship of intraocular pressure with blood pressure and to emphasize on the necessity to check intraocular pressure periodically in hypertensive patients. Also, to increase awareness about ocular complications of hypertension, population based screening would help to reduce blindness due to glaucoma.

AIMS AND OBJECTIVES

To study the relationship between blood pressure and intraocular pressure in systemic hypertensive patients and non-hypertensive patients attending BLDEU's Shri. B. M. Patil Medical College, Hospital & Research Centre.

REVIEW OF LITERATURE

Anatomy

The 2 main structures related to the aqueous humour dynamics are the ciliary body, which is the site of aqueous humour production and the anterior chamber angle including the trabecular meshwork, which is the principle site of aqueous humor outflow.

The ciliary body forms a part of the anterior chamber angle and gets attached to the scleral spur creating a potential space known as the supraciliary space between the sclera and itself. On cross section the ciliary body is shaped like a right angled triangle with the anterior posterior length of the ciliary body in the adult eye being about 4.6 to 5.2 mm nasally and 5.6 to 6.3 mm temporally. It is divided into 2 regions, the anterior part known as the pars plicata and the posterior part, the pars plana. The ciliary processes which occupy the innermost and anterior most portion of the pars plicata or corona ciliaris are the site of aqueous humour production. They consist of 70 to 80 radial ridges (major ciliary processes) between which are interdigitated an equal number of small ridges (minor and intermediate ciliary processes). The pars plicata region also has smooth muscle, which helps in accommodation and uveoscleral outflow of aqueous humour. The posterior portion of the ciliary body called pars plana or orbicularis ciliaris has a flatter inner surface and joins the choroid at ora serrata.

The anterior chamber angle is comprised of the following structures from posterior to anterior: the root of iris, ciliary body band, scleral spur, trabecular meshwork which bridges the Schlemm’s canal and the Schwalbe’s line.

The scleral sulcus, which is an indentation on the inner surface of the limbus, has a sharp posterior margin, the scleral spur and a sloping anterior wall that extends to the inner aspect of the peripheral cornea. The schwalbe's line marks the transition from trabecular meshwork to corneal endothelium and the thinning and termination of descemet's membrane. It is formed by the oblique insertion of uveal trabecular meshwork into the limbal stroma

The trabecular meshwork is a sieve like structure that bridges the scleral sulcus and converts it into a tube, the Schlemm's canal which is connected to the episcleral veins by the intrascleral channels. It is divided into 3 portions a) Uveal meshwork, b) Corneo-scleral meshwork c) Juxtacanalicular meshwork

The Uveal meshwork is the innermost portion of the trabecular meshwork, adjacent to the anterior chamber. It is arranged in bands or rope like trabeculae that extend from the iris root and ciliary body to peripheral cornea. The Corneoscleral meshwork is made up of sheets of trabeculum. It is the middle layer which extends from the scleral spur to the lateral wall of the scleral sulcus. The sheets of trabeculae are perforated with elliptical openings. The Juxtacanalicular tissue is the outermost part of meshwork consisting of a layer of connective tissue lined by endothelium. The inner layer is continuous with the remainder of the trabecular endothelium. The outermost layer forms the inner wall of the Schlemm's canal.

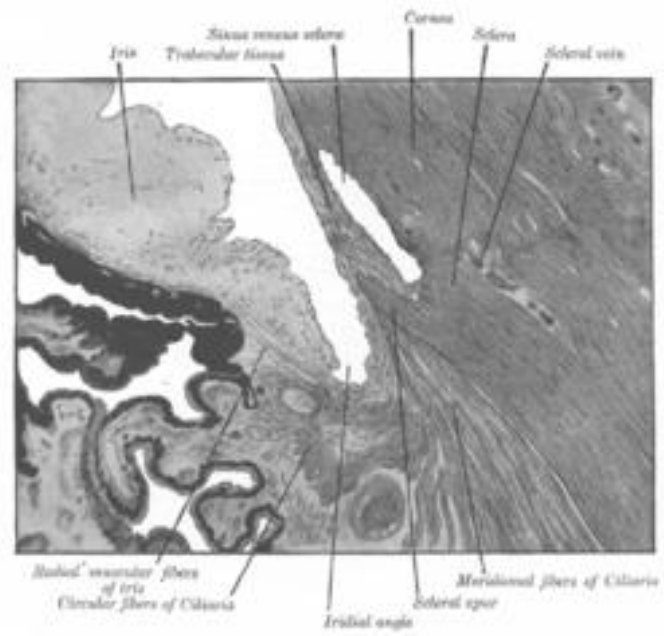


Figure1: Enlarged general view of the iridial angle. When enlarged, visible with older label of trabecular tissue.

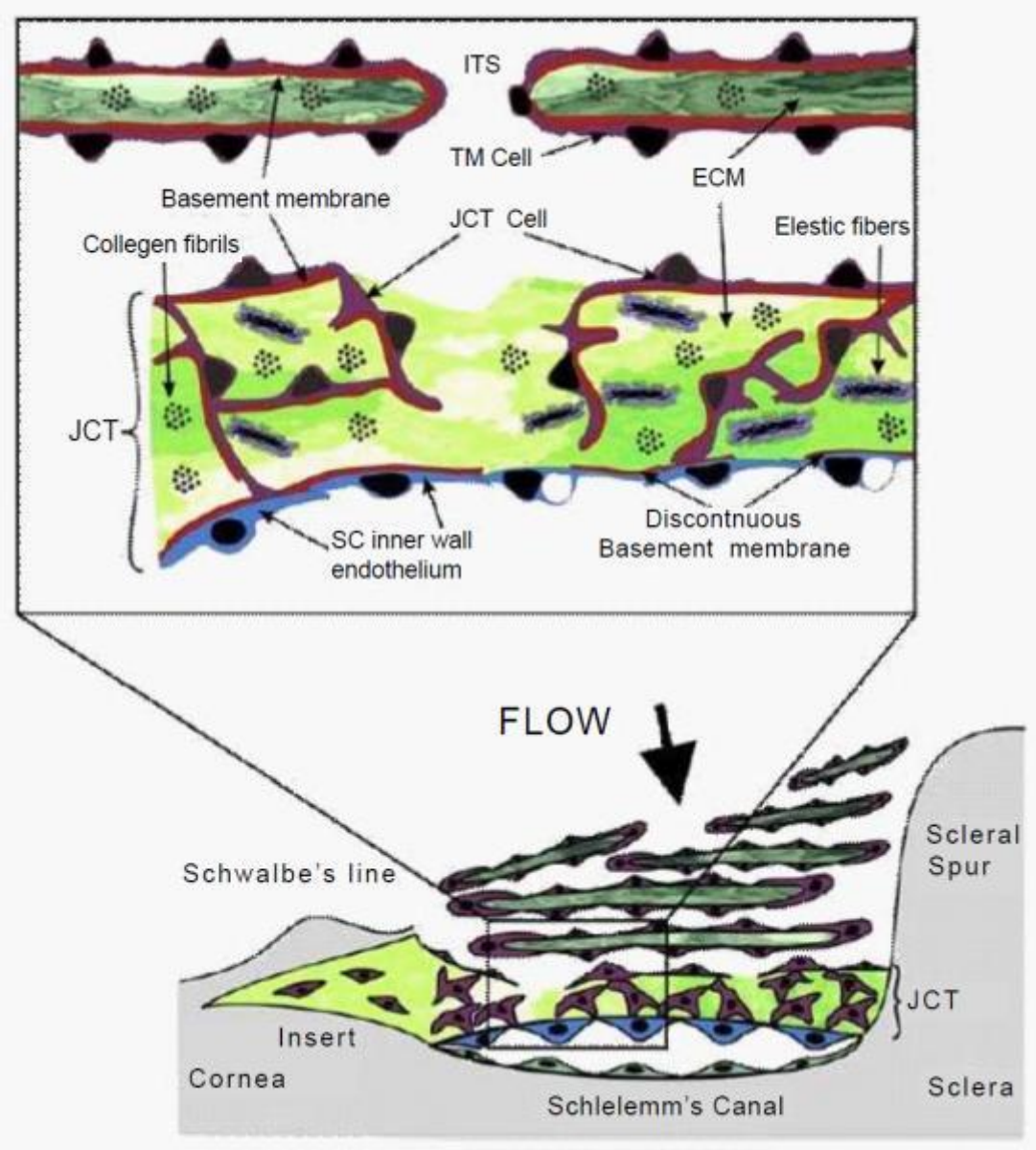


Figure 2.Outflow pathway through the TM and JCT

The lower portion of the figure shows a side view of the TM (radial section). The arrow indicates the direction of AH flow across the TM until it enters SC. The upper inset represents an expanded view of the JCT region. Once the AH passes through the intratrabecular spaces (ITS) of corneoscleral meshwork, it goes to the JCT region, and then through the inner wall endothelial lining of SC.

The trabecular meshwork is composed of multiple layers, each of which consists of a collagenous connective tissue core covered by a continuous endothelial layer covering. It is the site of pressure dependent outflow of aqueous. It functions as a one-way valve that permits aqueous to leave the eye by bulk flow but limits flow in the other direction, independent of energy.[15]

The Schlemm's canal is a single channel with an average diameter of approximately 370 microns and is traversed by tubules. The inner wall of Schlemm's canal contains giant vacuoles that have direct communication with the intertrabecular spaces. Aqueous moves both across and between the endothelial cells lining the inner wall of Schlemm's canal.[15,16] The outer wall is actually a single layer of endothelial cells that do not contain pores. A complex system of vessels connects the Schlemm's canal to the episcleral veins.[15] Thus the main route of aqueous humour outflow is via the trabecular meshwork, Schlemm's canal, and intrascleral channels.

Hypertensive retinopathy

Hypertensive retinopathy is damage to the retina and retinal circulation due to high blood pressure (i.e. hypertension).

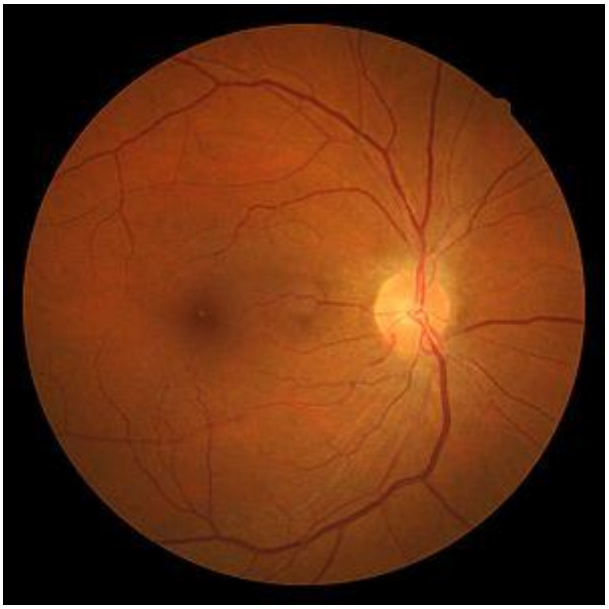


Figure 3.Hypertensive retinopathy with AV nicking and mild vascular tortuosity

Signs and symptoms

Most patients with hypertensive retinopathy have no symptoms. However, some may report decreased or blurred vision, [17] and headaches.[18]

Signs

Signs of damage to the retina caused by hypertension include:

- Arteriolar changes, such as generalized arteriolar narrowing, focal arteriolar narrowing, arteriovenous nicking, changes in the arteriolar wall (arteriosclerosis) and abnormalities at points where arterioles and venules cross. Manifestations of these changes include Copper wire arterioles where the central light reflex occupies most of the width of the arteriole and Silver wire arterioles where the central light reflex occupies all of the width of the arteriole, and "arterio-venular (AV) nicking" or "AV nipping", due to venous constriction and banking.

- advanced retinopathy lesions, such as micro aneurysms, blot hemorrhages and/or flame hemorrhages, ischemic changes (e.g. "cotton wool spots"), hard exudates and in severe cases swelling of the optic disc (optic disc edema), a ring of exudates around the retina called a "macular star" and visual acuity loss, typically due to macular involvement.

Mild signs of hypertensive retinopathy can be seen quite frequently in normal people (3–14% of adult individuals aged ≥40 years), even without hypertension.[19] Hypertensive retinopathy is commonly considered a diagnostic feature of a hypertensive emergency although it is not invariably present.[20]

Keith Wagener Barker (KWB) Grades

Grade 1

Vascular Attenuation

Grade 2

As grade 1 + irregularly located, tight constrictions - Known as "AV nicking" or "AV nipping" - Salus's sign

Grade 3

As grade 2 + Retinal edema, cotton wool spots and flame-hemorrhages "Copper Wiring" + Bonnet's Sign + Gunn's Sign

Grade 4

As grade 3 + optic disc edema + macular star "Silver Wiring"

There is an association between the grade of retinopathy and mortality. In a classic study in 1939, Keith and colleagues [5] described the prognosis of people with differing severity of retinopathy. They showed 70% of those with grade 1 retinopathy were alive after 3 years whereas only 6% of those with grade 4 survived. The most widely used modern classification system bears their name.[19] The role of retinopathy

grading in risk stratification is debated, but it has been proposed that individuals with signs of hypertensive retinopathy signs, especially retinal hemorrhages, microaneurysms and cotton-wool spots, should be assessed carefully.[19]

The changes in hypertensive retinopathy result from damage and adaptive changes in the arterial and arteriolar circulation in response to the high blood pressure.[17]

Several other diseases can result in retinopathy that can be confused with hypertensive retinopathy. These include diabetic retinopathy, retinopathy due to autoimmune disease, anemia, radiation retinopathy, central retinal vein occlusion.[18]

A major aim of treatment is to prevent, limit, or reverse target organ damage by lowering the patient's high blood pressure and reduce the risk of cardiovascular disease and death. Anti-hypertensive drug treatment may be required to control the high blood pressure.

Grading of anterior chamber angle:

The most commonly used anterior chamber angle grading system are the Shaffer and Modified Shaffer system which grades the angle from 0 to 4 based on the degrees of the angle (Shaffer) and the structures visible on gonioscopy.[21]

Table A.

	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
Shaffer's grading	Closed	10^0	20^0	30^0	40^0
Modified Shaffer's grading	Schwalbe's line not visible	Schwalbe's line visible	Anterior trabecular meshwork visible	Scleral spur visible	Ciliary body band visible

Aqueous humor dynamics:

An understanding of aqueous humour dynamics is essential for the evaluation and management of glaucoma. Aqueous humour formation is a biological process that is subject to circadian rhythms. [15] Aqueous humour is formed by the ciliary processes, each of which is composed of a double layer of epithelium over a core of stroma and a rich supply of fenestrated capillaries. Each of the 80 or so processes contains a large number of capillaries, which are supplied mainly by the branches of the major arterial circle of the iris. The apical layers of both the outer and inner nonpigmented layers of epithelium face each other and are joined by tight junctions which are an important component of the blood aqueous barrier.[15]

Aqueous is derived from the plasma within the capillary network of the ciliary processes and secreted into the posterior chamber by three mechanisms:

A. Diffusion is the process by which lipid-soluble substances are transported through the lipid portions of the cell membrane proportional to a concentration gradient across the membrane.

B. Ultrafiltration is the process by which water and water-soluble substances, limited by size and charge, flow through theoretical micropores in the cell membrane in response to an osmotic gradient or hydrostatic pressure in the ciliary processes. The hydrostatic pressure difference between capillary pressure and Intraocular Pressure (IOP) favours fluid movement into the eye whereas the oncotic gradient between the two resists fluid movement.[15,16] It is influenced by intraocular pressure, blood pressure in the ciliary capillaries, and plasma oncotic pressure.

Diffusion and ultrafiltration are both passive mechanisms, by which lipid and water-soluble substances from the capillary core traverse the stroma and pass between the pigmented epithelial cells and get limited by the tight junctions of the non-pigmented epithelial cells

C. Active transport (secretion) - This is the most important mechanism involved in aqueous humour formation. Water-soluble substances of larger size or greater charge are actively transported across the cell membrane, requiring the energy expenditure. Na-K ATPase and glycolytic enzyme complexes which are present in the nonpigmented epithelial cells are used for the active transport of these substances. This process is decreased by hypoxia, hypothermia, and any inhibitor of active metabolism.

The mechanisms involved in regulation of IOP remain largely unknown. It is suggested that humoral or neurohumoral pathways influence the steady state level of IOP by altering the rate of aqueous production.[15,22,23] Aqueous humor formation decreases with sleep, advancing age, uveitis, retinal detachment and ciliochoroidal detachment. Decreased aqueous humor formation with increased IOP (pseudofacility) has been disputed by recent studies indicating that rate of aqueous formation is relatively pressure-insensitive.[15]

Aqueous humour outflow occurs by 2 mechanisms, which are the pressure dependent outflow and pressure independent outflow. The mean outflow facility of the aqueous humour ranges from 0.22 to 0.30 micL/min/mmHg. Outflow facility

decreases with age and is affected by surgery, trauma, medications and endocrine factors. Patients with glaucoma and elevated IOP have decreased outflow facility.[16]

The trabecular outflow is the main route of aqueous humour outflow and under normal conditions active secretion accounts for perhaps 80% to 90% of total aqueous humor outflow. Recent evidence questions the exact ratio of trabecular to uveoscleral outflow. As with outflow facility, this ratio is affected by age and by ocular health. The aqueous humor, secreted into the posterior chamber of the eye, enters the anterior chamber through the pupil. It then passes through the pupil and circulates within the anterior chamber of the eye, by the convection current created by the temperature difference between the warm iris and the cooler cornea so that it rises posteriorly and falls anteriorly.. Aqueous humor drains from the anterior chamber via trabecular meshwork to schlemm's canal. From the Schlemm's canal the aqueous is further transported by various mechanisms for which there are different theories such as the vacuolation theory, leaky endothelial cells, Sonderman's canals, contractile microfilaments and pores. From this canal, 30 collector channels weave toward the surface of the sclera, lined by vascular endothelium. These canals are wide at the origin and have no valves. They are divided into two systems which are the direct system in which 8 larger vessels run a short intrascleral course and terminate directly into episcleral veins and the indirect system in which numerous finer collector channels drain into three interconnecting venous plexuses; the deep intrascleral plexus, middle intrascleral plexus and episcleral venous plexus before eventually going into the episcleral veins which drain into cavernous sinus via anterior ciliary and superior ophthalmic vein. On slit lamp examination they appear as clear vessels with aqueous and are known as the aqueous veins of Ascher.[15]

Uveoscleral outflow is the second major route of aqueous drainage through the face of the ciliary body and iris root to the ciliary muscle and then into the supraciliary and suprachoroidal space. The fluid then exits the eye through the intact sclera or along the nerves and vessels which penetrate it. It is also termed pressure independent outflow though it reportedly may improve with IOP elevation, presumably due to ultrafiltration of aqueous into uveal vessels. It accounts for an estimated 5 – 15 % of total outflow and is influenced by age. Recent studies indicate that it may be a higher percentage of total outflow especially in normal eyes of young people. The uveoscleral outflow is increased by cycloplegics, adrenergic agents, prostaglandin analogues and is decreased by miotics.

Uveovortex outflow - Tracer substances have also been demonstrated to traverse vessels of the iris, ciliary muscle, and anterior choroid, eventually reaching the vortex veins and this pathway is called the uveovortex outflow. It is not energy dependent, nor clinically significant.[15,16] Contraction of ciliary muscles (e.g. with parasympathomimetics) increases trabecular outflow and decreases uveoscleral outflow. Relaxation of ciliary muscles (e.g. with cycloplegics) decreases trabecular outflow and increases uveoscleral outflow.

Intraocular pressure

A number of large epidemiological studies indicate that the mean (+ SD) IOP in the general population is approximately 16 (± 3) mmHg. However, IOP has a non Gaussian distribution with a skew towards higher pressures, especially in individuals over 40 years of age. The value of 22 mmHg (greater than 2 standard deviations above mean) has been used in the past both to separate normal and abnormal pressures and to define which patients require ocular hypotensive therapy. This

division was based on the erroneous assumption that glaucomatous damage is caused exclusively by intraocular pressures that are higher than normal and that normal IOP does not cause damage. Over the years, other factors such as optic nerve head (ONH) ischaemia and various vasogenic factors have also been implicated in glaucomatous ONH damage. However elevation of IOP is still seen as a very important risk factor for the development of glaucomatous optic nerve damage, because although other risk factors affect the susceptibility to glaucomatous damage, IOP is the only one that can be effectively altered at present.

IOP varies with a number of factors; such as, elevated episcleral venous pressure due to valsalva manouvere, tight collar/tie, elevated central venous pressure, intubation, direct pressure on the eye in case of blepharospasm, hormonal influences, thyroid ophthalmopathy and drugs like Topiramate and Corticosteroids which can increase IOP. Many factors such as aerobic exercise, anaesthetic drugs like ketamine and succinylcholine, metabolic and respiratory acidosis, pregnancy and alcohol decrease IOP.

There is normal diurnal variation of IOP by 2 to 6 mm Hg over a 24 hour period, due to changes in aqueous humour production and aqueous outflow. A diurnal fluctuation of greater than 10 mmHg is suggestive of glaucoma. The impact of IOP fluctuations on the optic nerve remains largely unknown.[15]

Tonometry - There are various techniques for tonometry, with the most commonly used techniques being indentation and applanation tonometry. Indentation tonometry is the measurement of the IOP by relating a deformation of the globe to the force responsible for the deformation. A low ocular rigidity yields a falsely low IOP reading and this occurs in high myopia, miotic therapy, previous intraocular surgery

and vasodilator therapy. A high ocular rigidity yields a falsely high IOP reading and possible causes include high hyperopia, vasoconstrictor therapy, blood volume alterations and steeper or thicker corneas which may displace more fluid on indentation, resulting in falsely high IOP measurement. Moses effect; seen with indentation tonometry where the cornea may mould into the space between the plunger and the hole in the tonometer footplate, pushing up the plunger, can also give a falsely high IOP reading.[15]

Applanation tonometry is more accurate than indentation tonometry and its prototype is the Goldmann's tonometer. It is based upon modification of the Imbert-Fick law for ideal, thin walled spheres:

Pt = W/A => W = Pt x A

W = External force against sphere

Pt = Pressure within sphere

A = Area flattened (applanated) by external force

Applanation tonometry measurements are affected by central corneal thickness (CCT), such that increased CCT may give an artificially high IOP reading and a lower CCT may produce an artificially low IOP reading. Normal CCT varies over a wide range of with the mean CCT being between 537 and 554 microns. The ocular hypertension treatment study (OHTS)[24] found that a thinner central cornea was a strong predictive factor for the development of glaucoma in subjects with ocular hypertension. Subjects with corneal thickness of 555 microns or less had a three fold greater risk of developing POAG as compared to participants who had a CCT of more than 588 microns. Whether this increased risk of glaucoma is due to underestimating actual IOP in patients with thin corneas or whether thin corneas are actually a risk

factor independent of IOP measurement has not been completely determined, but the OHTS found CCT to be a risk factor for progression of POAG, independent of IOP level.[16] In a cross-sectional, population based study in an east Asian population, a small but highly significant decrease in CCT was found with increasing age. Due to the variation in IOP measurement attributable to the variation in CCT, it is difficult to fully elucidate the true relationship between glaucomatous optic neuropathy and IOP without taking into account CCT variation.[25]

ESTIMATION OF OCULAR PERFUSION PRESSURE

Perfusion pressure usually represents the difference between arterial and venous pressure. In the eye, venous pressure approximates the IOP, so that mean OPP can be taken as the difference between the mean ophthalmic artery pressure ($MAP_{ophthalmic}$) and IOP,[26,27] as given in Equation 1.

$$OPP = MAP_{ophthalmic} - IOP$$

$MAP_{ophthalmic}$ is not readily measured in clinical practice. Instead, the brachial arterial pressure ($MAP_{brachial}$) is most commonly measured in clinical settings using an arm cuff sphygmomanometer in an upright position. This is a useful estimate of $MAP_{ophthalmic}$ as the blood pressures in both the ophthalmic and brachial arteries are related in the absence of vascular pathology.[28] Measured by ophthalmodynamometry, systolic ophthalmic arterial pressure is approximately three-quarters the systolic brachial arterial pressure, whereas diastolic ophthalmic arterial pressure is approximately two-thirds of the diastolic brachial arterial pressure.[29,30] Therefore, Equation 1 can be reformulated for clinical application as follows:

$$OPP = \frac{2}{3} \cdot MAP_{brachial} - IOP$$

$MAP_{brachial}$ is determined from the systolic blood pressure (SBP) and diastolic blood pressure (DBP) as shown in Equation 3. The scaling factor 2/3 in Equation 2 accounts for the difference in blood pressure between the brachial and ophthalmic arteries in humans when measured in the sitting or standing positions.[31] In many non-primate models, such a scaling factor is not required as the animals are habitually in a prone position.

$$MAP = DBP + \frac{1}{3}(SBP - DBP)$$

Equation 2 is of clinical significance, as it indicates that the OPP can be reduced either by lowering the mean blood pressure (MAP) or by increasing the IOP.107,108 Thus, low blood pressure can undermine the effect of IOP lowering therapy to improve OPP in glaucoma patients. This may explain why some patients continue to develop visual field loss despite effective therapeutic IOP reduction. Consistent with this idea one study[32] has shown that not only IOP but also ocular blood flow correlate with the progression of glaucoma in terms of visual field loss.

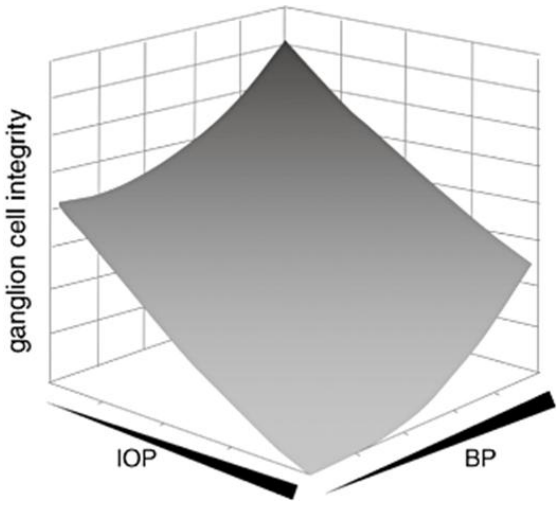


Figure 4

Hypothesis derived from Equation 2 and a clinical trial113 showing the interplay of intraocular pressure (IOP) and blood pressure as risk factors of glaucoma.

Several caveats exist when Equation 2 is used to determine the OPP. First, although the use of $MAP_{brachial}$ as a surrogate for $MAP_{ophthalmic}$ is appropriate under normal conditions, it does not account for local vascular pathology, such as atherosclerosis induced by chronic high blood pressure. Once hypertension becomes severe enough to produce atherosclerosis or even total tissue infarction, local perfusion pressure will drop even with high blood pressure. In this setting, systemic blood pressure will not be a good surrogate for local blood pressure. Second, IOP elevation can also induce mechanical compression on axons, which cannot be reversed by lowering blood pressure, as this produces local hypoperfusion.[33] The OPP concept cannot account for this mechanical compression.

EVIDENCE FOR BLOOD PRESSURE INVOLVEMENT

In contrast to the vast body of literature arising from clinical trials and epidemiological studies, few experimental studies have directly addressed the effect of blood pressure on glaucoma susceptibility. To our knowledge, no study has successfully induced 'normal tension glaucoma' in an animal model by lowering blood pressure alone. Only a few experiments have considered the effect of IOP and blood pressure modulation simultaneously. The first report by Grehn and Prost[34] goes back to 1983. Specifically, ganglion cell function in cats was assessed by axonal impulse conduction, which remained unimpaired when the OPP was above 20 mmHg, regardless of whether IOP was 40 or 135 mmHg. This is of interest as the data suggest that the primary determinant of ganglion cell health is the integrity of the blood flow. There appears to be little influence from a mechanical mechanism of acute IOP, as

one would have expected a greater mechanical effect in the presence of an IOP of 135 mmHg than 40 mmHg. This study was then extended to the measurement of full-field electroretinogram (ERG) (the bipolar cell b-wave) and pattern ERG by Siliprandi and associates[35] in 1988. The pattern ERG has been shown to depend mainly on ganglion cell integrity.[36] Like the Grehn and Prost study, 115 the pattern ERG was attenuated either by increasing IOP or by reducing blood pressure in cats. These studies indicate that the key determinant to retinal function is OPP, rather than IOP or blood pressure alone.

Studies that measure ocular blood flow are in agreement with the functional data, supporting the hypothesis that OPP plays a dominant role in determining retinal function. Kiel and Van Heuven[37] reported that blood pressure and IOP manipulations can produce an equivalent change in choroidal blood flow in rabbits, measured with laser-Doppler flowmetry. Most recently, Liang and associates[38] found that impaired ONH blood flow arising from elevated IOP is exacerbated in monkeys with hypotension (mean arterial blood pressure of 56 mmHg), compared with those with normal blood pressure (mean arterial blood pressure of 102 mmHg). These findings are consistent with those reported by Grehn and Prost,[34] as they indicate that the primary insult associated with IOP challenge is a vascular compromise.

Taken together, these studies consistently show that OPP is a key determinant of blood flow and visual function, which is in agreement with the concept that low blood pressure exacerbates IOP-induced ischaemia, whereas high blood pressure, at least in the short term, appears to provide some protection against it.[39]

It is important to note that these studies altered IOP and blood pressure over only short periods of time (a maximum of 10 minutes). Although they provide crucial insights into the relationship between IOP, blood pressure and ganglion cell integrity, these experiments do not explore the more chronic effects needed to better model open-angle glaucoma and essential hypertension in humans. In particular, acute short-term hypertension does not cause atherosclerosis, cardiac hypertrophy or renal impairment, which frequently occur in long-standing systemic hypertension. Therefore, a model of chronic elevation of IOP and blood pressure would yield greater clinical insight into understanding the relationship between autoregulation, systemic hypertension and glaucoma. In this regard, Hayreh and colleagues[40,41] induced experimental atherosclerosis (using a high-cholesterol diet) and systemic hypertension (by renal artery occlusion) in monkeys for several years before chronic IOP elevation was achieved by laser photocoagulation of the trabecular meshwork. Surprisingly, these two reports showed that neither systemic hypertension nor atherosclerosis has much influence on retinal and optic nerve changes induced by IOP elevation. The authors attributed the outcome to inadequate sample size and statistical power. To our knowledge, no other animal experiment has examined the effect of chronic hypertension on glaucoma, possibly due to the technical difficulties associated with producing and monitoring chronic hypertension and IOP elevation simultaneously.

BLOOD FLOW AUTOREGULATION

A small reduction in OPP does not always result in blood flow deficiency, as the retina strives to maintain its circulation even under extreme environmental insults. This has been known since Hill and Flack[42] in 1912 found that the choroidal circulation in cats would not arrest until the IOP was raised to levels approximating

the carotid artery pressure. Ocular blood flow is determined not only by OPP but also by blood vessel resistance, which in turn is related to blood viscosity (η) and vessel diameter (R), all of which contribute to regulate blood flow (Q) as expressed by the Hagen–Poiseuille law:

$$Q = \frac{\pi R^4 \Delta P}{8 \eta L}$$

ΔP represents the pressure gradient between the two ends of a cylindrical pipe. In the case of blood vessels in the eye, ΔP can be taken to represent ocular perfusion pressure; L is the length of the blood vessel.

Autoregulation of blood flow is defined as the intrinsic ability of an organ to maintain constant blood flow despite changes in perfusion pressure. When there is a change in OPP (ΔP), the retina tends to maintain its blood flow (Q) by adjusting other parameters in Equation 4. Any modification in blood vessel length (L) or blood viscosity (η) is negligible during such an event. Therefore, blood vessel diameter (R) has a major role in determining both the vessel resistance and autoregulatory capacity of blood flow. It is worth noting that Equation 4, in its strictest sense, only applies to fluid flowing through a rigid pipe, where none of the parameters interacts with the others. However, in living tissue, Equation 4 is complicated by other factors. In particular, a change in vessels caliber (R) will interfere with local blood pressure (ΔP). For example, the vasodilatory calcium channel blockers can increase blood vessel diameter (R) and thereby improve blood flow, even though the drug has a systemic blood pressure lowering effect.[43] Likewise, despite an increase in systemic blood pressure, L-nitro-arginine methyl ester (L-NAME) causes a reduction in ophthalmic blood flow in rabbits due to its strong local vasoconstriction effect.[44,45]

This is not surprising given the exponent '4' of parameter R in Equation 4, which means that the vasomotor response has a much greater capacity to regulate local blood flow, compared with a proportional change in any other parameter. Not surprisingly, extensive clinical and experimental evidence has shown that autoregulation acts via changes in vessel diameter. By photographing retinal blood vessels, a compensatory vasodilation of blood vessels has been demonstrated during IOP elevation in glaucoma patients. Furthermore, the degree of change in diameter was associated with the level of IOP elevation.[26,27] This vasomotor response to IOP challenge was less effective in patients with glaucoma than in healthy subjects. Mice genetically deficient in endothelial nitric oxide synthase (eNOS; a potent vasoactive peptide), show impaired blood flow autoregulation and increased vulnerability to ischaemic insult such as cerebral infarction, when compared with the wild-type mice.[46]

More direct evidence of ocular autoregulation comes from measurement of blood flow during OPP variation. When autoregulation is removed in cats undergoing euthanasia, ocular blood flow measured with laser-Doppler flowmetry drops linearly with OPP reduction.[47] On the other hand ocular blood flow in normal human subjects is well regulated over a wide range of changes in OPP induced by IOP[48] or blood pressure elevation.[49] Although measured in different species, the sharp contrast between Figures 4A and 4B illustrates the capacity of the ONH to maintain a relatively constant blood flow in response to blood pressure and IOP challenge.

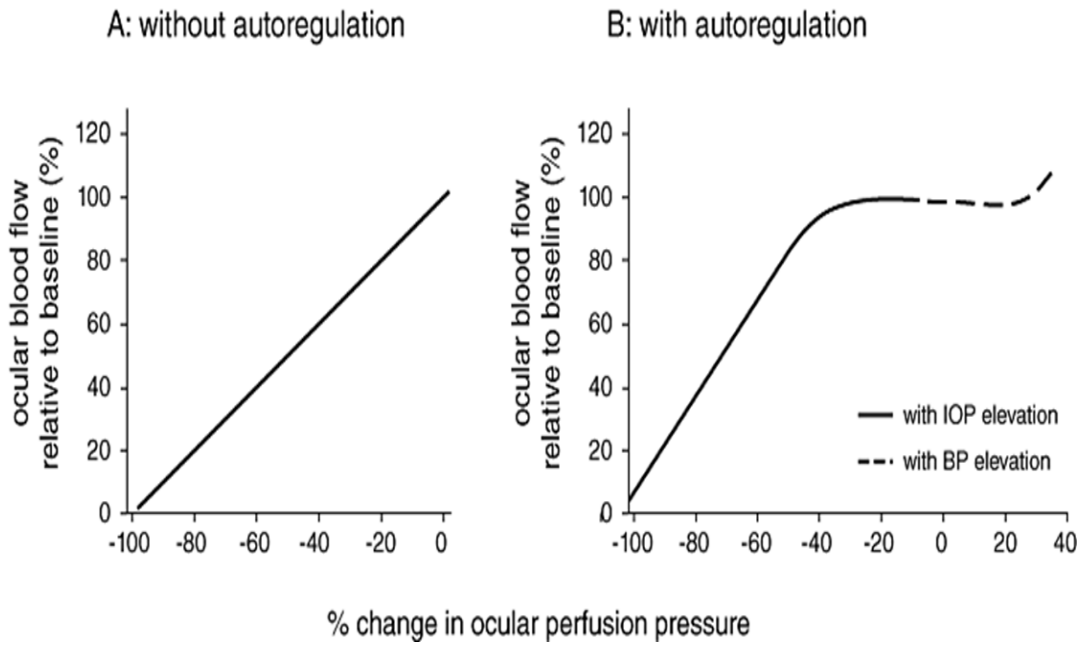


Figure5.

Ocular blood flow measured by laser Doppler flowmetry across a range of ocular perfusion pressures (induced by intraocular pressure or blood pressure manipulation), summarized from a number of studies.[47,49,50]

A: There is a linear relationship between ocular blood flow and ocular perfusion pressure during euthanasia in cats, which lack autoregulation capacity.[47]

B: Ocular blood flow in healthy human subjects remains stable over a range of ocular perfusion pressure levels. Ocular perfusion pressure changes are induced either by blood pressure elevation (dashed curve) 130 or by IOP elevation (solid curve).[50]

RANGE OF AUTOREGULATION

While the existence of autoregulation is well established, a question of interest is ‘to what extent can autoregulation sustain function during OPP challenge?’ In normal human subjects, autoregulation at the optic nerve is effective for IOP below 27–30 mmHg. This represents an OPP reduction of some 40–50 per cent from baseline (Figure 4B) for a mean arterial pressure of 100 mmHg (2/3*100–IOP).[51] At

the other extreme, blood flow remains unchanged until the OPP is elevated by more than 30 ± 8 per cent above baseline (Figure 4B), which in human studies is usually achieved by blood pressure elevation via isometric exercise.[49] Other studies have reported that this upper limit of autoregulation can be as high as 34–60 per cent above the baseline ocular perfusion pressure.[28,52-54]

The autoregulation curve represents the data collected from two different studies, one where OPP was lowered by IOP elevation[55] and the other where OPP was increased by raising blood pressure.[49] It is worth noting that combining the two sets of data assumes that IOP increase and blood pressure lowering modify the autoregulation curve in the same manner. This assumption has yet to be proven. In fact, at least one study showed that blood flow regulation in the choroidal circulation was more effective with blood pressure reduction rather than IOP elevation.[55] Chemtob and colleagues[56,57] characterized the blood flow across a wide range of blood pressure by infusing radioactive microspheres into the retina, choroid and brain of newborn piglets. Although the absolute values of blood flow vary across different tissues, the profiles of the flow–pressure relationship bare a striking resemblance. In particular, a blood flow plateau exists for blood pressures between 50–100 mmHg, consistent with the presence of strong autoregulation in the retina, choroid and brain.

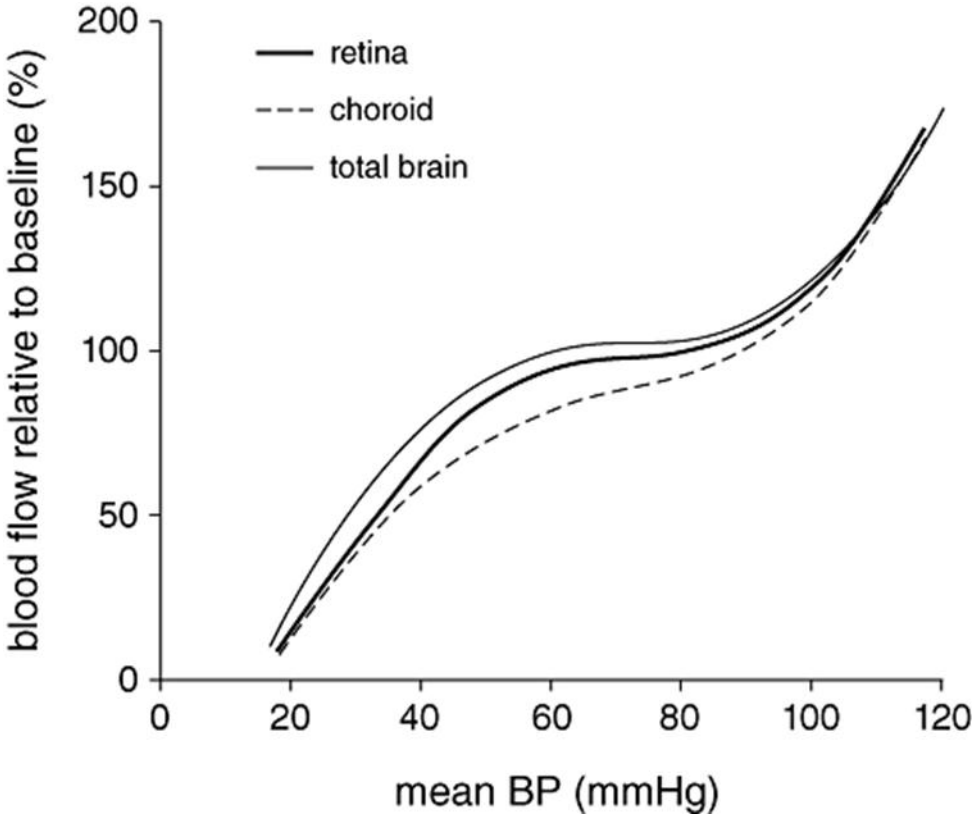


Figure 6

Range of blood flow autoregulation in the retina, choroid137 and brain138 in newborn piglets. Blood flow is measured with radioactive microspheres during blood pressure variation induced by aortic occlusion.

The changes to the autoregulation curve in systemic hypertension, ageing and glaucoma are yet to be fully understood. An age- or disease-related shift in the curve to higher blood pressures, a steeper curve or a narrower autoregulatory range may make neurons more susceptible to reductions in OPP.

MECHANISMS OF AUTOREGULATION

The mechanisms underlying vascular autoregulation are still under investigation. Our current understanding of ocular blood flow autoregulation is based on investigations in the cerebral and systemic circulations. It is likely that ocular autoregulation involves both myogenic and metabolic mechanisms, through the action of endothelium-derived vasoactive factors that modulate smooth muscle tone and pericytes. In the eye, the role of hormonal components (epinephrine and norepinephrine) in autoregulation is relatively minor as there is no autonomic innervation of retinal and ONH blood vessels; however, it is worth noting that the choroidal circulation has strong autonomic input.[58,59] In addition, alpha- and beta-adrenergic as well as cholinergic receptors are present on ocular blood vessels.[60] Thus, higher systemic concentrations of catecholamines, as seen in hypertension or higher local concentration due to the use of anti-glaucoma agents (beta-blocker and alpha agonists), may impact local blood flow.[61]

In myogenic autoregulation, it is thought that changes in perfusion pressure are sensed by mechano-transducers located on the endothelial cells of the blood vessels, which in turn respond to the pressure challenge by releasing vasoactive mediators. By patch-clamping the aortic endothelial cell membrane, Lansman and colleagues[62] demonstrated the presence of stretch-activated ion channels, which respond to mechanical pressure, thus forming a set of mechano-transducers. These channels are permeable to Ca2+. One consequence of Ca2+ influx is that this cation acts as a second messenger, which mediates the synthesis and release of endothelium-derived vasoactive factors. In isolated bovine eyes, a graded contraction of retinal arteries occurs when intraluminal pressure is elevated from 10 to 60 mmHg, which

acts to maintain vessel diameter. At pressures above 60 mmHg the vessel diameter increases linearly with pressure, signalling the failure of this myogenic mechanism.[63] The suppression of this autoregulatory response by the calcium channel blocker nifedipine shows that it is mediated by extracellular calcium.[63]

Blood flow is also closely coupled with tissue metabolic activity. Evidence for metabolic autoregulation comes from studies showing that blood flow in the eye can be modified in the absence of pressure change. Specifically, retinal vessels constrict in response to hyperoxia (increased PaO2),10,[64-66] whereas vasodilation and increased retinal blood flow can be induced by either hypoxia (decreased PaO2) or hypercapnia (accumulation of CO2) in order to meet the needs of neuronal tissues.[67,68] Likewise, an increase in retinal metabolism induced by flickering light also leads to compensatory vasodilation.[69,70] These findings strongly suggest that a metabolic-dependent mechanism is involved in blood flow autoregulation in the retina and optic nerve.

Both myogenic and metabolic mechanisms of autoregulation are achieved via the release of contracting and relaxing substances from the vascular endothelium, glial cells or neurons, with the latter two cell types mainly involved in the metabolic pathway of autoregulation. Is a schematic of the endothelial-dependent mediators, among which nitric oxide (NO; vasodilation) and endothelin-1 (ET-1; vasoconstriction) are probably the most important factors and have opposing actions in ocular blood flow autoregulation.

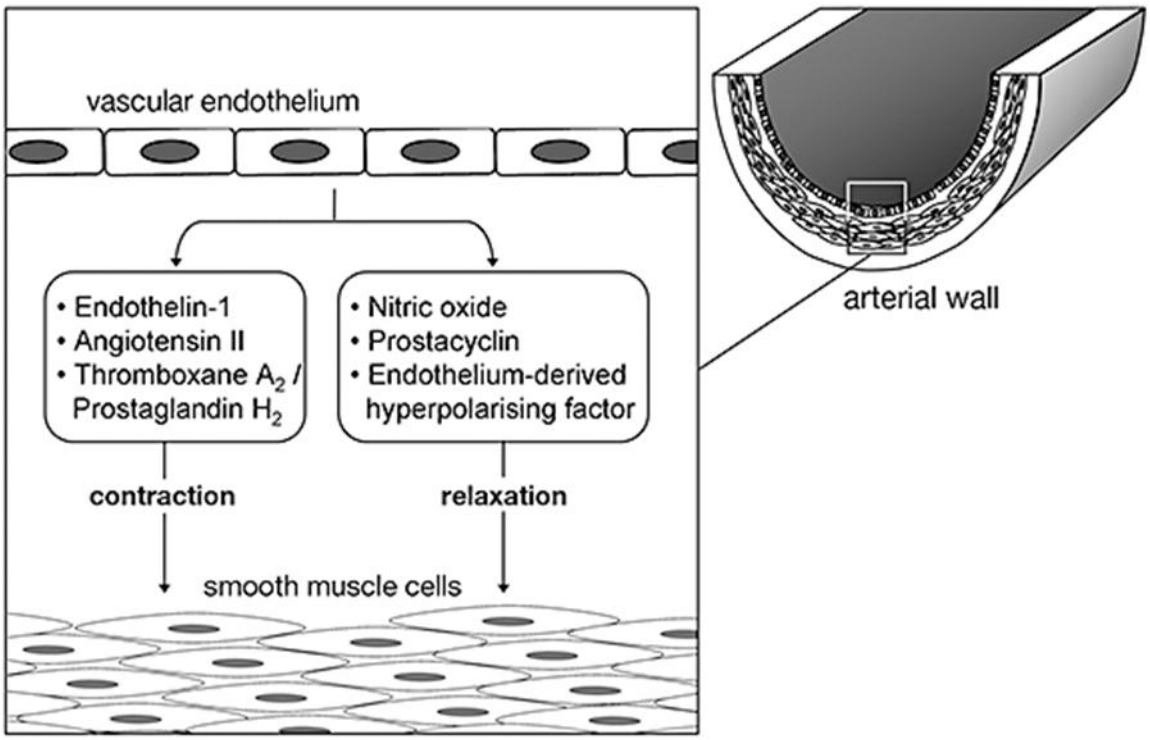


Figure 7. Schematic of endothelium-derived vasoactive factors that are involved in autoregulation of ocular blood flow.

In vascular endothelial cells, L-arginine is converted to NO via the enzyme NO synthase (NOS). On release from endothelial cells, NO exerts a potent vasodilatory effect via the activation of guanylyl cyclase in the cyclic guanosine monophosphate (cGMP) pathway, thereby reducing blood flow.[71] Among the three isoforms of NOS, the endothelial NOS (eNOS or NOS-1) and neuronal NOS (nNOS or NOS-3) are constitutively expressed and are important in sustaining blood flow with normal variations in IOP and blood pressure. The inducible NOS (iNOS or NOS-2) is expressed under pathological conditions such as low OPP. The NO produced with iNOS can be excessive, leading to vascular dysregulation and cellular apoptosis. In human donor eyes, iNOS was found only in glaucomatous laminar cribrosa but not

in normal tissue.153 Exposure to excess levels of NO produced by iNOSat the ONH has been implicated in the pathogenesis of glaucoma.[72]

Studies in both ocular[73] and cerebral tissues[74] demonstrate the existence of a basal release of nitric oxide, which means that there is active vasodilation under physiological conditions. This basal level of vasodilation allows the vascular tone to be either increased (constricted) or decreased quickly during changes in the perfusion pressure. For example, when NO release was suppressed by systemic infusion of a NOS inhibitor (L-NAME), choroidal blood flow reduced, leading to a downward shift of the autoregulation curve.[44] This shows that basal- and pressure-induced NO release are both important in autoregulation.

The vasodilatory effect of NO is counteracted by vasoconstricting factors such as ET-1, which binds to the ETA receptor on the membrane of vascular smooth muscle cells. Altered ET-1 vasoreactivity has been implicated in the pathogenesis of vascular dysregulation and systemic hypertension,[75] potentially increasing vulnerability to ischaemic insult. More importantly, clinical and experimental evidence exists to support the role of ET-1 in the development of normal tension glaucoma. Higher plasma levels of ET-1 have been found in patients with normal tension glaucoma than in healthy subjects,[76] implying a generalised vasoconstriction and reduction in blood flow. In rabbits, intravitreal injection of ET-1 causes blood flow reduction in the ONH.[76] In another study, although plasma ET-1 levels were similar in glaucoma patients and normal controls, ET-1 elevation was greater in those with glaucoma following cold provocation.[77] Additionally, Henry and colleagues[78] showed that the vasodilation induced by an ETA receptor antagonist (BQ123; intra-

arterial infusion) was reduced in patients with normal tension glaucoma when compared with age-matched controls. Taken together, these studies suggest a link between systemic hypertension, vascular dysregulation and glaucoma.

VASCULAR DYSREGULATION AND GLAUCOMA

Abnormalities in autoregulation have been divided into primary and secondary vascular dysregulation (without or with underlying disease, respectively). Flammer and Mozaffareih[79] and Moore and associates[80] have reviewed how abnormalities of autoregulation might increase the risk of glaucoma. In this section, we focus on the role of systemic hypertension and its implications for secondary vascular dysregulation and glaucoma.

As described above (Table 1 and Figure 2), several studies have found that paradoxically, chronic hypertension may increase the risk of glaucoma, an observation that does not explain the protection that should be afforded by an improved OPP. The presence of secondary vascular dysregulation could increase the vulnerability of the optic nerve to small changes in IOP, blood pressure and metabolic needs. One way that this may occur is if vascular dysregulation reduces the effectiveness of autoregulation. Thus, the same change in OPP can cause a greater reduction in blood flow. Autoregulation confers a wide 'normal range' and thus an increased capacity to cope with changes in the OPP. On the other hand, the absence of autoregulation means that smaller changes in the OPP are needed to push blood flow outside of the 'normal range'.

Systemic hypertension[81-83] has been shown to alter autoregulation in systemic circulation, via endothelial cell damage/dysfunction and abnormal release of

vasoactive substances; however, the influence of hypertension on ocular blood flow autoregulation is difficult to assess in epidemiological studies, as few studies have measured blood flow over an adequately wide ocular perfusion pressure range. The influence of hypertension has been considered in laboratory studies of cerebral but not of ocular blood flow. In particular, Harper and Bohlen[84] showed that the autoregulatory capacity of cerebral blood flow in spontaneously hypertensive rats is rightward shifted to higher pressure (Figure 8), consistent with an effort to compensate for the potential hyperaemia during increased cerebral perfusion pressure. This observation has also been reported in baboons[85,86] and humans.[87]

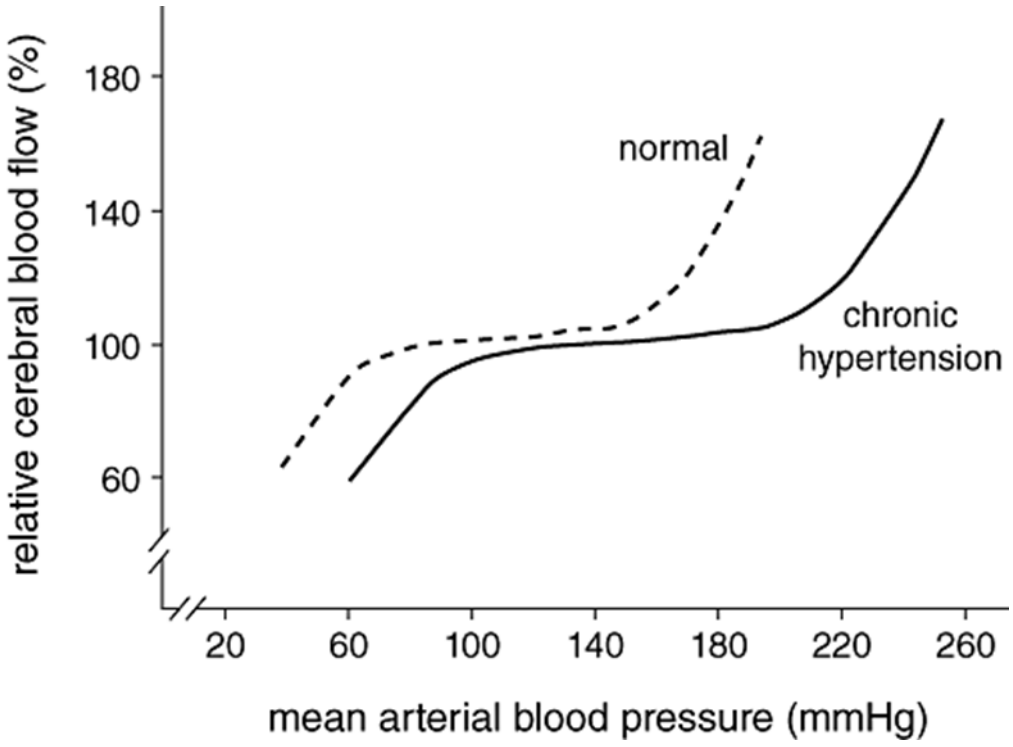


Figure 8 :

Effect of chronic hypertension on cerebral blood flow is associated with a rightward shift in blood pressure range over which autoregulation occurs[84-87]

If the above findings in brain also apply to ocular blood flow, then the lower limit of the 'normal range' would be reset to a higher OPP in chronic hypertension. This 'on face' value means that blood flow will be reduced below the 'normal range' (grey area) at a higher OPP in those with hypertension. When the pre-treatment habitual blood pressure (unfilled circles) is taken into account, the actual OPP change needed to reduce blood flow below the 'normal range' is actually the same. Thus, the data derived from the cerebral circulation do not account for an increased risk of optic nerve injury with chronic hypertension. Some other mechanism must be at play. One possibility is that hypertensive treatment dissociates the post-treatment blood pressure (filled circle, Figure 9B) from the 'set point' (unfilled circle, Figure 9B) of the autoregulation range. That is, the middle of the autoregulation range is set to the higher pre-treatment blood pressure (unfilled circle), creating a mismatch with the lower post-treatment blood pressure (filled circle). What this would mean is that the medically treated (post-treatment) hypertensive patient is now closer to the lower limit of their 'normal range'. Thus, a smaller reduction in the OPP would be needed to yield a blood flow that cannot sustain normal function.

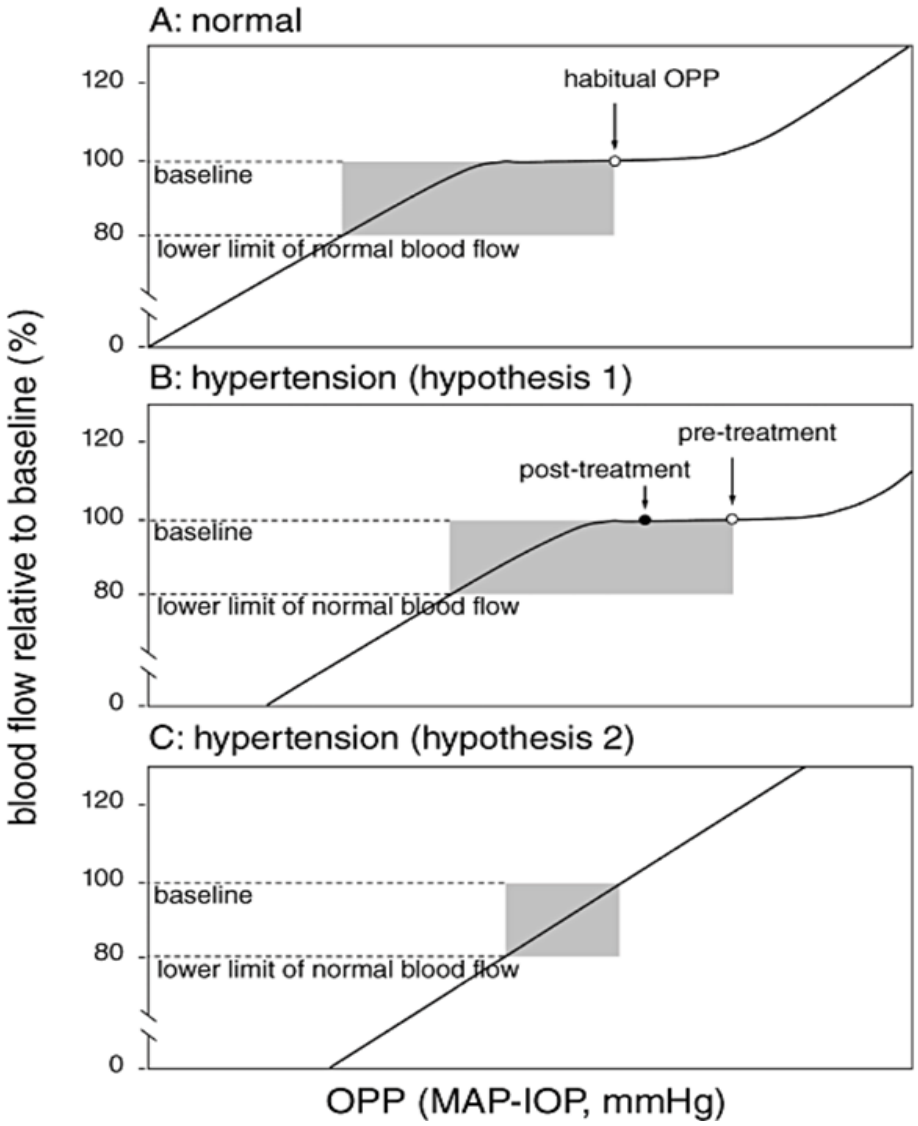


Figure 9.

Potential effects of chronic hypertension on ocular blood flow autoregulation.

A: Autoregulation in normal subjects.

B: (Hypothesis 1) Hypertension shifts the autoregulation curve to higher ocular perfusion pressure (OPP). Patients who have their blood pressure lowered with medications are closer to the lower limit of their normal range (grey area).

C: (Hypothesis 2) Hypertension narrows or removes the autoregulation plateau, increasing the risk for blood flow deficiency, with small reductions in ocular perfusion pressure. These people have the least capacity to regulate blood flow for a given ocular perfusion pressure change, thereby compromising neural perfusion.

A second possibility is that chronic hypertension affects ocular autoregulation differently from cerebral blood flow, to produce a narrower autoregulatory plateau. Figure 9C shows one extreme where the plateau has been removed, which means that smaller changes in the OPP would be needed to reduce blood flow below the 'normal range'. A narrower autoregulatory range might arise due to atherosclerosis, such that blood vessels are less able to change their calibre in response to stimulation by vasoactive factors. However, neither epidemiological studies nor animal experiments[40,41] have identified atherosclerosis as an important risk factor for open-angle glaucoma. An alternative may be aberrant production of vasoactive peptides (Figure 6) involved in autoregulation. Other contributing factors may also play a role in linking glaucoma and impaired autoregulation in hypertension. For example, it has been well established that patients with hypertension also demonstrate increased blood viscosity,[88-91] which impacts negatively on blood flow (Equation 4).

FUTURE DIRECTIONS

Although it is clear that blood pressure plays a role in the pathogenesis of glaucoma, the underlying aetiology and mechanisms are not fully understood. A better understanding of this potential link requires clinical studies of glaucoma that take into account the mode and aggressiveness of treatment for systemic hypertension. The Thessaloniki Eye Study has shown that zealous treatment of systemic hypertension in patients without glaucoma is associated with increased cup-to-disk ratio. Further studies should extend this link to patients with concurrent hypertension and glaucoma. Specifically, the aggressiveness of anti-hypertensive treatments may correlate with the progression of glaucoma. If this were the case, it would reinforce the role of OPP as an important risk factor of glaucoma, as well as provide guidance for clinicians in treating these conditions. In terms of laboratory studies, a more

comprehensive understanding of the cellular processes and the manner by which they interact with vasoactive peptides to drive the autoregulation of ocular blood flow represents a formidable challenge but one that must be undertaken. Understanding these pathways may eventually lead to the discovery of therapeutic intervention.

During a challenge to the OPP, autoregulation acts as a compensatory mechanism not only to maintain a constant blood flow (vascular reserve), but also in a broader sense to preserve neuronal function even when blood flow is compromised (functional reserve). As shown schematically in Figure 10, the vascular reserve is driven by a compensatory vasodilation. When vasodilation reaches its maximal capacity and the OPP is further reduced, blood flow will decline proportionately with the OPP. At moderate to low OPP, there is an increase in tissue oxygen extraction from the residual arterial blood, which may be adequate to maintain oxygen metabolism for a further period of time. This hypothesis is supported by studies in the brain,[92-95] which have frequently found that increased oxygen extraction during ischaemia and/or anemia allows oxygen metabolism and neural function to be maintained. In the brain, this functional reserve has been shown to depend largely on intact mitochondrial function during the early stage of ischaemia.[96-98] When ischaemia becomes severe enough to impair mitochondrial function, then irreversible neuronal damage (infarction) ensues. These findings derived from the brain should prompt research to further define the thresholds for both vascular and functional reserves in the eye. To test this hypothesis, it is essential to measure both ocular blood flow and ganglion cell function simultaneously over a gradient of OPP variation. Furthermore, it will be of interest to see if such a 'safety buffer' is reduced with older age or in patients with atherosclerosis or diabetes.

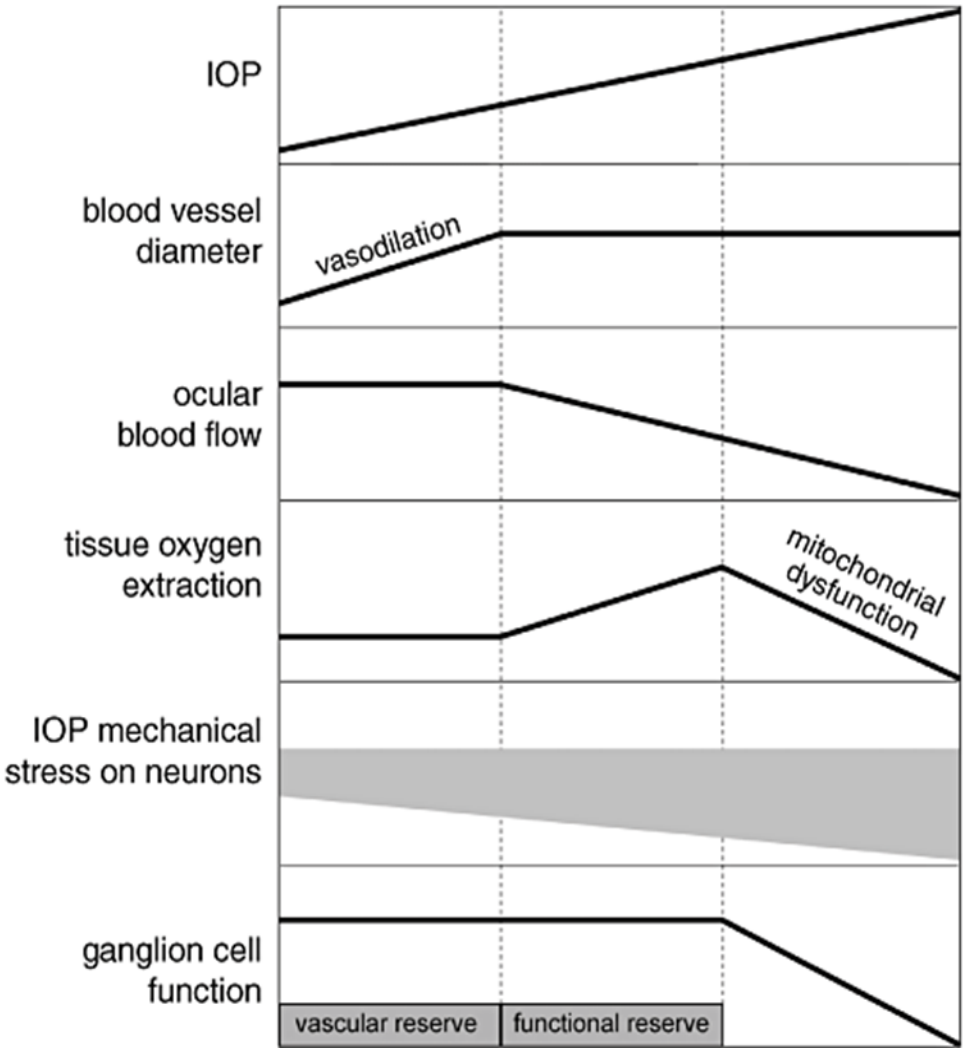


Figure 10.

Homeostatic responses to falling ocular perfusion pressure (OPP). Vascular reserve (blood flow autoregulation) is driven by vasodilation, which modulates ocular blood flow. Functional reserve of the retina is the result of increased oxygen extraction from residual blood flow that depends on the integrity of mitochondria. If ocular perfusion pressure challenge is induced by IOP elevation, the overall effect of blood flow, tissue oxygen extraction and IOP mechanical stress determines retinal function. Modified from Allen and colleagues.[99,100]

In summary, it is clear that IOP alone does not determine the risk of glaucoma development. While epidemiological studies have shown that there is a host of

potential risk factors along with IOP, how these risk factors interact with IOP to modify glaucomatous neuropathy remains unclear. Although certainly not the only risk factor, there is adequate evidence to show that abnormalities in blood pressure and blood flow play a central role in glaucoma pathogenesis. In particular, low blood pressure predisposes to low OPP, which increases the likelihood of hypoxic or ischaemic stress. This is pertinent in that nocturnal IOP elevations and blood pressure dips can act synergistically to produce substantial OPP troughs over a diurnal cycle, which have been implicated in the development of normal tension glaucoma. An epidemiological study has shown that over-treatment of hypertension increases the risk of glaucoma.99 Although the role of low blood pressure in glaucoma is clearly detrimental, the effect of high blood pressure is more complex. In the short term, high blood pressure can improve the OPP and provide some protection against IOP-induced ischaemia.[34-38] In chronic presentations, the influence of hypertension on glaucoma remains controversial among epidemiological studies and is not well established in animal experiments. The most recent evidence from an epidemiological trial106 showed that hypertension predisposes to the development of glaucoma. This is in line with the widespread vascular damage frequently associated with chronic hypertension, which would act to impair ocular blood flow and autoregulation (secondary vascular dysregulation). The presence of impaired autoregulation means that the eye is less able to cope with episodes of low OPP and over time a cumulative effect could produce ganglion cell loss. In an attempt to adapt to chronic high blood pressure, a rightward shift of the cerebral blood flow autoregulatory curve has been found in patients with hypertension168 and animal models.[85,86] If this can be extrapolated to the eye, it provides an explanation of why patients with hypertension are more vulnerable to low OPP. From a clinical point of view, it is important to

consider not only the IOP but also the blood pressure status in patients with glaucoma. Specifically, it is important to avoid under- or over-treatment of chronic hypertension to achieve an optimal OPP range.

SYSTEMIC BLOOD PRESSURE AND INTRAOCULAR PRESSURE

ASSOCIATION OF SYSTOLIC BLOOD PRESSURE (SBP) AND IOP

SBP was positively associated with IOP in the Barbados Eye Study, which excluded subjects with OAG from analysis.[8] The 4-year and 9-year follow-up data from the Barbados Incidence Study of Eye Diseases I and II (BISED I and BISED II), which examined the surviving cohort of the Barbados Eye Study, demonstrated a trend of increase in IOP with increasing SBP.[101,102] Similarly positive correlation between SBP and IOP was evident in the Baltimore Longitudinal Study of Aging (BLSA) and 2 large Japanese studies that included normal subjects.[103-105] In addition to a positive correlation in normal individuals, several studies have consistently demonstrated a positive correlation between BP and IOP, in populations that include patients with OAG. In general, each 10 mm Hg increment in SBP at baseline leads to mean 0.23-0.31 mm Hg rise in IOP.[9,10,105-107] Similarly the Beaver Dam Study shows that an increase of SBP by ≥ 10 mm Hg from baseline leads to 0.44 mm Hg rise in IOP whereas a decrease of SBP by ≤ 10 mm Hg from baseline leads to 0.59 mm Hg decrease in IOP, over a 5-year interval.[108] The positive correlation between SBP and IOP is observed across all races in both healthy individuals and OAG patients. The Rotterdam Study, the Egna-Neumarkt Study and the Beaver Dam Study were each conducted on populations predominantly of European descent. However, the Barbados Eye Study that had predominantly African ancestry participants, the Baltimore Eye Survey in which almost one half of the patients were of African

ancestry, and the Tanjong Pagar Study that was conducted on entirely Asian population, all confirm a strong correlation between SBP and IOP, as well.[9,105,107] A recent report from Los Angeles Latino Eye Study (LALES) confirmed higher systolic blood pressure as one of the two major factor associated with elevated IOP in the Latino population (patients with glaucoma were excluded), other being higher CCT.[109] A 20 mm Hg higher SBP was associated with 0.7 mm Hg higher IOP. Further, higher mean blood pressure was significantly correlated with higher IOP in a study of 2597 Japanese adults without glaucoma. Each mm Hg increase in BP was associated with increase in IOP by 0.022 mm Hg.[110]

ASSOCIATION OF DIASTOLIC BLOOD PRESSURE (DBP) AND IOP

The evidence for a positive relationship between DBP and IOP is contradictory. DBP was associated with a marginally significant rise of 0.15 mm Hg in IOP over 9 years follow-up in BISED II.[102] In LALES higher DBP was associated with elevated IOP, however the association was not as strong as between SBP and elevated IOP.15 DBP contributed to 2% of IOP variance compared to 4% contribution by SBP, on univariate analysis. On multivariate analysis the correlation between SBP and IOP continued to be strong whereas the correlation between DBP and IOP weakened to 0.09% contribution of DBP to IOP variance. In contrast; BLSA and the Japanese studies demonstrated no apparent correlation between DBP and IOP.Similar to SBP, DBP is positively correlated with IOP in patients with OAG; each 10 mm Hg increment in DBP at baseline leads to 0.19-0.6 mm Hg rise in IOP[9,10,105,111] Over a 5-year interval, there was a mean increase of 0.06 mm Hg in IOP for subjects with DBP within 10 mm Hg of their baseline DBP compared to an increase of 0.85 mm Hg for those whose DBP increased by ≥ 10 mm Hg and a decrease of 0.79 mm Hg in IOP for those whose DBP decreased by ≥ 10 mm Hg.[107] There is no satisfactory explanation

for the difference in the results between patients with glaucoma and normal subjects. This difference could be due to the gender and racial differences amongst studies. The pathopysiologic basis for the relationship between BP and IOP is not known. It has been proposed that the positive correlation between SBP and IOP is related to increased BP leading to increased aqueous humor ultrafiltration by means of increased ciliary artery pressure, and thus an increase of IOP. Conversely roles for common physiologic factors such as generalized sympathetic tone or serum corticosteroids also have been proposed.[111]

Klein BEK et al in 2005[107] concluded that Intraocular pressures were significantly correlated with systolic and diastolic blood pressures at both baseline and follow up. There were significant direct correlations between changes in systemic blood pressures and changes in intraocular pressure. There was a 0.21 (95% CI: 0.16 to0.27) mm Hg increase in IOP for a 10 mm Hg increase in systolic and 0.43 (0.35 to 0.52) mm Hg increase in IOP for a 10 mm Hg increase in diastolic blood pressure.

Deokule S in 2009[112] concluded that there is a strong positive association between SBP and IOP, and a weaker association between DBP and IOP. This association is present across the racial lines. However, the actual change in IOP with increasing BP is relatively small. The cross-sectional studies suggest a marginal increase in OAG prevalence with increasing BP.

Kisan R et al in 2012[113] concluded that persons with hypertension and advancing age need to be monitored for high IOP. In persons with an elevated IOP, periodic BP monitoring may be indicated. Hence, a population based screening for an elevated IOP and its control could reduce the number of people who are at the greatest

risk of glaucoma, which is the second commonest cause for blindness and visual impairment in India and also worldwide.

Sajja S et al in 2013[114] concluded that elevated IOP is the major risk factor for developing glaucoma or glaucomatous optic neuropathy. From this study it was evident that IOP increases as systemic BP increase & advancing age was associated with elevated IOP. Persons with hypertension and advancing age should be monitored for high IOP. In persons with elevated IOP, periodic BP monitoring may be indicated. A population based screening for elevated IOP could reduce the number of people who were at greater risk of developing glaucoma, which is the second commonest cause for blindness and visual impairment in India.

Yoshida M et al in 2013[115] concluded that several previous studies of Europeans and Americans have reported an increase in IOP after the age of 40 years and a decrease in IOP among elderly populations, although IOP was also found to decrease with age in Asian populations. In the present study, a positive association with IOP was observed for SBP, DBP, and BMI in both men and women. Many such studies have observed a positive association of IOP with SBP and BMI and others have found a positive association between IOP and both SBP and DBP. Elevated SBP might elevate IOP by increasing ultrafiltration of the aqueous humour through the elevation of ciliary artery pressure.

Grippo TM et al in 2013[116] did a study to characterize the 24-hour pattern of intraocular pressure (IOP) in untreated ocular hypertensive (OHTN) patients. The authors found mean sitting and supine IOPs were significantly higher in the OHTN group than in the healthy control but not the glaucoma group. Similar to the glaucoma group, the OHTN group demonstrated significant differences from healthy controls in

diurnal IOP variation and IOP changes upon awakening in habitual and supine positions. The 24-hour IOP curve acrophases and amplitudes for OHTNs were closer to those of the glaucoma than the healthy control group in the habitual position. Thirty-three percent of OHTNs developed glaucoma during a mean follow-up period of 4.3 ± 3.8 years. Similar to findings in the glaucoma group, habitual IOP curve phase delay, habitual IOP variation, diurnal-to-nocturnal IOP changes, and IOP changes upon awakening of the converters were significantly different from those in healthy controls. There were no differences between nonconverters and other groups. The authors concluded that Baseline 24-hour IOP pattern in OHTN patients is similar to that in glaucomatous patients. In contrast to nonconverters, OHTN patients who converted to glaucoma are significantly different from healthy controls.

Khawaja AP et al in 2014[117] did a Population-based, cross-sectional study to determine the association between systemic medication use and intraocular pressure (IOP). The authors found Use of systemic β-blockers (−0.92 mmHg; 95% CI, −1.19, −0.65; P<0.001) and nitrates (−0.63 mmHg; 95% CI, −1.12, −0.14; P = 0.011) were independently associated with lower IOP. The observed associations between statin or aspirin use with IOP were no longer significant after adjustment for β-blocker use. The authors demonstrated that clinically significant differences in IOP among participants using systemic β-blockers or nitrates. Lower IOP observed in participants using statins or aspirin was explained by concurrent systemic β-blocker use. The study findings may have implications for the management of glaucoma patients with comorbidity, and may provide insight into the pathophysiologic processes underlying IOP.

Irum S et al in 2015[118] concluded that their study had determined high readings of mean IOP with increasing grades of hypertension. Considering IOP as a traditional still in-use, one of the screening means of glaucoma detection, it would be necessary to implement further studies to determine the normal range and distribution of IOP in our population. There is also a need to educate doctors and all hypertensive patients about regular monitoring of IOP so that all cases of subclinical glaucoma and ocular hypertension can be picked up earlier.

Baisakhiya S et al in 2015[119] concluded that there exists a positive correlation between IOP and BP. High blood pressure is a risk factor for development of raised IOP which can lead to glaucoma. Periodic checking of IOP in hypertensive subjects and vice-versa is the key to the prevention of irreversible blindness due to glaucoma. Thus population based screening would reduce the burden of blindness due to glaucoma.

Monisha A et al in 2016[120] in a study examined 200 subjects aged above 40 years to find out the relationship between blood pressure and intraocular pressure. They were further divided into four groups (a), (b), (c) and (d) according to their blood pressure and each group consisted of 50 subjects. The group (a) constituted subjects having systolic BP 160 mmHg and diastolic >100 mmHg. The authors concluded that Elevated IOP is the major risk factor for developing glaucoma or glaucomatous optic neuropathy. Glaucoma is the second commonest cause of irreversible blindness and visual impairment. Glaucoma is a chronic disease with insidious onset. If it is diagnosed early and treated appropriately, its progression can be arrested. IOP which is a major risk factor for glaucoma is influenced by other systemic parameters. From this study it is evident that, • IOP increases as systemic

blood pressure increases. • Advancing age is associated with elevated intraocular pressure. • Females are at higher risk for developing elevated intraocular pressure. It can be concluded that, persons with hypertension and advancing age need to be monitored for high intraocular pressure and periodic BP monitoring may be indicated. Hence a population based screening for elevated IOP and its control could reduce the number of people at greatest risk of glaucoma, which is the second commonest cause for blindness and visual impairment in India and worldwide.

Budenza DL et al in 2017[121] in a Prospective cohort study determined the cumulative incidence of optic disc hemorrhage (ODH) before and after development of primary open-angle glaucoma (POAG); determine the prognostic significance of ODH for the development of POAG; and identify predictive factors for ODH. The authors found after a median follow-up of 13 years, 1 or more ODHs were detected in 179 eyes of 169 participants. The incidence of ODH was 0.5% per year during an average of 13 years before the development of POAG and 1.2% per year during an average of 6 years after the development of POAG. The cumulative incidence of POAG in eyes with ODH was 25.6% compared with 12.9% in eyes without ODH. The occurrence of an ODH increased the risk of developing POAG 2.6-fold in the multivariate analysis (95% confidence interval, 1.7–4.0; P < .0001). Randomization to the observation group, older age, thinner central corneal thickness, larger vertical cup-to-disc ratio, higher intraocular pressure, and self-reported black race were identified as risk factors for ODH. The authors concluded that ODH is an independent predictive factor for the development of POAG in patients with ocular hypertension (OHT) and the predictive factors for ODH are very similar to those for POAG in OHT patients.

IOP which is a major risk factor for glaucoma is influenced by other systemic parameters. From this study it is evident that, • IOP increases as systemic blood pressure increases. • Advancing age is associated with elevated intraocular pressure. • It can be concluded that, persons with hypertension and advancing age need to be monitored for high intraocular pressure and periodic BP monitoring may be indicated. Hence a population based screening for elevated IOP and its control could reduce the number of people at greatest risk of glaucoma, which is the second commonest cause for blindness and visual impairment in India and worldwide.

MATERIAL AND METHODS

A hospital based comparative study was conducted with 256 patients to compare Intraocular Pressure in systemic hypertensive patients and in non-hypertensive patients. The patients were divided into following groups:

Normotensive: 128 non-hypertensive patients were included in this group.

Hypertensive: 128 systemic hypertensive patients were included in this group.

Based on blood pressure, the patients were divided into the following groups according to JNC 7 classification i.e. Normotensive, Prehypertension, Stage 1 hypertension, Stage 2 hypertension.

STUDY DESIGN: A Comparative study.

SOURCE OF DATA:

The present study was conducted on patients attending outpatient department in Ophthalmology and Medicine Department in B.L.D.E.U'S Shri B.M.Patil Medical College, Hospital and Research Centre, Vijaypur during the period of Oct 2015 – April 2017.

Duration of study

October 2015 – April 2017

SAMPLE SIZE: 208 Patients

In the study of Deb A et al[122], it was found that the proportion of glaucoma suspect in systemic hypertensive patients was 13.7% and in normotensive 7%. Considering 95% confidence level & 80% in the power the sample size was minimum 208 as per below calculation:

$$n = \frac{(Z\alpha + Z\beta)^2 \times 2 \times p \times q}{d^2}$$

$Z\alpha$ = Z value at α level

$Z\beta$ = Z value at β level

p = proportion value of hypertensive

q = 1 – p

d = difference between two parameters

Hence, a minimum of 104 systemic hypertensive and 104 non-hypertensive cases were included in the study.

INCLUSION CRITERIA

1. A minimum 104 male & female subjects with normal BP above 30 years.
2. A minimum 104 male & female subjects with systemic hypertension above 30 years.

EXCLUSION CRITERIA

1. Subjects with previous ocular surgery and other ocular diseases.
2. Subjects below 30 year.
3. Subjects with diabetes mellitus.

METHODOLOGY

The study was carried out in the department of Ophthalmology of B.L.D.E.U'S Shri B.M.Patil Medical College, Hospital and Research Centre, Vijayapur. The study included a minimum 208 adult subjects divided into two groups 104 systemic hypertensive and 104 non hypertensive patients (> 30 years) randomly selected from the patients visiting Medicine and Ophthalmology OPD. On the basis of blood pressure the subjects were divided into these groups i.e. normotensive, prehypertension, stage 1 hypertension, stage 2 hypertension and isolated systolic hypertension. The mean IOP difference were compared amongst the these categories. The systolic and diastolic blood pressure in these categories were as follows:

Blood pressure classification according to JNC 7

	Systolic blood pressure (mmHg)	Diastolic blood Pressure (mmHg)
Normotensive	< 120	< 80
Pre hypertension	120 - 139	or 80 -89
Stage 1 hypertension	140 - 159	or 90 – 99
Stage 2 hypertension	>160	or > 100
Isolated systolic hypertension	> 140	and < 90

A detailed personal history, Family history of diabetes, hypertension and glaucoma were recorded. The blood pressure was recorded using mercury sphygmomanometer in supine position. The ocular examination included visual acuity, slit lamp examination, Gonioscopy (if required), fundus examination, intraocular pressure recording by Goldmann's applanation tonometer, Perimetry (if required).

Investigations or interventions required in this study were routine standardized procedures.

Detailed history was taken and clinical examination was done in all patients as per the study proforma. Patients' history included age, sex, history of acute or chronic ocular disease, ocular surgery in the past 6 months, history of previous eye trauma, history of undergoing any medical therapy for glaucoma, history of consumption of corticosteroids or beta-blockers through any route of administration, history of any systemic illness like diabetes mellitus or hypertension.

Clinical examination

a) Visual acuity

Distance (unaided, pinhole) and near visual acuity was recorded on Snellen's' optotype charts.

b) Slit lamp examination

Detailed adnexal (lids and lashes) and anterior segment (conjunctiva, cornea, sclera, AC, pupil, iris, lens) examination was carried out.

c) Intraocular pressure measurement.

(IOP) was measured with Goldmanns' Applanation Tonometer.

d) Fundus Examination

Dilated fundus examination was carried out by binocular indirect ophthalmoscopy and fundus biomicroscopy using +78 D or +90D lens or direct ophthalmoscopy.

The intraocular pressure was measured with the Goldmann's Applanation Tonometer (INAMI Applanation Tonometer.CAT NO L-5110A911).

Technique for Applanation Tonometry

- It was ensured that the tonometer was disinfected with isopropyl alcohol 70% (methylated spirit) or sodium hypochlorite 1%. The disinfectant was allowed to act for 1 min and then wiped dry with a clean swab (residue of the disinfectant may cause a caustic burn on the cornea).
- The graduation marked '0' on the measuring prism was aligned with the white marker point on the tonometer head.
- The calibrated dial of the tonometer was set at 10 mmHg.
- It was ensured that the patient was sitting comfortably on the slit lamp: at the right height, with chin on the rest and forehead against the headband.
- The magnification of the slit lamp was set at x10.
- Local anaesthetic drops (0.5% Proparacaine) were instilled in the patient's eyes were stained with fluorescein (Fluorescein sodium strip 1mg). A very small amount of fluorescein was needed.
- The slit beam of the slit lamp was aligned to shine into the tonometer head.
- The filters were arranged such that the cobalt blue filter was used to produce a blue beam.
- The beam of light was as wide as possible, and the light bright enough which helped visualize the fluorescein rings easier (with the slit diaphragm fully open).
- The patient was asked to look straight ahead, open both eyes wide, fix his or her gaze and keep perfectly still.
- If the patient had difficulty in opening the eye, then only the upper eyelid was gently held to keep it open taking care not to put any pressure on the eye.
- The blue light from the slit lamp was directed onto the prism head.

- The tonometer head was made perpendicular to the eye.
- The tonometer was moved forward slowly until the prism rested gently on the centre of the patient's cornea.
- With the other hand, the calibrated dial on the tonometer was turned clockwise or anticlockwise until the two fluorescein semi-circles in the prism head were seen to meet.
- (Note: the correct end point is when the inner edges of the two fluorescein semi-circle images just touch)
- The reading on the dial was recorded.
- The prism was withdrawn from the corneal surface.
- The procedure was repeated for the other eye.

STATISTICAL ANALYSIS

Quantitative data is presented with the help of Mean and Standard deviation. Comparison among the study groups is done with the help of unpaired t test as per results of normality test. Qualitative data is presented with the help of frequency and percentage table. Association among the study groups is assessed with the help of Fisher test, student 't' test and Chi-Square test. 'p' value less than 0.05 is taken as significant**.**

Pearson's chi-squared test

$$\mathrm{X}^2 = \sum_{i=1}^{n} \frac{(O_i - E_i)^2}{E_i}$$

Where X2 = Pearson's cumulative test statistic.

Oi = an observed frequency;

Ei = an expected frequency, asserted by the null hypothesis;

n = the number of cells in the table.

Results were graphically represented where deemed necessary.

Appropriate statistical software, including but not restricted to MS Excel, SPSS ver. 20 will be used for statistical analysis. Graphical representation will be done in MS Excel.

OBSERVATIONS AND RESULTS

A hospital based comparative study was conducted with 256 patients to compare Intraocular Pressure in systemic hypertensive patients and in non-hypertensive patients. The patients were divided into following groups:

Normotensive: 128 non-hypertensive patients were included in this group.

Hypertensive: 128 systemic hypertensive patients were included in this group.

Based on blood pressure, the patients were divided into the following groups according to JNC 7 classification i.e. Normotensive, Prehypertension, Stage 1 hypertension, Stage 2 hypertension.

EXCLUSION CRITERIA

1. Patients with previous ocular surgery and other ocular diseases.
2. Patients below 30 years.
3. Patients with diabetes mellitus.

Table 1: Distribution of Age between Hypertensive and Non-Hypertensive cases

Age (Yrs)	Non hypertensive		Hypertensive	
	N	%	N	%
30-35	32	25	32	25
36-40	32	25	32	25
41-45	32	25	32	25
46-50	32	25	32	25
Total	128	100	128	100

A total of 128 Non-Hypertensive patients and 128 Hypertensive patients were equally divided into four age-matched groups.

Graph 1: Distribution of Age between Hypertensive and Non-Hypertensive cases.

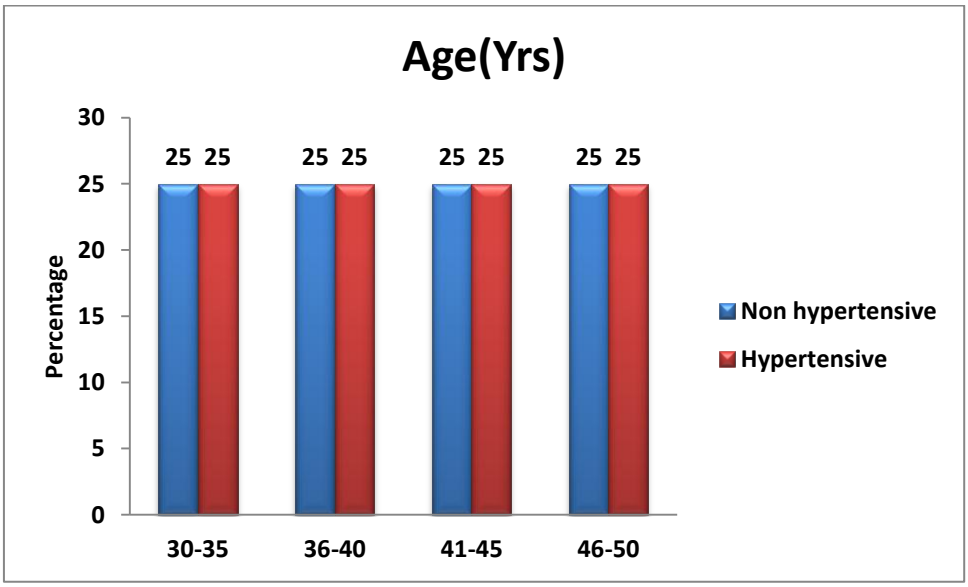


Table 2: Distribution of Sex between Hypertensive and Non-Hypertensive cases

Sex	Non hypertensive		Hypertensive	
	N	%	N	%
Male	64	50	64	50
Female	64	50	64	50
Total	128	100	128	100

There was equal distribution of male and female patients in all the four groups in Non-Hypertensive and Hypertensive patients**.**

Graph 2: Distribution of Sex between Hypertensive and Non-Hypertensive cases

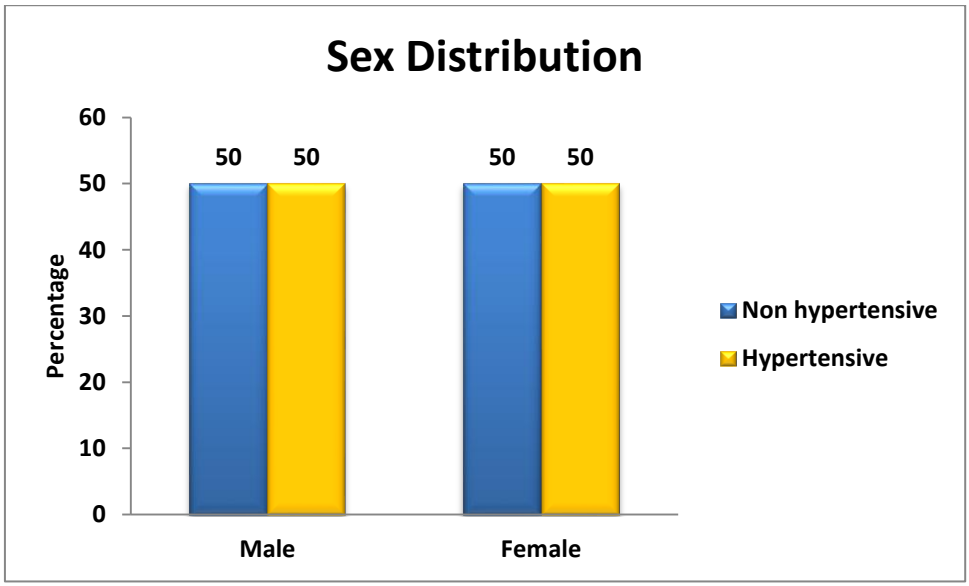


Table 3: Distribution of mean IOP according to sex

Eye	Male		Female		p value
	Mean	SD	Mean	SD	
Right eye	14.1	2.9	13.9	2.8	0.662
Left eye	14.4	3.0	13.8	2.8	0.139
Total	14.2	2.9	13.9	2.8	0.401

The mean IOP in Males was 14.1 mmhg in RE and 14.4 mmHg in LE whereas the mean IOP in Females was 13.9 mmHg in RE and 13.8mmHg. The total mean IOP in RE was 14.2 and 13.9 in LE which is not statistically significant.

Graph 3: Graph Showing Distribution of Mean IOP according to Sex

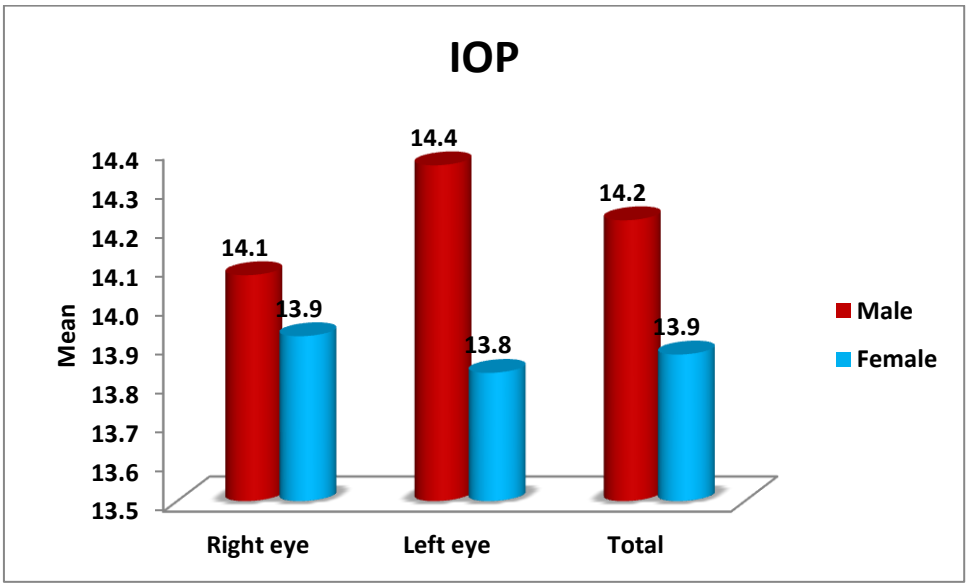


Table 4: Distribution of mean IOP according to Age

Age (Yrs)	IOP Right eye		IOP Left eye		IOP total	
	Mean	SD	Mean	SD	Mean	SD
30-35	14.13	3.02	14.06	3.06	14.09	3.04
36-40	13.75	2.61	14.06	2.78	13.91	2.69
41-45	13.91	2.82	14.03	2.91	13.97	2.86
46-50	14.22	3.01	14.22	2.79	14.22	2.90
p value	0.789		0.983		0.89	

The mean IOP in 30-35 yr group was 14.13 in RE and 14.06 in LE, mean in BE 14.09 while the mean IOP in 36-40 yr group was 13.75 in RE and 14.06 in LE, mean in BE 14.09. The mean IOP in 41-45 yr group was 13.91 in RE and 14.03 in LE, mean in BE 14.22 whereas the mean IOP in 46-50 yr group was 14.22 in RE, LE and BE. It was observed that IOP increased as age advances, which was statistically not significant.

Graph 4: Graph showing distribution of mean IOP according to age

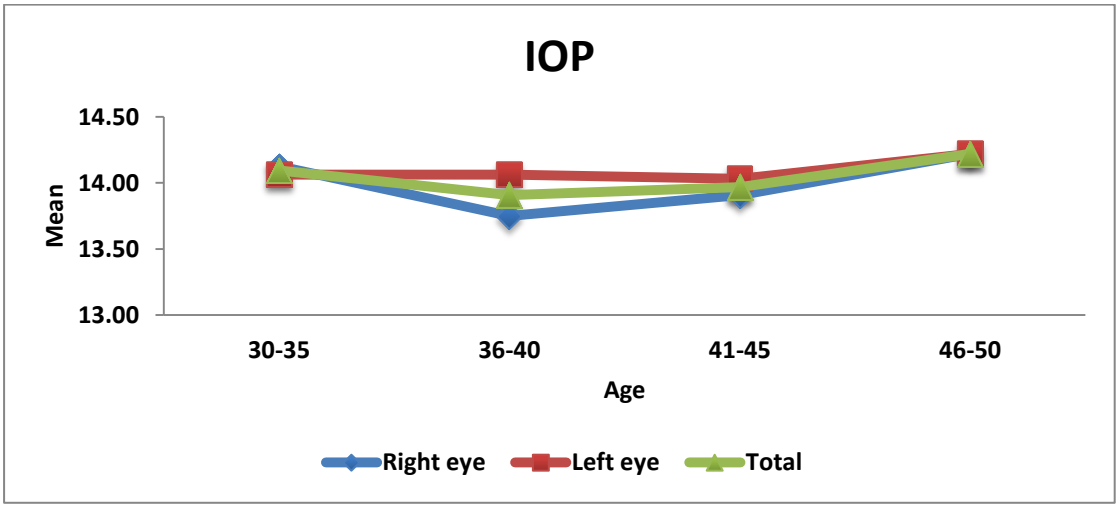


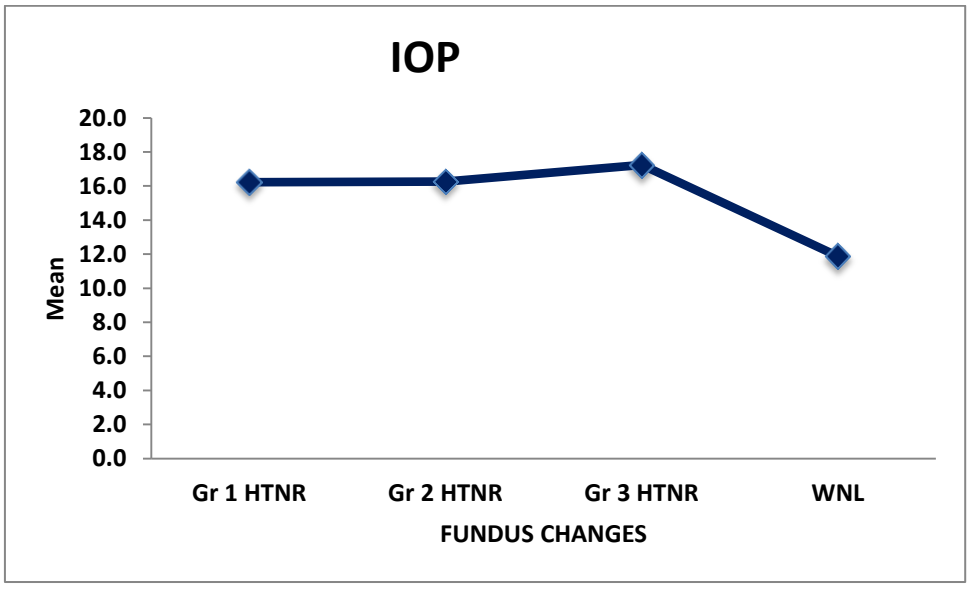
Table 5: Distribution of Mean IOP according to Fundus Changes

FUNDUS CHANGES	Number of eyes	IOP		p value
		Mean	SD	
Gr 1 HTNR	176	16.2	2.0	<0.001*
Gr 2 HTNR	54	16.3	2.3	
Gr 3 HTNR	26	17.2	2.6	
WNL	256	11.9	1.5	
Total	512	14.0	2.9	

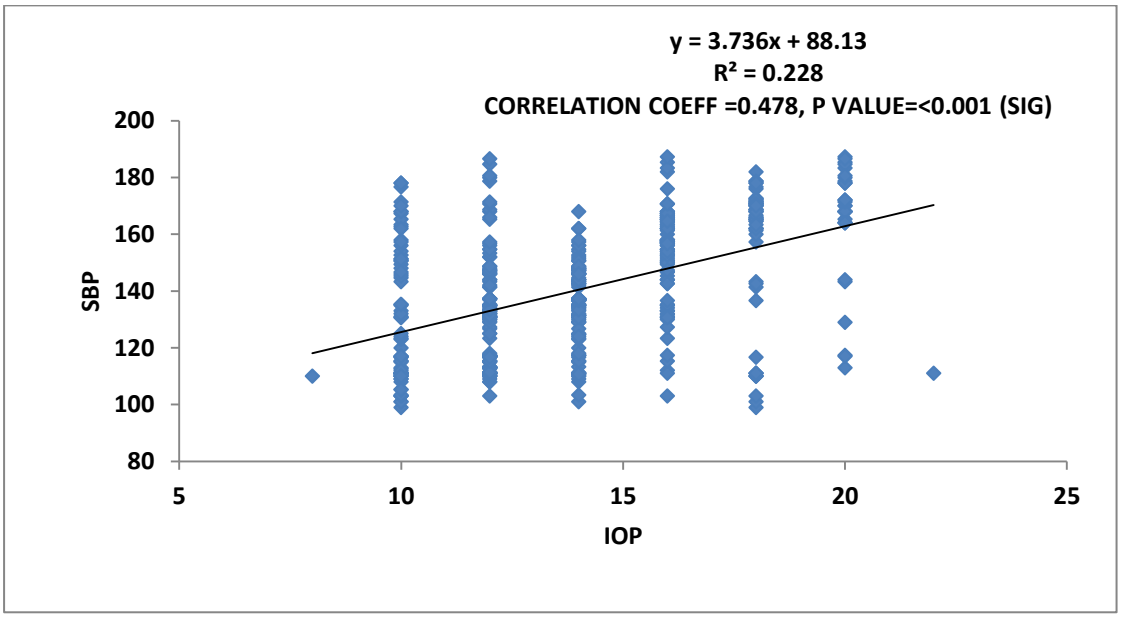
Note: * significant at 5% level of significance (p<0.05)

The mean IOP in Gr 1 HTNR was 16.2mmHg while the mean IOP in Gr 2 HTNR was 16.3mmHg. The mean IOP in Gr 3 HTNR was 17.2 mmHg whereas the mean IOP in Normal patients was 11.9 mmHg. The total mean IOP was 14 mmHg, which is statistically significant.

Graph 5: Graph showing distribution of Mean IOP according to Fundus Changes

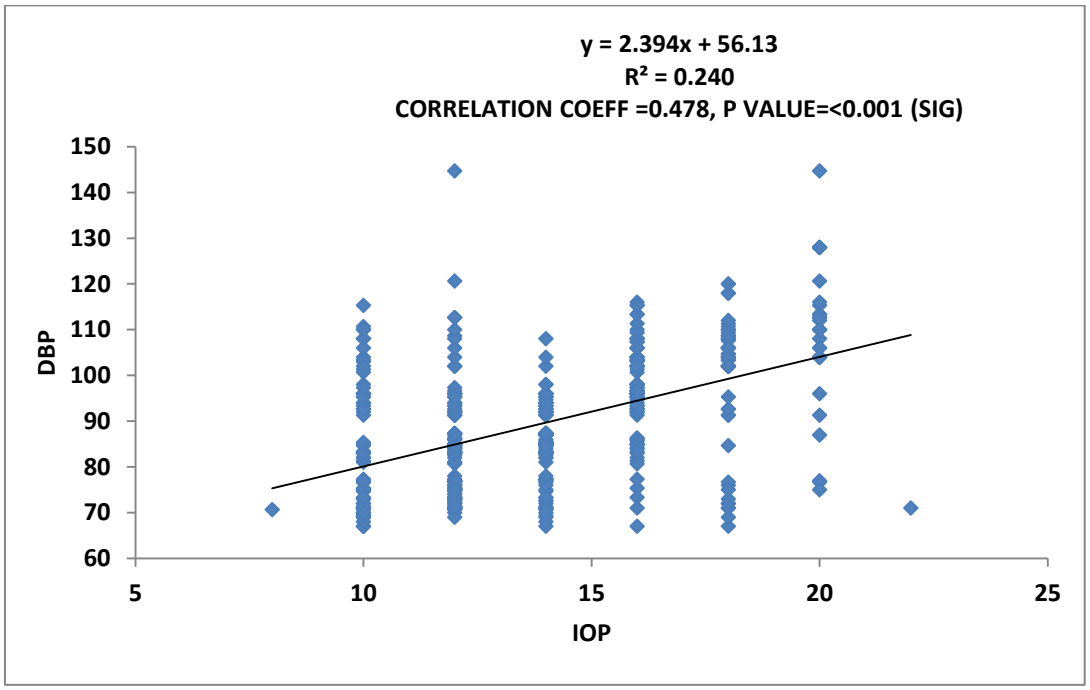


Graph 6: Scattered Plot between IOP and SBP



The above table shows IOP is increasing as Systolic Blood Pressure increases, which is statistically significant.

Graph 7: Scattered Plot between IOP and DBP



The above table shows IOP is increasing as Diastolic Blood Pressure increases, which is statically significant.

Table 6: Distribution of Fundus changes between Hypertensive and Non-Hypertensive cases

Parameters		Right Eye								Left Eye							
		Normo		Prehyper		Grade I HTN		Grade II HTN		Normo		Prehyper		Grade I HTN		Grade II HTN	
		N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Fundus	Gr 1 HTNR	0	0.0	0	0.0	62	95.4	26	41.3	0	0.0	0	0.0	62	95.4	27	42.9
	Gr 2 HTNR	0	0.0	0	0.0	1	1.5	26	41.3	0	0.0	0	0.0	1	1.5	26	41.3
	Gr 3 HTNR	0	0.0	0	0.0	0	0.0	11	17.5	0	0.0	0	0.0	0	0.0	10	15.9
	WNL	66	100.0	62	100.0	2	3.1	0	0.0	66	100.0	62	100.0	2	3.1	0	0.0
Total		66	100.0	62	100.0	65	100.0	63	100.0	66	100.0	62	100.0	65	100.0	63	100.0

The above table shows distribution of patients according to hypertensive retinopathy in Normotensive, Pre-Hypertensive, Grade 1 Hypertensive and Grade 2 Hypertensive patients.

Table 7: Distribution of Mean Age according to Hypertension level

Hypertension	Age (Yrs)		p value
	Mean	SD	
Normotensive	40.29	6.46	0.869
Prehypertensive	40.94	5.72	
Grade I hypertensive	40.50	6.31	
Grade II hypertensive	41.10	6.11	
Total	40.70	6.13	

The above table shows distribution of mean age. Mean age of Normotensive patient was 40.29 and standard deviation was 6.46. Mean age among Pre-Hypertensive patients was 40.94 and standard deviation was 5.72. Mean age amongst Grade 1 Hypertensive patient was 40.50 and standard deviation was 6.31. Mean age among Grade 2 Hypertensive patients was 41.10 and standard deviation was 6.11. P value is 0.869, which is statically significant.

Graph 8: Distribution of Mean Age according to Hypertension level

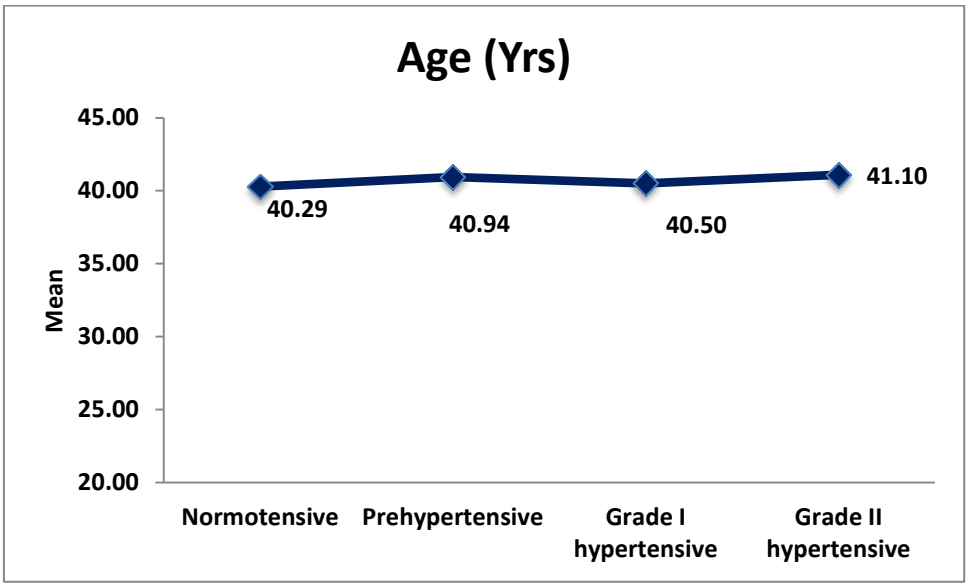


Table 8: Distribution of Mean SBP according to Hypertension level

Hypertension	SBP		p value
	Mean	SD	
Normotensive	112.23	5.85	<0.001*
Prehypertensive	133.01	5.65	
Grade I hypertensive	150.02	5.01	
Grade II hypertensive	170.18	6.95	
Total	140.63	22.38	

Note: *means significant at 5% level of significance (p<0.05)

The mean SBP of patients in Normotensive Group was 112.23 mmHg and 133.01 mmHg in Prehypertensive group , 150.02 in Grade 1 Hypertensive group , 170.18 mmHg in Grade 2 Hypertensive Group and mean SBP was 140.63 , P value <0.001 which is statically significant.

Graph 9: Distribution of Mean SBP according to Hypertension level

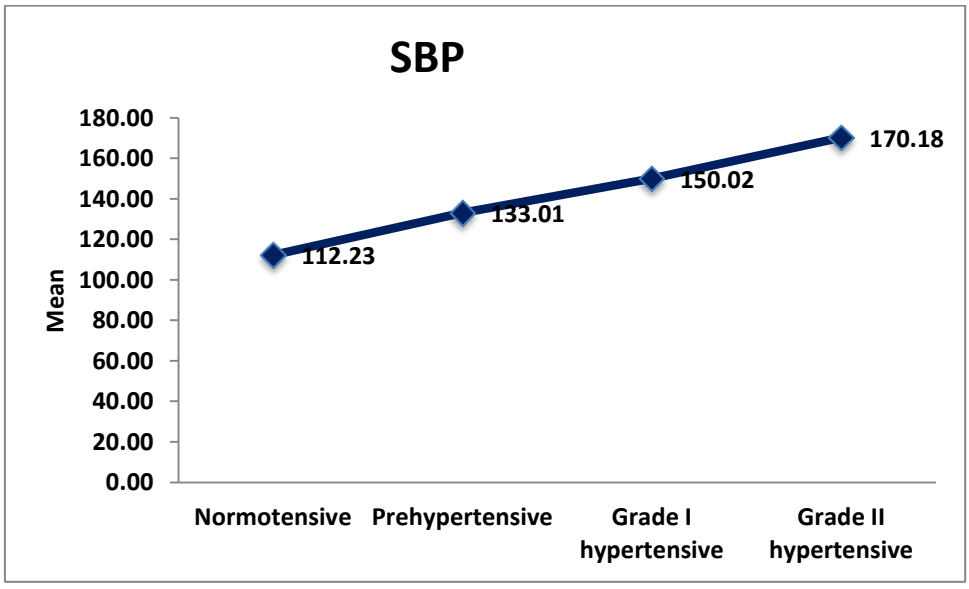


Table 9: Distribution of Mean DBP according to Hypertension level

Hypertension	DBP		p value
	Mean	SD	
Normotensive	73.60	5.16	<0.001*
Prehypertensive	84.23	3.97	
Grade I hypertensive	94.54	2.03	
Grade II hypertensive	108.42	7.80	
Total	89.77	13.98	

Note: *means significant at 5% level of significance (p<0.05)

The mean DBP of patients in Normotensive Group was 73.60 mmHg as compared to 84.23 mmHg in Pre-Hypertensive Group, 94.54 mmHg in Grade 1 Hypertensive group, 108.42 mmHg in Grade 2 Hypertensive group and Total mean DBP was 89.77 mmHg. The difference was statistically significant as per Student t-test (**p<0.05**).

Graph 10: Distribution of Mean DBP according to Hypertension level

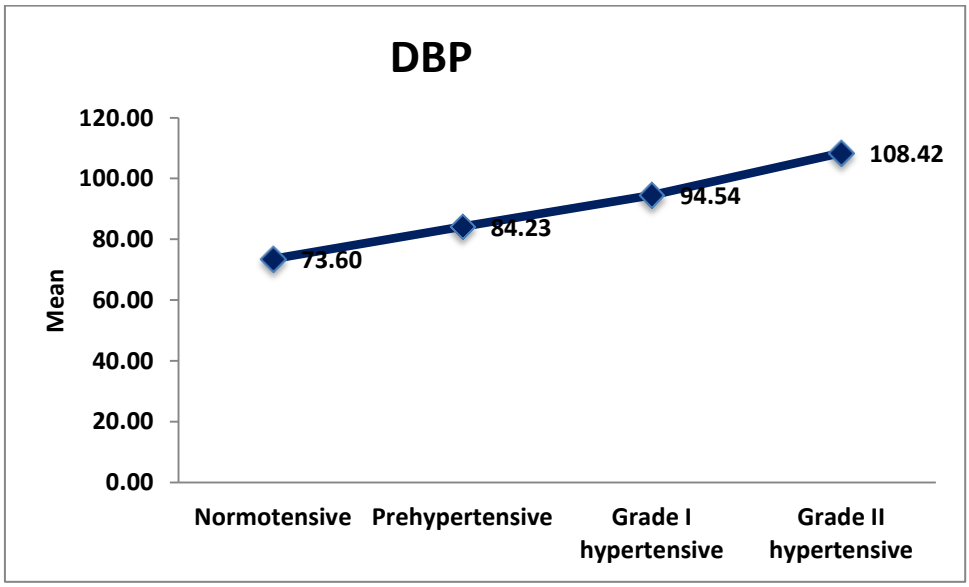


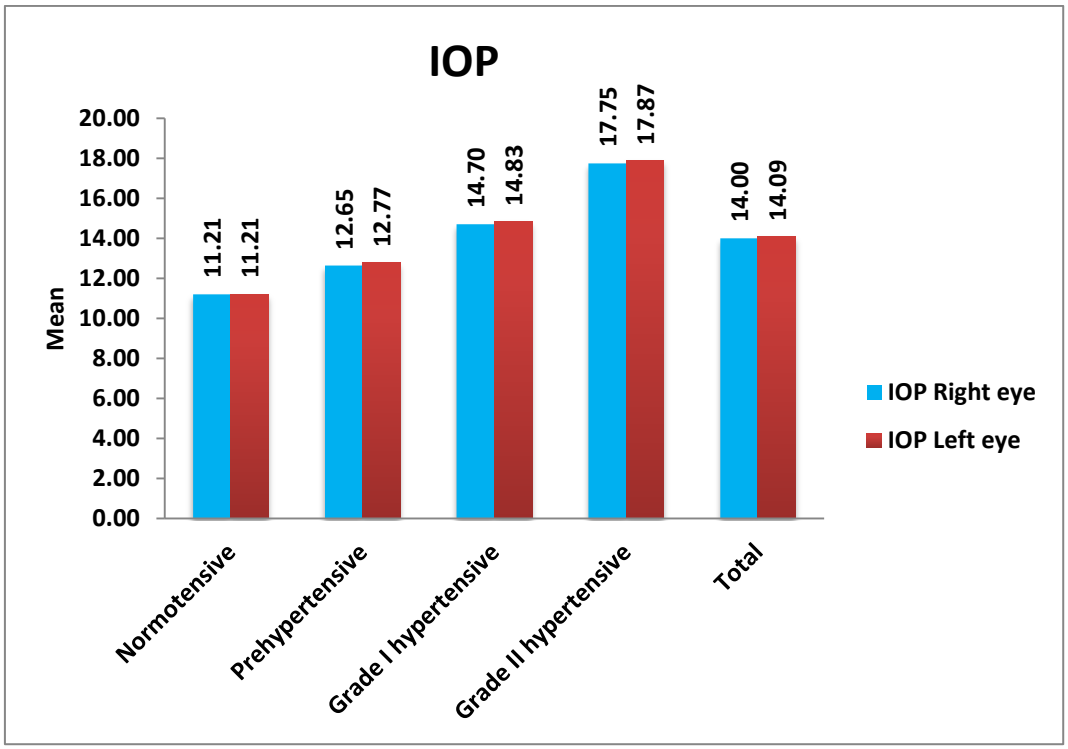
Table 10: Distribution of Mean IOP according to Hypertension level

Hypertension	IOP Right eye		p value	IOP Left eye		p value
	Mean	SD		Mean	SD	
Normotensive	11.21	1.34	<0.001*	11.21	1.25	<0.001*
Prehypertensive	12.65	1.50		12.77	1.26	
Grade I hypertensive	14.70	1.27		14.83	1.24	
Grade II hypertensive	17.75	1.59		17.87	1.76	
Total	14.00	2.86		14.09	2.87	

Note: *means significant at 5% level of significance (p<0.05)

The mean IOP in Normotensive patients was 11.21 mmHg, 12.65mmHg in RE and 12.77mmHg in LE in Pre-Hypertensive patients, 14.70mmHg in RE and 14.87mmHg in LE in Grade 1 Hypertensive patients, 17.75mmHg in RE and 17.87mmHg in LE in Grade 2 Hypertensive patients. Mean total IOP 14mmHg in RE and 14.09mmHg in LE, which is statically significant.

Graph 11: Distribution of Mean IOP according to Hypertension level



DISCUSSION

A hospital based comparative study was conducted with 256 patients to compare Intraocular Pressure in systemic hypertensive patients and in non-hypertensive patients. The patients were divided into following groups:

Normotensive: 128 non-hypertensive patients were included in this group.

Hypertensive: 128 systemic hypertensive patients were included in this group.

Based on blood pressure, the patients were divided into the following groups according to JNC 7 classification i.e. Normotensive, Prehypertension, Stage 1 hypertension, Stage 2 hypertension.

Hypertension is an important public health challenge in both economically developing and developed countries. We have found that change in Systemic blood pressure is directly and significantly associated with changes in IOP. This would suggest that treatment of blood pressure might have an effect on the risk of developing glaucoma, as IOP is probably the most important risk factor for glaucoma in general populations. Becker B[123] demonstrated that variations in systolic blood pressure resulted in (small) changes in aqueous humour formation, possibly related to increase capillary pressure in the ciliary body. This could result in increased IOP. Blood pressure may affect episcleral venous pressure, which is important in regulating the flow of aqueous across the trabecular meshwork into schlemm's canal.

Lack of knowledge about hypertension makes the general population prone to various complications. Most patients seldom realized that they were hypertensive until complication occurred. Monisha NS et al[120] study on correlation of blood pressure and intraocular pressure in hypertensive patients showed that systolic and diastolic blood pressure is positively related to IOP regardless of gender. It is thought that physiological basis for this IOP blood pressure relationship may be an increased production of aqueous humor by ultrafiltration through the elevated ciliary artery pressure. Systemic hypertension can lead to increased IOP through this relationship, but other physiological factors such as sympathetic tone, sclerotic changes or serum corticosteroids should be considered.

In the present study, the age distribution in Non-hypertensive and hypertensive cases were 30-35 (32, 25%), 36-40 (32, 25%), 41-45 (32, 25%), 46-50 (32, 25%) respectively. A total of 128 Non-Hypertensive patients and 128 Hypertensive patients were equally divided into four age-matched groups. There was equal distribution of male and female patients in all the four groups in Non-Hypertensive and Hypertensive patients**.**

Irum S et al[118] cross sectional descriptive study to determine the mean intraocular pressure in various grades of hypertension found 88 (49.6%) patients were male and 90 (50.6%) were female. The mean age was 50.08 ± 5.87 years (range 40-60 years).

The mean IOP in Males was 14.1 mmhg in RE and 14.4 mmHg in LE whereas the mean IOP in Females was 13.9 mmHg in RE and 13.8mmHg. The total mean IOP in RE was 14.2 and 13.9 in LE which is not statistically significant.

The mean IOP in 30-35 yr group was 14.13 in RE and 14.06 in LE, mean in BE 14.09 while the mean IOP in 36-40 yr group was 13.75 in RE and 14.06 in LE, mean in BE 14.09. The mean IOP in 41-45 yr group was 13.91 in RE and 14.03 in LE, mean in BE 14.22 whereas the mean IOP in 46-50 yr group was 14.22 in RE, LE and BE. It was observed that IOP increased as age advances, which was statistically not significant.

The mean IOP in Gr 1 HTNR was 16.2mmHg while the mean IOP in Gr 2 HTNR was 16.3mmHg. The mean IOP in Gr 3 HTNR was 17.2 mmHg whereas the mean IOP in Normal patients was 11.9 mmHg. The total mean IOP was 14 mmHg, which is statistically significant.

Irum S et al[118] cross sectional descriptive study to determine the mean intraocular pressure in various grades of hypertension reported differences of intraocular pressure (IOP) among male and female subjects was not found to be significant [{Males (n = 88): 16.98 ± 4.02} {Female (n = 90): 17.22 ± 4.23}, (p = 0.706)}]. There was a statistically significant difference between groups as determined by one way ANOVA ($p < 0.001$).

Shiose Y et al[124] study reported mean IOP to be 13.3 mmHg for normal people aged over 40 years. In the Beaver Dam study[107], the median IOP was 15.34 ± 2.07 mmHg. Different studies presented with considerable variations in their results in terms of IOP determining factors.

It was observed that IOP increased as Systolic Blood Pressure increases, which are statistically significant. Similarly IOP increases as Diastolic Blood Pressure increases, which is statically significant.

Tektas OY et al[125] and Tielsch JM et al[9] found systemic and ocular hypertension to be interlinked. There is also longitudinal data from developed countries which suggests that baseline systolic BP is directly connected with mean IOP measured at follow up of 4 years and 8 years.[126]

All the major studies, including the Beaver Dam Eye Study[107], the Tanjong Pagar study[108], the Barbados Eye Study[127] have shown positive involvement of systolic and diastolic blood pressure with intraocular pressure.

The distribution of patients according to hypertensive retinopathy in Normotensive, Pre-Hypertensive, Grade 1 Hypertensive and Grade 2 Hypertensive patients showed the following results: For Right Eye, in Normotensive and Pre-hypertensive group all patients had no hypertensive retinopathy while 62 (95.4%) patients in Grade 1 Hypertensive group and 26 (41.3%) patients in Grade 2 Hypertensive group had Grade 1 hypertensive retinopathy. 1 (1.5%) patient in Grade 1 Hypertensive group and 26 (41.3%) patients in Grade 2 Hypertensive group had Grade 2 hypertensive retinopathy. 11 (17.5%) patients in Grade 2 Hypertensive group had Grade 3 hypertensive retinopathy.

For Left Eye, in Normotensive and Pre-hypertensive group all patients had no hypertensive retinopathy while 62 (95.4%) patients in Grade 1 Hypertensive group and 27 (42.9%) patients in Grade 2 Hypertensive group had Grade 1 hypertensive retinopathy. 1 (1.5%) patient in Grade 1 Hypertensive group and 26 (41.3%) patients in Grade 2 Hypertensive group had Grade 2 hypertensive retinopathy. 10 (15.9%) patients in Grade 2 Hypertensive group had Grade 3 hypertensive retinopathy.

Williams BI[128] study on Abnormal intraocular pressure control in systemic hypertension and diabetic mellitus reported detailed analysis of the relationship between the state of the disc, veins, arteries, and arteriovenous crossings of both eyes of all our subjects was performed. The authors failed to find a significant association between the mean rise of pressure at 0 min or 15 min and abnormality of any 1 of the above retinal variables within the hypertensive group. However, the presence of abnormal arteriovenous crossings was associated with a lower mean rise of pressure at 0 min than that found in their absence, and the correlation approached significance (2P=0 059). Conversely the mean values at 15 min were very similar in the presence or absence of this abnormality.

In the present study, mean age of Normotensive patient was 40.29 and standard deviation was 6.46. Mean age among Pre-Hypertensive patients was 40.94 and standard deviation was 5.72. Mean age amongst Grade 1 Hypertensive patient was 40.50 and standard deviation was 6.31. Mean age among Grade 2 Hypertensive patients was 41.10 and standard deviation was 6.11. P value is 0.869, which is statically significant.

Williams BI[128] study on Abnormal intraocular pressure control in systemic hypertension and diabetic mellitus reported average age of the 3 groups of patients were 34-5 years for the control subjects, 49 3 years for patients with hypertension, and 53 3 years for patients with diabetes mellitus. The authors found no significant differences in the abnormal rises of intraocular pressure associated with change of posture seen in hypertensive and diabetic subjects are dependent on this age difference. hypertensive group patients showed rises of intraocular pressure greater than 19 mmHg (mean + SD for control subjects) when measured at 15 minutes did not

fall into any particular age group, such rises occurring in patients as young as 18 years and as old as 70 years.

In our study, the mean SBP of patients in Normotensive Group was 112.23 mmHg and 133.01 mmHg in Prehypertensive group, 150.02 in Grade 1 Hypertensive group, 170.18 mmHg in Grade 2 Hypertensive Group and mean SBP was 140.63 , P value <0.001 which is statically significant.

Wu SY et al[8] in Barbados Eye Study, which excluded subjects with OAG from analysis reported SBP was positively associated with IOP. Hennis A et al[101] and Wu SY et al[102] 4-year and 9-year follow-up data from the Barbados Incidence Study of Eye Diseases I and II (BISED I and BISED II), demonstrated a trend of increase in IOP with increasing SBP.

McLeod S et al[103] [Baltimore Longitudinal Study of Aging (BLSA)], Nomura H et al[104] and Nalano T et al[105] studies that included normal subjects reported positive correlation between SBP and IOP.

Yip J et al[108] and Beaver Dam[107] studies showed that an increase of SBP by ≥ 10 mm Hg from baseline leads to 0.44 mm Hg rise in IOP whereas a decrease of SBP by ≤10 mm Hg from baseline leads to 0.59 mm Hg decrease in IOP, over a 5-year interval.

In present study, the mean DBP of patients in Normotensive Group was 73.60 mmHg as compared to 84.23 mmHg in Pre-Hypertensive Group, 94.54 mmHg in Grade 1 Hypertensive group, 108.42 mmHg in Grade 2 Hypertensive group and Total mean DBP was 89.77 mmHg. The difference was statistically significant as per Student t-test (**p<0.05**).

Wu SY et al[102] reported the evidence for a positive relationship between DBP and IOP is contradictory. DBP was associated with a marginally significant rise of 0.15 mm Hg in IOP over 9 years follow-up in BISED II.

Los Angeles Latino Eye Study[109] reported higher DBP was associated with elevated IOP, however the association was not as strong as between SBP and elevated IOP. DBP contributed to 2% of IOP variance compared to 4% contribution by SBP, on univariate analysis. On multivariate analysis the correlation between SBP and IOP continued to be strong whereas the correlation between DBP and IOP weakened to 0.09% contribution of DBP to IOP variance.

McLeod S et al[103], Nomura H et al[104] and Nalano T et al[105] demonstrated no apparent correlation between DBP and IOP.

Similar to SBP, DBP is positively correlated with IOP in patients with OAG; each 10 mm Hg increment in DBP at baseline leads to 0.19-0.6 mm Hg rise in IOP[9-10,105,111]

It was observed in our study that the mean IOP in Normotensive patients was 11.21 mmHg, 12.65mmHg in RE and 12.77mmHg in LE in Pre-Hypertensive patients, 14.70mmHg in RE and 14.87mmHg in LE in Grade 1 Hypertensive patients, 17.75mmHg in RE and 17.87mmHg in LE in Grade 2 Hypertensive patients. Mean total IOP 14mmHg in RE and 14.09mmHg in LE, which is statically significant.

Irum S et al[118] cross sectional descriptive study to determine the mean intraocular pressure in various grades of hypertension reported overall mean intraocular pressure in hypertensive adults was 17.10 ± 4.12 mmHg. The differences of intraocular pressure (IOP) among male and female subjects was not found to be significant [{Males (n = 88): 16.98 ± 4.02} {Female (n = 90): 17.22 ± 4.23}, (p =

0.706)}]. There was a statistically significant difference between groups as determined by one way ANOVA ($p < 0.001$). Tukey post hoc tests of multiple comparisons revealed significant differences between grade l and grade ll ($p < 0.001$), grade l and grade lll ($p < 0.001$), and grade ll and grade lll ($p = 0.004$).

Shiose Y et al[124] study on new perspectives and intraocular pressure reported mean IOP to be 13.3 mmHg for normal people aged over 40 years. Klein BE et al[107] in the Beaver Dam Eye study on intraocular pressure and systemic blood pressure reported the median IOP was 15.34 ± 2.07 mmHg.

Monisha NS et al[120] study on correlation of blood pressure and intraocular pressure in hypertensive patients indicated systolic BP and diastolic BP, were positively independently correlated to IOP and were statistically significant. The IOP rises and falls by 1 mmHg with every heartbeat. During systole the central retinal artery compress the accompanying vein to increase the vascular resistance in this vessel. It was hypothesized that increased BP in early course of systemic hypertension, prior to the onset of small vessel damage might result in increased blood flow or greater hydrostatic resistance to closure of small vessels and therefore protect the ganglion cells and their axons from damage.

Williams BI[128] et al study reported mean IOP rise recorded varied between 0 and 8 5 mmHg with an overall mean value for the group of 3 5 42 5 mmHg. Since these values are of a higher order than those we found for the groups of control patients. The pattern of the rise of intraocular pressure associated with change of position was different in the 2 groups. In the control group the mean rise, when measured at 0 min, was significantly higher than the mean rise measured at 15 min, 1-02 mmHg compared to 0 60 mmHg (P< 05). In the hypertensive group the mean rise

at 15 min was significantly higher than that occurring at 0 min, that is, 1-21 mmHg compared to 0 61 mmHg (P<00005). When the control was compared with the hypertensive group, the difference in the rise of pressure occurring at 0 min was not significant (P-007), while the difference occurring at 15 min was significant (P<0 005). This difference was tested after exclusion of hypertensive subjects who were not matched for age with control subjects, and the difference found was again significant (P<0 05). It therefore appeared that this difference was not dependent upon age.

Deb AK et al[122] cross-sectional observational study on relationship between blood pressure (BP), intraocular pressure (IOP) reported In the hypertensive group, IOP varied from 10 to 24 mm Hg with a mean IOP of 15.37 mm Hg ± 2.01 mm Hg (216 eyes of 108 patients). In the control group, IOP varied between 9 and 23 mm Hg with a mean IOP of 13.41 mm Hg ± 2.82 mm Hg (200 eyes of 100 participants). Using unpaired t-test, the means in the two groups were found to differ significantly (P < 0.0001).

Qureshi IA[129] study on correlation of age and intraocular pressure showed that menopause significantly increases intraocular pressure. He concluded that mean IOP of postmenopausal hypertensive women was significantly higher than that of postmenopausal normotensive women. Nirmala N et al[130] descriptive comparative study reported Mean IOP of postmenopausal hypertensive women was significantly higher than that of postmenopausal normotensive women.

Longstanding hypertension might also reflect a compromised peripheral vascular capacity and autoregulation to a higher IOP. Studies have also indicated that chronically elevated BP results in arteriosclerotic changes in the size of precapillary arterioles and capillary dropout leading to increased resistance to blood flow and thus reduced perfusion.[131]

CONCLUSION

Glaucoma which is second most common cause for irreversible blindness has to be diagnosed early and treated appropriately along with risk factors.

Elevated Intraocular pressure is the major risk factor for developing glaucoma or glaucomatous optic neuropathy.

Systemic blood pressure increases Intraocular pressure significantly and advancing age is also associated with elevated intraocular pressure.

Hence, person with systemic hypertension and advancing age need periodic Blood Pressure and Intraocular pressure monitoring and control. This will help in control / reduce progression of glaucoma.

SUMMARY

A hospital based comparative study was conducted with 256 patients to compare Intraocular Pressure in systemic hypertensive patients and in non-hypertensive patients. The patients were divided into following groups:

Normotensive: 128 non-hypertensive patients were included in this group.

Hypertensive: 128 systemic hypertensive patients were included in this group.

Based on blood pressure, the patients were divided into the following groups according to JNC 7 classification i.e. Normotensive, Prehypertension, Stage 1 hypertension, Stage 2 hypertension.

The following observations were noted:

1. The age distribution in Non-hypertensive and hypertensive cases were 30-35 (32, 25%), 36-40 (32, 25%), 41-45 (32, 25%), 46-50 (32, 25%) respectively. A total of 128 Non-Hypertensive patients and 128 Hypertensive patients were equally divided into four age-matched groups.
2. There was equal distribution of male and female patients in all the four groups in Non-Hypertensive and Hypertensive patients**.**
3. The mean IOP in Males was 14.1 mmhg in RE and 14.4 mmHg in LE whereas the mean IOP in Females was 13.9 mmHg in RE and 13.8mmHg. The total mean IOP in RE was 14.2 and 13.9 in LE which is not statistically significant.
4. The mean IOP in 30-35 yr group was 14.13 in RE and 14.06 in LE, mean in BE 14.09 while the mean IOP in 36-40 yr group was 13.75 in RE and 14.06 in LE, mean in BE 14.09. The mean IOP in 41-45 yr group was 13.91 in RE and

14.03 in LE, mean in BE 14.22 whereas the mean IOP in 46-50 yr group was 14.22 in RE, LE and BE. It was observed that IOP increased as age advances, which was statistically not significant.

5. The mean IOP in Gr 1 HTNR was 16.2mmHg while the mean IOP in Gr 2 HTNR was 16.3mmHg. The mean IOP in Gr 3 HTNR was 17.2 mmHg whereas the mean IOP in Normotensive patients was 11.9 mmHg. The total mean IOP was 14 mmHg, which is statistically significant.

6. It was observed that IOP increased as Systolic Blood Pressure increases, which are statistically significant. Similarly IOP increases as Diastolic Blood Pressure increases, which is statically significant.

7. The distribution of patients according to hypertensive retinopathy in Normotensive, Pre-Hypertensive, Grade 1 Hypertensive and Grade 2 Hypertensive patients showed the following results: For Right Eye, in Normotensive and Pre-hypertensive group all patients had no hypertensive retinopathy while 62 (95.4%) patients in Grade 1 Hypertensive group and 26 (41.3%) patients in Grade 2 Hypertensive group had Grade 1 hypertensive retinopathy. 1 (1.5%) patient in Grade 1 Hypertensive group and 26 (41.3%) patients in Grade 2 Hypertensive group had Grade 2 hypertensive retinopathy. 11 (17.5%) patients in Grade 2 Hypertensive group had Grade 3 hypertensive retinopathy.

8. For Left Eye, in Normotensive and Pre-hypertensive group all patients had no hypertensive retinopathy while 62 (95.4%) patients in Grade 1 Hypertensive group and 27 (42.9%) patients in Grade 2 Hypertensive group had Grade 1 hypertensive retinopathy. 1 (1.5%) patient in Grade 1 Hypertensive group and

26 (41.3%) patients in Grade 2 Hypertensive group had Grade 2 hypertensive retinopathy. 10 (15.9%) patients in Grade 2 Hypertensive group had Grade 3 hypertensive retinopathy.

9. Mean age of Normotensive patient was 40.29 and standard deviation was 6.46. Mean age among Pre-Hypertensive patients was 40.94 and standard deviation was 5.72. Mean age amongst Grade 1 Hypertensive patient was 40.50 and standard deviation was 6.31. Mean age among Grade 2 Hypertensive patients was 41.10 and standard deviation was 6.11. P value is 0.869, which is statically significant.

10. The mean SBP of patients in Normotensive Group was 112.23 mmHg and 133.01 mmHg in Prehypertensive group, 150.02 in Grade 1 Hypertensive group, 170.18 mmHg in Grade 2 Hypertensive Group and mean SBP was 140.63 , P value <0.001 which is statically significant.

11. The mean DBP of patients in Normotensive Group was 73.60 mmHg as compared to 84.23 mmHg in Pre-Hypertensive Group, 94.54 mmHg in Grade 1 Hypertensive group, 108.42 mmHg in Grade 2 Hypertensive group and Total mean DBP was 89.77 mmHg. The difference was statistically significant as per Student t-test (**p<0.05**).

12. The mean IOP in Normotensive patients was 11.21 mmHg in BE, 12.65mmHg in RE and 12.77mmHg in LE in Pre-Hypertensive patients, 14.70mmHg in RE and 14.87mmHg in LE in Grade 1 Hypertensive patients, 17.75mmHg in RE and 17.87mmHg in LE in Grade 2 Hypertensive patients. Mean total IOP 14mmHg in RE and 14.09mmHg in LE, which is statically significant.

REFERENCES

1. Sihota R, Tandon R, (2015). Parsons Diseases Of The Eye. 22nd Edition. Ch 2. Page no 16-18. Reed Elsevier India Private Limited.)
2. Sithole HL, Arbee T, Nxumalo N, Tshatsha ND, Perumal K, Mohamed Ali Z, Souza T, et al. A correlational study of systemic blood pressure and intraocular pressure in a young South African adult population. South African Optom 2009 68(4) 192-197.
3. Bengtsson B. Some factors affecting the distribution of intraocular pressures in a population. Acta Ophthalmol (Copenh) 1972;50:33–46.
4. Bulpitt CJ, Hodes C, Everitt MG. Intraocular pressure and systemic blood pressure in the elderly. Br J Ophthalmol 1975;59:717–20.
5. Kahn HA, Leibowitz HM, Ganley JP, et al. The Framingham Eye Study. II. Association of ophthalmic pathology with single variables previously measured in the Framingham Heart Study. Am J Epidemiol 1977;106:33–41.
6. Klein BE, Klein R. Intraocular pressure and cardiovascular risk variables. Arch Ophthalmol 1981;99:837–9.
7. Klein BE, Klein R, Linton KL. Intraocular pressure in an American community. The Beaver Dam Eye Study. Invest Ophthalmol Vis Sci 1992;33:2224–8.
8. Wu SY, Leske MC. Associations with intraocular pressure in the Barbados Eye Study. Arch Ophthalmol 1997;115:1572–6.
9. Tielsch JM, Katz J, Sommer A, et al. Hypertension, perfusion pressure, and primary open-angle glaucoma. A population-based assessment. Arch Ophthalmol 1995;113:216–21.

10. Dielemans I, Vingerling JR, Algra D, et al. Primary open-angle glaucoma, intraocular pressure, and systemic blood pressure in the general elderly population. The Rotterdam Study. Ophthalmology 1995;102:54–60.
11. Healey PR, Mitchell P, Smith W, et al. The influence of age and intraocular pressure on the optic cup in a normal population. J Glaucoma 1997;6:274–8.
12. Foster PJ, Machin D, Wong TY, et al. Determinants of intraocular pressure and its association with glaucomatous optic neuropathy in Chinese Singaporeans: the Tanjong Pagar Study. Invest Ophthalmol Vis Sci 2003;44:3885–91.
13. Leske MC, Warheit-Roberts L, Wu SY. Open-angle glaucoma and ocular hypertension: the Long Island Glaucoma Case-control Study. Ophthalmic Epidemiol 1996;3:85–96.
14. Piltz-Seymour JR, Stone RA. Glaucoma associated with systemic disease. In: Ritch R, Shields MB, Krupin T, eds. The glaucomas. 2nd ed. St Louis: Mosby, 1996:1157–76.
15. Rand AR, Damji KF, Shields MB. Shield's textbook of glaucoma, 5th ed. Lippincott:2005;9:197.
16. American Academy of Opthalmology. Glaucoma 2009-2010:6-8,31-36, 53-58.
17. Bhargava M, Ikram MK, Wong TY. "How does hypertension affect your eyes?". Journal of Human Hypertension. 26 (2): 71–83.
18. Myron Y, Duker JS. (2009-01-01). Ophthalmology. Elsevier Health Sciences. ISBN 0323043321.

19. Wong TY, Mcintosh R (2005). "Hypertensive retinopathy signs as risk indicators of cardiovascular morbidity and mortality". British Medical Bulletin. 73-74: 57–70.

20. Cremer A, Amraoui F, Lip GYH, Morales E, Rubin S, Segura J, Van den Born BJ, Gosse P. (2016-08-01). "From malignant hypertension to hypertension-MOD: a modern definition for an old but still dangerous emergency". Journal of Human Hypertension. 30 (8): 463–466.

21. South East Asia Glaucoma Interest Group. Asia Pacific Glaucoma Guidelines 2003-2004:79.

22. Caprioli J, Sears M, Bausher L, Gregory D, Mead A. Forskolin lowers intraocular pressure by reducing aqueous inflow. Invest Ophthalmol Vis Sci,1999;25:268-277

23. Macri FJ. Experimental Aqueous Humour Drainage. Arch Ophthalmol 1962;68(1):150-151.

24. Gordon MA, Beiser JA, Brandt JD, Heuer DK, Higginbotham EJ, Johnson CA, et al. The Ocular Hypertension Treatment Study: Baseline Factors That Predict the Onset of Primary Open-Angle Glaucoma. Arch Ophthalmol. 2002;120:714-720.

25. Foster PJ, Baasanhu J, Alsbirk PH, Munkhbayar D, Uranchimeg D, Johnson G. Central Corneal Thickness and Intraocular Pressure in a Mongolian Population. Ophthalmology 1998; 105:969-973.

26. Dobree JH. Calibre changes in retinal vessels occurring in raised ocular tension; circulatory compensation in chronic glaucoma. Br J Ophthalmol 1956; 40: 1–13.

27. Russell RW. Evidence for autoregulation in human retinal circulation. Lancet 1973; 2: 1048–1050.

28. Robinson F, Riva CE, Grunwald JE, Petrig BL, Sinclair SH. Retinal blood flow autoregulation in response to an acute increase in blood pressure. Invest Ophthalmol Vis Sci 1986; 27: 722–726.

29. Grosvenor T. Primary Care Optometry, 5th ed. Hong Kong: Butterworth–Heinemann Elsevier, 2006.

30. Lovasik JV, Kothe AC, Kergoat H. Comparison of noninvasive methods to derive the mean central retinal artery pressure in man. Optom Vis Sci 1993; 70: 1005–1011.

31. Bill A. Ocular circulation. In: Adler FH, Moses RA, eds. Adler's Physiology of the Eye. St Louis, Missouri: The CV Mosby Co, 1975. p 215.

32. Satilmis M, Orgul S, Doubler B, Flammer J. Rate of progression of glaucoma correlates with retrobulbar circulation and intraocular pressure. Am J Ophthalmol 2003; 135: 664–669.

33. Gehlbach PL, Purple RL. A paired comparison of two models of experimental retinal ischemia. Curr Eye Res 1994; 13: 597–602.

34. Grehn F, Prost M. Function of retinal nerve fibers depends on perfusion pressure: neurophysiologic investigations during acute intraocular pressure elevation. Invest Ophthalmol Vis Sci 1983; 24: 347–353.

35. Siliprandi R, Bucci MG, Canella R, Carmignoto G. Flash and pattern electroretinograms during and after acute intraocular pressure elevation in cats. Invest Ophthalmol Vis Sci 1988; 29: 558–565.

36. Maffei L, Fiorentini A, Bisti S, Hollander H. Pattern ERG in the monkey after section of the optic nerve. Exp Brain Res 1985; 59: 423–425.

37. Kiel JW, van Heuven WA. Ocular perfusion pressure and choroidal blood flow in the rabbit. Invest Ophthalmol Vis Sci 1995; 36: 579–585.

38. Liang Y, Downs JC, Fortune B, Cull G, Cioffi GA, Wang L. Impact of systemic blood pressure on the relationship between intraocular pressure and blood flow in the optic nerve head of nonhuman primates. Invest Ophthalmol Vis Sci 2009; 50: 2154–2160.

39. He Z, Vingrys AJ, Armitage JA, Bui BV. Effect of ocular perfusion pressure on retinal function in rats. In: ARVO e-Abstract 2752-D676. Ft Lauderdale, FL, USA, 2009.

40. Hayreh SS, Jonas JB, Zimmerman MB. Parapapillary chorioretinal atrophy in chronic high-pressure experimental glaucoma in rhesus monkeys. Invest Ophthalmol Vis Sci 1998; 39: 2296–2303.

41. Hayreh SS, Pe'er J, Zimmerman MB. Morphologic changes in chronic high-pressure experimental glaucoma in rhesus monkeys. J Glaucoma 1999; 8: 56–71.

42. Hill L, Flack M. The relation between capillary pressure and secretion. II. The secretion of the aqueous and the intraocular pressure. Proc Roy Soc B 1912; 85: 439.

43. Harino S, Riva CE, Petrig BL. Intravenous nicardipine in cats increases optic nerve head but not retinal blood flow. Invest Ophthalmol Vis Sci 1992; 33: 2885–2890.

44. Kiel JW. Modulation of choroidal autoregulation in the rabbit. Exp Eye Res 1999; 69: 413–429.

45. Seligsohn EE, Bill A. Effects of NG-nitro-L-arginine methyl ester on the cardiovascular system of the anaesthetized rabbit and on the cardiovascular response to thyrotropin-releasing hormone. Br J Pharmacol 1993; 109: 1219–1225.

46. Huang Z, Huang PL, Ma J, Meng W, Ayata C, Fishman MC, Moskowitz MA. Enlarged infarcts in endothelial nitric oxide synthase knockout mice are attenuated by nitro-L-arginine. J Cereb Blood Flow Metab 1996; 16: 981–987.

47. Riva CE, Petrig BL. Choroidal blood flow by laser Doppler flowmetry. Optical Engineering 1995; 34: 746–752.

48. Riva CE, Hero M, Titze P, Petrig B. Autoregulation of human optic nerve head blood flow in response to acute changes in ocular perfusion pressure. Graefes Arch Clin Exp Ophthalmol 1997; 235: 618–626.

49. Movaffaghy A, Chamot SR, Petrig BL, Riva CE. Blood flow in the human optic nerve head during isometric exercise. Exp Eye Res 1998; 67: 561–568.

50. Riva CE, Titze P, Hero M, Petrig BL. Effect of acute decreases of perfusion pressure on choroidal blood flow in humans. Invest Ophthalmol Vis Sci 1997; 38: 1752–1760.

51. Riva CE, Grunwald JE, Petrig BL. Autoregulation of human retinal blood flow. An investigation with laser Doppler velocimetry. Invest Ophthalmol Vis Sci 1986; 27: 1706–1712.

52. Dumskyj MJ, Eriksen JE, Dore CJ, Kohner EM. Autoregulation in the human retinal circulation: assessment using isometric exercise, laser

Doppler velocimetry, and computer-assisted image analysis. Microvasc Res 1996; 51: 378–392.

53. Harris A, Arend O, Bohnke K, Kroepfl E, Danis R, Martin B. Retinal blood flow during dynamic exercise. Graefes Arch Clin Exp Ophthalmol 1996; 234: 440–444.

54. Jeppesen P, Sanye-Hajari J, Bek T. Increased blood pressure induces a diameter response of retinal arterioles that increases with decreasing arteriolar diameter. Invest Ophthalmol Vis Sci 2007; 48: 328–331.

55. Polska E, Simader C, Weigert G, Doelemeyer A, Kolodjaschna J, Scharmann O, Schmetterer L. Regulation of choroidal blood flow during combined changes in intraocular pressure and arterial blood pressure. Invest Ophthalmol Vis Sci 2007; 48: 3768–3774.

56. Chemtob S, Beharry K, Rex J, Chatterjee T, Varma DR, Aranda JV. Ibuprofen enhances retinal and choroidal blood flow autoregulation in newborn piglets. Invest Ophthalmol Vis Sci 1991; 32: 1799–1807.

57. Chemtob S, Beharry K, Rex J, Varma DR, Aranda JV. Changes in cerebrovascular prostaglandins and thromboxane as a function of systemic blood pressure. Cerebral blood flow autoregulation of the newborn. Circ Res 1990; 67: 674–682.

58. Laties AM, Jacobowitz D. A comparative study of the autonomic innervation of the eye in monkey, cat and rabbit. Anat Rec 1966; 156: 383–395.

59. Ruskell GL. An ocular parasympathetic nerve pathway of facial nerve origin and its influence on intraocular pressure. Exp Eye Res 1970; 10: 319–330.

60. Alm A. Ocular circulation. In: Kaufman PL, Alm A, Adler FH, eds. Adler's physiology of the Eye: Clinical Application. 10th ed. St Louis: Mosby, 2003.

61. Costa VP, Harris A, Stefansson E, Flammer J, Krieglstein GK, Orzalesi N, Heijl A et al. The effects of antiglaucoma and systemic medications on ocular blood flow. Prog Retin Eye Res 2003; 22: 769–805.

62. Lansman JB, Hallam TJ, Rink TJ. Single stretch-activated ion channels in vascular endothelial cells as mechanotransducers? Nature 1987; 325: 811–813.

63. Delaey C, Van de Voorde J. Pressure-induced myogenic responses in isolated bovine retinal arteries. Invest Ophthalmol Vis Sci 2000; 41: 1871–1875.

64. Jean-Louis S, Lovasik JV, Kergoat H. Systemic hyperoxia and retinal vasomotor responses. Invest Ophthalmol Vis Sci 2005; 46: 1714–1720.

65. Riva CE, Grunwald JE, Sinclair SH. Laser Doppler velocimetry study of the effect of pure oxygen breathing on retinal blood flow. Invest Ophthalmol Vis Sci 1983; 24: 47–51.

66. Riva CE, Pournaras CJ, Tsacopoulos M. Regulation of local oxygen tension and blood flow in the inner retina during hyperoxia. J Appl Physiol 1986; 61: 592–598.

67. Pournaras C, Tsacopoulos M, Chapuis P. Studies on the role of prostaglandins in the regulation of retinal blood flow. Exp Eye Res 1978; 26: 687–697.

68. Tsacopoulos M, David NJ. The effect of arterial PCO2 on relative retinal blood flow in monkeys. Invest Ophthalmol 1973; 12: 335–347.

69. Formaz F, Riva CE, Geiser M. Diffuse luminance flicker increases retinal vessel diameter in humans. Curr Eye Res 1997; 16: 1252–1257.

70. Michelson G, Patzelt A, Harazny J. Flickering light increases retinal blood flow. Retina 2002; 22: 336–343.

71. Toda N, Nakanishi-Toda M. Nitric oxide: ocular blood flow, glaucoma, and diabetic retinopathy. Prog Retin Eye Res 2007; 26: 205–238.

72. Neufeld AH, Hernandez MR, Gonzalez M. Nitric oxide synthase in the human glaucomatous optic nerve head. Arch Ophthalmol 1997; 115: 497–503.

73. Pellanda N, Flammer J, Haefliger IO. L-NAME- and U 46619-induced contractions in isolated porcine ciliary arteries versus vortex veins. Klin Monbl Augenheilkd 2001; 218: 366–369.

74. Dieguez G, Garcia JL, Fernandez N, Garcia-Villalon AL, Monge L, Gomez B. Role of NO in goat basal cerebral circulation and after vasodilatation to hypercapnia or brief ischemias. Am J Physiol 1993; 265: R1410–R1415.

75. Ortega Mateo A, de Artinano AA. Highlights on endothelins: a review. Pharmacol Res 1997; 36: 339–351.

76. Sugiyama T, Moriya S, Oku H, Azuma I. Association of endothelin-1 with normal tension glaucoma: clinical and fundamental studies. Surv Ophthalmol 1995; 39 Suppl 1: S49–S56.

77. Nicolela MT, Ferrier SN, Morrison CA, Archibald ML, LeVatte TL, Wallace K, Chauhan BC et al. Effects of cold-induced vasospasm in glaucoma: the role of endothelin-1. Invest Ophthalmol Vis Sci 2003; 44: 2565–2572.

78. Henry E, Newby DE, Webb DJ, Hadoke PW, O'Brien CJ. Altered endothelin-1 vasoreactivity in patients with untreated normal-pressure glaucoma. Invest Ophthalmol Vis Sci 2006; 47: 2528–2532.

79. Flammer J, Mozaffarieh M. Autoregulation, a balancing act between supply and demand. Can J Ophthalmol 2008; 43: 317–321.

80. Moore D, Harris A, Wudunn D, Kheradiya N, Siesky B. Dysfunctional regulation of ocular blood flow: A risk factor for glaucoma? Clin Ophthalmol 2008; 2: 849–861.

81. Blann AD, Waite MA. von Willebrand factor and soluble E-selectin in hypertension: influence of treatment and value in predicting the progression of atherosclerosis. Coron Artery Dis 1996; 7: 143–147.

82. Iiyama K, Nagano M, Yo Y, Nagano N, Kamide K, Higaki J, Mikami H et al. Impaired endothelial function with essential hypertension assessed by ultrasonography. Am Heart J 1996; 132: 779–782.

83. Muiesan ML, Salvetti M, Monteduro C, Rizzoni D, Zulli R, Corbellini C, Brun C, et al. Effect of treatment on flow-dependent vasodilation of the brachial artery in essential hypertension. Hypertension 1999; 33: 575–580.

84. Harper SL, Bohlen HG. Microvascular adaptation in the cerebral cortex of adult spontaneously hypertensive rats. Hypertension 1984; 6: 408–419.

85. Strandgaard S, Jones JV, MacKenzie ET, Harper AM. Upper limit of cerebral blood flow autoregulation in experimental renovascular hypertension in the baboon. Circ Res 1975; 37: 164–167.

86. Jones JV, Fitch W, MacKenzie ET, Strandgaard S, Harper AM. Lower limit of cerebral blood flow autoregulation in experimental renovascular hypertension in the baboon. Circ Res 1976; 39: 555–557.

87. Strandgaard S, Olesen J, Skinhoj E, Lassen NA. Autoregulation of brain circulation in severe arterial hypertension. Br Med J 1973; 1: 507–510.

88. Dintenfass L. Hyperviscosity in Hypertension. Sydney: Pergamon Press, 1981.

89. Fowkes FG, Lowe GD, Rumley A, Lennie SE, Smith FB, Donnan PT. The relationship between blood viscosity and blood pressure in a random sample of the population aged 55 to 74 years. Eur Heart J 1993; 14: 597–601.

90. Letcher RL, Chien S, Pickering TG, Sealey JE, Laragh JH. Direct relationship between blood pressure and blood viscosity in normal and hypertensive subjects. Role of fibrinogen and concentration. Am J Med 1981; 70: 1195–1202.

91. Tibblin G, Bergentz SE, Bjure J, Wilhelmsen L. Hematocrit, plasma protein, plasma volume, and viscosity in early hypertensive disease. Am Heart J 1966; 72: 165–176.

92. Hayashi T, Watabe H, Kudomi N, Kim KM, Enmi J, Hayashida K, Iida H. A theoretical model of oxygen delivery and metabolism for physiologic interpretation of quantitative cerebral blood flow and metabolic rate of oxygen. J Cereb Blood Flow Metab 2003; 23: 1314–1323.

93. Hirakata H, Yao H, Osato S, Ibayashi S, Onoyama K, Otsuka M, Ichiya Y, et al. CBF and oxygen metabolism in hemodialysis patients: effects of anemia correction with recombinant human EPO. Am J Physiol 1992; 262: F737–F743.

94. Mountz JM, Liu HG, Deutsch G. Neuroimaging in cerebrovascular disorders: measurement of cerebral physiology after stroke and assessment of stroke recovery. Semin Nucl Med 2003; 33: 56–76.

95. Zheng Y, Martindale J, Johnston D, Jones M, Berwick J, Mayhew J. A model of the hemodynamic response and oxygen delivery to brain. Neuroimage 2002; 16: 617–637.

96. Ginsberg MD, Mela L, Wrobel-Kuhl K, Reivich M. Mitochondrial metabolism following bilateral cerebral ischemia in the gerbil. Ann Neurol 1977; 1: 519–527.

97. Rehncrona S, Mela L, Siesjo BK. Recovery of brain mitochondrial function in the rat after complete and incomplete cerebral ischemia. Stroke 1979; 10: 437–446.

98. Schutz H, Silverstein PR, Vapalahti M, Bruce DA, Mela L, Langfitt TW. Brain mitochondrial function after ischemia and hypoxia. I. Ischemia induced by increased intracranial pressure. Arch Neurol 1973; 29: 408–416.

99. Leske MC, Wu SY, Nemesure B, Hennis A. Incident open-angle glaucoma and blood pressure. Arch Ophthalmol 2002; 120: 954–959.

100. Allen CMC, Lueck CJ, Dennis M. Neurological disease. In: Boon NA, Colledge NR, Walker BR, Hunter JAA, eds. Davidson's Principles and Practise of Medicine, 20th ed. Edinburgh: Churchill Livingstone, 2006.

101. Hennis A, Wu SY, Nemesure B, et al. Hypertension, diabetes and longitudinal changes in intraocular pressure. Ophthalmology 2003;110:908-14.

102. Wu SY, Nemesure B, Hennis A, Leske C, et al. Nine-Year changes in intraocular pressure: the Barbados Eye Studies. Arch Ophthalmol 2006;124:1631-36.

103. McLeod S, West S, Quigley H, Fozard J. A longitudinal study of the relationship between intraocular and blood pressure. Invest Ophthalmol Vis Sci 1990;30:2361-66.

104. Nomura H, Shimokata H, Ando F, Miyake Y, et al. Age-related changes in intraocular pressure in a large Japanese population: A cross-sectional and longitudinal study. Ophthalmology 1999;106: 2016-22.

105. Nalano T, Tatemichi M, Miura Y, Sugita M, et al. Long-term physiologic changes of intraocular pressure: A 10-year longitudinal analysis in young and middle aged Japanese men. Ophthalmology 2005;112:609-16.

106. Bonomi L, Marchini G, Marraffa M, et al. Vascular risk factors for primary open angle glaucoma. The Egna-Neumarkt Study. Ophthalmology 2000;107:1287-93.

107. Klein BK, Klein R, Knudtson MD. Intraocular pressure and systemic blood pressure: longitudinal perspective: the Beaver Dam Eye Study. Br J Ophthalmol 2005;89(3):284-87

108. Yip J, Aung T, Wong TY, et al. Socioeconomic status, systolic blood pressure and intraocular pressure: the Tanjong Pagar Study. Br J Ophthalmol 2007;91:56-61.

109. Associations with intraocular pressure in Latinos: The Los Angeles Latino Eye Study. The Los Angeles Latino Eye Study Group. Am J Ophthalmol 2008;146:69-76.

110. Kawase K, Tomidokoro A, Araie M, et al. Ocular and systemic factors related to intraocular pressure in Japanese adults: The Tajimi Study. Br J Ophthalmol 2008;92:1175-79.

111. Hulsman CA, Vingerling JR, Hofman A, et al. Blood pressure, arterial stiffness and open angle glaucoma. The Rotterdam Study. Arch Ophthalmol 2007;125:805-12.

112. Deokule S. How is Systemic Blood Pressure and Intraocular Pressure Related. Journal of Current Glaucoma Practice. January-April 2009;1–4.

113. Kisan R, Kisan SR, Anitha OR, Chandrakala SP, Koujalagi RS. Correlation Between the Intraocular Pressure and the Blood Pressure in Different Age Groups. Journal of Clinical and Diagnostic Research, 2012 May (Suppl-2), Vol-6(4): 581-585.

114. Sajja S, Saha M. Effect of Hypertension on intraocular pressure in rural population of Andhra Pradesh. International Journal of Biological & Medical Research.2013;4(3):3637-3641.

115. Yoshida M, Take S, Ishikawa M, Karita K, Kokaze A, Harada M, et al. Interrelationship among blood pressure, intraocular pressure, and life-style in middle-aged and older Japanese residents. Health . 2013;05(10): 1527–32.

116. Grippo TM, Liu JHK, Zebardast N, Arnold TB, Moore GH, Weinreb RN. Twenty-Four–Hour Pattern of Intraocular Pressure in Untreated Patients with Ocular Hypertension. Investigative Ophthalmology & Visual Science January 2013, Vol.54, 512-517. doi:10.1167/iovs.12-10709.

117. Khawaja AP, Chan MPY, Broadway DC, et al. Systemic Medication and Intraocular Pressure in a British Population: The EPIC-Norfolk Eye Study. Ophthalmology.2014;121(8):1501-1507.

118. Irum S, Malik AM, Saeed M, Shahid M. Pak Armed Forces Medical Journal. 2015;65(1):73-6.

119. Baisakhiya S, Singh S, Manjhi P. Correlation between intraocular pressure and blood pressure in North Indian subjects. International Journal of Advanced Research.2015;3(7):1545–54.

120. Monisha A, Neki NS, Kumar H, Chovan V, Meena NK, Singh A, Kaushal D, Vaid A. A correlation of blood pressure and intraocular pressure in hypertensive patients above 40 years. Annals of Geriatric Education and Medical Sciences, January-December,2016;1(1):10-13

121. Budenza DL, Hueckerb JB, Geddec SJ, Gordon M, Kass M. Thirteen-Year Follow-up of Optic Disc Hemorrhages in the Ocular Hypertension Treatment Study. American Journal of Ophthalmology. 2017, Volume 174, Pages 126-133.

122. Deb A, Kaliaperumal S, Rao V, Sengupta S. Relationship between systemic hypertension, perfusion pressure and glaucoma: A comparative study in an adult Indian population. Indian J Ophthalmol. 2014;62(9):917.

123. Becker B. The effect of hypothermia on aqueous humor dynamics: III. Turnover of ascorbate and sodium. Am J Ophthalmol 1961;51;1032.

124. Shiose Y. Intraocular pressure: new perspectives. Surv Ophthalmol 1990; 34:413-35.

125. Tektas OY, Lütjen-Drecoll E. Structural changes of the trabecular meshwork in different kinds of glaucoma. Exp Eyes Res. 2009; 88:769-75.

126. Nakano T, Tatemichi M, Miura Y, Sugita M, Kitahara K. Long-term physiologic changes of intraocular pressure: a 10-year longitudinal analysis in young and middle-aged Japanese men. Ophthalmol 2005; 112:609-16.

127. Nemesure B, Wu SY, Hennis A, Leske MC. Factors related to the 4-year risk of high intraocular pressure: The Barbados eye studies. Arch Ophthalmol 2003; 121:856-6

128. Williams BI, Peart WS, E. Letley E. Abnormal intraocular pressure control in systemic hypertension and diabetic mellitus. British Journal of Ophthalmology, 1980, 64, 845-851

129. Qureshi IA. Age and intraocular pressure: how are they correlated? J Pak Med Assoc. 1995 Jun;45(6):150-2.

130. Nirmala N, Adhilakshmi A, Jain H, Karthika PU. A comparative study of intraocular pressure changes in postmenopausal normotensive and hypertensive women. Int J Res Med Sci 2014;2:876-80.

131. Stefansson E, Wagner HG, Seida M. Retinal blood flow and its auto regulation measured by intraocular hydrogen clearance. Exp Eye Res. 1988;47:669-78.

ANNEXURES

ETHICAL CLEARANCE CERTIFICATE

B.L.D.E.UNIVERSITY'S
SHRI.B.M.PATIL MEDICAL COLLEGE, BIJAPUR – 586103
INSTITUTIONAL ETHICAL COMMITTEE

No 158/2015
20/11/15

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this college met on 17-11-2015 *at* 03 pm *scrutinize the Synopsis of Postgraduate Students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected and revised version synopsis of the Thesis has accorded Ethical Clearance.*

Title "Comparison of intraocular pressure in systemic Hypertensive patients & in non Hypertensive patients"

Name of P.G. Student : Dr Prashant. M. Koranmath
Dept of Ophthalmology

Name of Guide/Co-investigator : Dr. M.H. Patil
Prof of Ophthalmology

DR.TEJASWINI VALLABHA
CHAIRMAN

CHAIRMAN
Institutional Ethical Committee
BLDEU's Shri B.M. Patil
Medical College,BIJAPUR-586103.

Following documents were placed before E.C. for Scrutinization
1)Copy of Synopsis/Research Project
2)Copy of informed consent form.
3)Any other relevant documents.

☐ **Hypertensive.** ☐ **Non-Hypertensive.**

PROFORMA FOR CASE TAKING

DEPARTMENT OF OPHTHALMOLOGY

B.L.D.E UNIVERSITY'S SHRI B.M.PATIL MEDICAL COLLEGE HOSPITAL & RESEARCH CENTRE, VIJAYPUR-586103

COMPARISON OF INTRAOCULAR PRESSURE IN SYSTEMIC HYPERTENSIVE PATIENTS AND NON HYPERTENSIVE PATIENTS.

Case No: OPD/IPD No Date

Name Age SEX

Occupation Address

Chief complaints -

PERSONAL HISTORY

Habit -

Any other disease-

Treatment history-

FAMILY HISTORY –

H/O Hypertension - Yes / No

H/O Diabetes - Yes / No

Recording under resting conditions.

Blood pressure reading	1st	2nd	3rd	Mean
Systolic				
Diastolic				

OPHTHALMIC EXAMINATION.

	Right eye	Left eye
External appearance		
Lids		
Conjunctiva		
Cornea		
Pupil		
Iris		
Anterior chamber		
Lens		

Visual acuity	Right eye	Left eye
Unaided		
Pinhole		
Near vision		

Intra ocular pressure measurement by Goldman's applanation tonometer.

	Right eye	Left eye
IOP		

GONIOSCOPY (if required)

Right eye Left eye

Fundus examination.

	RIGHT EYE	LEFT EYE
DISC		
BACKGROUND		
BLOOD VESSEL'S		
MACULA		

PERIMETRY (In selective patients only)

STUDY SUBJECT CONSENT STATEMENT:

I confirm that Dr. Prashant. M. Koranmath has explained to me the purpose of research, the study procedure, that I will undergo and the possible discomforts as well as benefits that I may experience in my own language. I have been explained all the above in detail in my own language and I understand the same. Therefore, I agree to give consent to participate as a subject in this research project.

_____ _____

(Participant) Date

_____ _____

(Witness to signature) Date

INJURY STATEMENT:

I understand that in the unlikely event of injury to me resulting directly from my participation in this study, if such injury were reported promptly, the appropriate treatment would be available to me. But, no further compensation would be provided by the hospital. I understand that by my agreements to participate in this study and not waiving any of my legal rights.

I have explained to _____the purpose of the research, the procedures required and the possible risks to the best of my ability.

_____ _____

Dr.Prashant.M.Koranmath. Date

(Investigator)

KEY TO MASTERCHART.

Sl.no – Serial number.

opd/ipd no – Out patient department/inpatient department.

T/H – Treatment history.

Conj – Conjunctiva.

RRR – Round regular reactive.

A/C – Anterior chamber.

DV – Distant vision.

P/H – Pinhole.

NV – Near vision.

IOP – Intraocular pressure.

WNL – within normal limits.

Gr1HTNR – Grade 1 hypertensive retinopathy.

Gr2HTNR – Grade 2 hypertensive retinopathy.

Gr3HTNR – Grade 3 hypertensive retinopathy.