"CORRELATION OF VISUAL FIELD DEFECTS TO OPTIC DISC DAMAGE IN PRIMARY OPEN ANGLE GLAUCOMA"

By

DR. SHIREEN ROKADIA

Dissertation Submitted to the
SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH
KOLAR

In partial fulfillment of
the requirements for the degree of

MASTER OF SURGERY
in
OPHTHALMOLOGY

Under the Guidance of
DR. D. KRISHNAMURTHY M.B.B.S., M.S.

DEPARTMENT OF OPHTHALMOLOGY
SRI DEVARAJ URS MEDICAL COLLEGE
Tamaka, Kolar

APRIL - 2012

Dedicated to

My *MOTHER*

Late Dr. *Shahnaz Fatima Rokadia*

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH

DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation entitled "**CORRELATION OF VISUAL FIELD DEFECTS TO OPTIC DISC DAMAGE IN PRIMARY OPEN ANGLE GLAUCOMA**" is a bonafide and genuine research work carried out by me under the guidance of **DR. D. KRISHNAMURTHY**, (M.B.B.S, D.O.M.S., M.S.) Professor, Department of Ophthalmology, Sri Devaraj Urs Medical College, Tamaka, Kolar in partial fulfillment for the award of M.S degree in Ophthalmology to be completed in 2012. This dissertation has not been submitted in part or full to any other university or towards any other degree before this below mentioned date.

Date:

Signature of the Candidate

Place: Kolar

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH

CERTIFICATE BY THE GUIDE

This is to certify that the dissertation entitled **"CORRELATION OF VISUAL FIELD DEFECTS TO OPTIC DISC DAMAGE IN PRIMARY OPEN ANGLE GLAUCOMA"** is a bonafide research work done **by DR. SHIREEN ROKADIA** in partial fulfillment of the requirement for the degree of **MASTER OF SURGERY IN OPHTHALMOLOGY** as per regulations of **Sri Devaraj Urs Academy Of Higher Education And Research, Kolar.** I have great pleasure in forwarding this to the university.

DATE

Place: Kolar

DR. D. KRISHNAMURTHY (M.B.B.S., D.O.M.S., M.S.)

Professor, Department of Ophthalmology,

Sri Devaraj Urs Medical College,

Tamaka, Kolar

ENDORSEMENT BY THE HEAD OF THE DEPARTMENT

This is to certify that the dissertation entitled **"CORRELATION OF VISUAL FIELD DEFECTS TO OPTIC DISC DAMAGE IN PRIMARY OPEN ANGLE GLAUCOMA"** is a bonafide research work done by **DR. SHIREEN ROKADIA** under the guidance of **Dr. D. KRISHNAMURTHY**, M.B.B.S., D.O.M.S, M.S., Professor, Department of Ophthalmology, Sri Devaraj Urs Medical College, Tamaka, Kolar.

Date: **Signature of the HOD**

Place: Kolar **DR. D.KRISHNAMURTHY,** MBBS, DOMS, MS

Professor and Head

Department of Ophthalmology

Sri Devaraj Urs Medical College,

Tamaka, Kolar

ENDORSEMENT BY THE HOD, PRINCIPAL / HEAD OF THE INSTITUTION

This is to certify that the dissertation entitled **"CORRELATION OF VISUAL FIELD DEFECTS TO OPTIC DISC DAMAGE IN PRIMARY OPEN ANGLE GLAUCOMA"** is a bonafide research work done by **DR. SHIREEN ROKADIA** under the guidance of **DR. D. KRISHNAMURTHY** , M.B.B.S., D.O.M.S, M.S., Professor, Department of Ophthalmology, Sri Devaraj Urs Medical College, Tamaka, Kolar.

DR. D. Krishnamurthy, MBBS, DOMS, MS
Professor & Head
Department of Ophthalmology,
Sri Devaraj Urs Medical College,
Tamaka, Kolar

Date:
Place: Kolar

Dr. M. B. Sanikop
Principal

Date:
Place: Kolar

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION & RESEARCH

TAMAKA , KOLAR , KARNATAKA

ETHICAL COMMITTEE CERTIFICATE

This is to certify that the Ethics committee of Sri Devaraj Urs Medical College, Tamaka, Kolar has unanimously approved **DR. SHIREEN ROKADIA,** Post-Graduate student in the subject of **OPHTHALMOLOGY** at **Sri Devaraj Urs Medical College, Kolar** to take up the Dissertation work entitled **"CORRELATION OF VISUAL FIELD DEFECTS TO OPTIC DISC DAMAGE IN PRIMARY OPEN ANGLE GLAUCOMA"** to be submitted to **Sri Devaraj Urs Academy Of Higher Education And Research Tamaka , Kolar , Karnataka.**

Member Secretary

Sri Devaraj Urs Medical College,

Kolar–563101

Date :

Place : Kolar

COPYRIGHT

DECLARATION BY THE CANDIDATE

I hereby declare that the Sri Devaraj Urs Academy of Higher Education and Research, Kolar shall have the rights to preserve, use and disseminate this dissertation in print or electronic format for academic / research purpose.

Date: Signature of the Candidate

DR. SHIREEN ROKADIA

ACKNOWLEDGMENT

It is with great reverence and the deepest respect that I would like to thank my teacher and guide, **DR. D. KRISHNAMURTHY M.B.B.S., D.O.M.S, M.S.,** Professor and Head, Department of Ophthalmology, Sri Devaraj Urs Medical College Tamaka, Kolar for his guidance and valuable insights during the entire period of this study and post graduation course.

I would like to express my heartfelt gratitude to my Professors, **Dr. Narendra P. Datti (MBBS, MS)** for the keen interest he has shown in my study; and **Dr. K. Kanthamani (MBBS, MS),** for their constant encouragement and suggestions throughout my postgraduation course.

I have profound admiration for my Assistant Professors, **Dr. Guruprasad, Dr. Prashanth** and **Dr. Tanuja,** for sharing their knowledge and experience with me.

I am immensely thankful to my PG Colleagues and dear friends **Dr. Tejal, Dr. Iffath**, **Dr. Poornima**, **Dr. Sarbjaya, Dr. Harsha and Dr. Anirudha** for their timely help and support.

Thanks to **Dr. M.B. Sanikop,** M.S. (Anatomy), Principal, Sri Devaraj Urs Medical College Tamaka, Kolar; and **Dr. Chandrashekhar Shetty**, M.S.(Ophthalmology), Vice Chancellor, Sri Devaraj Urs Academy of Higher

Education & Research, for letting me use the college resources and hospital facilities for my study.

I am eternally grateful to my beloved family; my parents, **Dr. Noor Mohd. Rokadia and (late)Dr. Shahnaz Fatima Rokadia** for placing their total confidence in me and also to my brother **Dr. Shoaib Rokadia** and my husband, **Dr. Faiz Muqtadir** without whose cheerful assistance, this study would not have been possible.

Last, but definitely not the least, I am filled with appreciation for all **my patients** who submitted themselves most gracefully to all examinations and whole heartedly participated in this study to make it a success.

I sincerely thank my esteemed institute Sri Devaraj Urs Medical College, Tamaka , Kolar for giving me a wonderful foundation and fountain of knowledge in the field of Ophthalmology which will stand me in good stead for the rest of my life.

Finally, I bow my head in a silent acknowledgement of all that **The Almighty** has blessed me with.

Date: **Signature of the Candidate**

LIST OF ABBREVIATIONS USED

FFA	>>	Fundus Fluorescein Angiography
HRT	>>	Heidelberg Retinal Tomography
IOP	>>	Intraocular pressure
MRI	>>	Magnetic resonance imaging
NTG	>>	Normal tension glaucoma
OH	>>	Ocular Hypertension
COAG	>>	Chronic Open Angle Glaucoma
POAG	>>	Primary Open Angle Glaucoma
RNFL	>>	Retinal Nerve Fibre Layer
OCT	>>	Optical Coherence Tomography
AVP	>>	Arterio-Venous Passage
RGC	>>	Retinal Ganglion Cells
ERG	>>	Electro-Retinogram
ONH	>>	Optic Nerve Head
DDLS	>>	Disc Damage Likelihood Scale
HPA	>>	Hodapp-Parish-Anderson

ABSTRACT

BACKGROUND: Glaucoma is characterized by progressive loss of retinal ganglion cells. Loss of optic disc neuroretinal rim tissue, defects in the nerve fibre layer and visual field defects are the clinical manifestations of glaucoma. Examination of the optic nerve is a crucial part of an evaluation for glaucoma. Traditionally cup to disc ratio has been used as an indicator for ONH status. **METHODS:** 100 eyes of 50 patients of COAG and glaucoma suspects were analysed and staged according to DDLS. Visual field testing was carried out and grading done by HPA criteria. Linear correlation, regression analysis and predictability were calculated. **OBJECTIVES**: This study was undertaken to assess the correlation of disc damage using DDLS with the visual field defects. **RESULTS:** There were 27 females and 23 males in our study with a mean age of 56.38 years. DDLS showed a coefficient correlation value of $r = 0.75$, $r = -0.62$ and $r = 4.48$ ($p<0.0001$) when plotted against HPA, MD and PSD respectively. It also had an excellent predictability compared to CDR. **INTERPRETATION & CONCLUSION:** Rim to disc ratio is a far more sensitive indicator of ON damage and superior predictor of VF defect. DDLS is an easy, inexpensive, quick method to document and manage early cases of COAG.

KEYWORDS: COAG, VFD, Armaly CDR, NRR, rim to disc ratio, Spaeth, Disc Damage Likelihood Scale, Hodapp-Parish Anderson criteria, HRT

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF PHOTOGRAPHS

INTRODUCTION

Glaucoma is a leading cause of irreversible blindness throughout the world. World Health Organization statistics, published in 1995, indicate that glaucoma accounts for blindness in 5.1 million persons, or 13.5% of global blindness (behind cataracts and trachoma at 15.8 million and 5.9 million persons, or 41.8% and 15.5% of global blindness, respectively). Worldwide, it has become the second most common cause of bilateral blindness. A 1996 study estimated the prevalence of open-angle and angle-closure glaucoma in the world by the year 2000 to be 66.8 million, with 6.7 million suffering from bilateral blindness.

CLASSIFICATION

TABLE 1: CLASSIFICATION OF THE GLAUCOMAS BASED ON INITIAL EVENTS[1]

A. Open-angle glaucomas without other known ocular or systemic disorders
    1. Chronic open-angle glaucoma
    2. Normal-tension glaucoma
B. Angle-closure glaucomas without other known ocular or systemic disorders
    1. Pupillary block glaucomas
    2. Combined mechanism glaucoma
C. Developmental glaucomas
D. Glaucomas associated with other ocular and systemic disorders.

CHRONIC OPEN-ANGLE GLAUCOMA

Among all the glaucomas, by far the most prevalent condition has been commonly referred to as primary open-angle glaucoma. Continued research, however, has suggested that the concept of primary and secondary glaucomas to be arbitrary and that the view of primary open-angle glaucoma as a single entity is no longer valid. Alternative terms that are more appropriate for this group of open-angle glaucomas are chronic open-angle glaucoma (COAG), idiopathic open-angle glaucoma, chronic simple glaucoma, and open-angle glaucoma with damage.

DEFINITION

A proposed definition of COAG is a multifactorial optic neuropathy in which there is characteristic atrophy of the optic nerve (modified from the American Academy of Ophthalmology Preferred Practice Guidelines, 2000). Within this large group of glaucomas, however, the most common form (or forms) is typically characterized by the following three criteria: (a) an intraocular pressure (IOP) consistently above 21 mm Hg in at least one eye; (b) an open, normal-appearing anterior chamber angle with no apparent ocular or systemic abnormality that might account for the elevated IOP; and (c) typical optic nerve head damage and/or glaucomatous visual field damage.

ANATOMICAL CONSIDERATIONS

Maintenance of intraocular pressure and pathophysiology of glaucoma revolves around the aqueous humour dynamics. The aqueous humour is involved with virtually all portions of the eye, although the principal ocular structures concerned

with it are ciliary body, posterior chamber, anterior chamber, angle of the anterior chamber and the aqueous outflow system. Aqueous humour is produced by the pars plicata of the ciliary body (which is forward continuation of the choroid at the ora serrata), from which it enters the posterior chamber, passes through the pupil, enters the anterior chamber and drains into the peripheral recess or angle of the anterior chamber[2].

The angle plays an important role in the process of aqueous drainage. Clinically, the angle structures can be visualized by gonioscope examination. Starting from posterior to anterior, the angle recess is formed by the following structures:

- The ciliary band

It is the posterior most landmark in the angle recess. It is formed by the anterior most part of the ciliary body between its attachment to the scleral spur and insertion of iris.

- Scleral spur

It is the posterior portion of the scleral sulcus, which usually appears as a prominent white line on gonioscopy. On it are attached ciliary body posteriorly and corneoscleral meshwork anteriorly. The scleral spur-roll is composed of 75% to 80% collagen and 5% elastic tissue[3].

- Schwalbe's line

It is a fine ridge seen just in front of the trabecular meshwork. It is formed by the prominent end of the Descemet's membrane of the cornea. It marks the anterior limit of the structures forming the angle of the anterior chamber.

- Aqueous outflow system

It includes the trabecular meshwork, Schlemm's canal, collector channels, aqueous veins and the episcleral veins[4].

- Trabecular meshwork

It is seen as a band just anterior to the scleral spur[5,6].

It is a sieve – like structure through which aqueous humour leaves the eye. It bridges the scleral sulcus and converts it into a tube, which accommodates Schlemm's canal[7]. The trabecular meshwork consists of three portions:

- Uveal meshwork

It is the innermost part of the trabecular meshwork and extends from the iris root and ciliary body to the Schwalbe's line. The arrangement of uveal trabecular bands creates irregular openings, which vary in size from 25 microns to 75 microns.

- Corneoscleral meshwork

It forms the larger middle portion and extends from the scleral spur to the lateral wall of the scleral sulcus. It consists of flat sheets of trabeculae, which are perforated by elliptical openings, which are smaller than those in the uveal meshwork (5-50 microns).

- Juxtacanalicular (endothelial) meshwork

It forms the outermost portion of the trabecular meshwork. This part of the trabecular meshwork offers the normal resistance to aqueous outflow[8].

- Schlemm's canal

This is an endothelial lined oval channel present circumferentially in the sclera sulcus[9]. The outer wall of the canal contains the numerous openings of the collector channels.

- Collector channels

These intrascleral aqueous vessels are about 25 - 35 in number and leave the Schlemm's canal at oblique angles to terminate ultimately into episcleral veins.

- Episcleral veins

Most of the aqueous vessels drain into the episcleral veins. The episcleral veins ultimately drain into the cavernous sinus via the anterior ciliary and superior ophthalmic veins.

FIGURE 1: ANGLE OF ANTERIOR CHAMBER

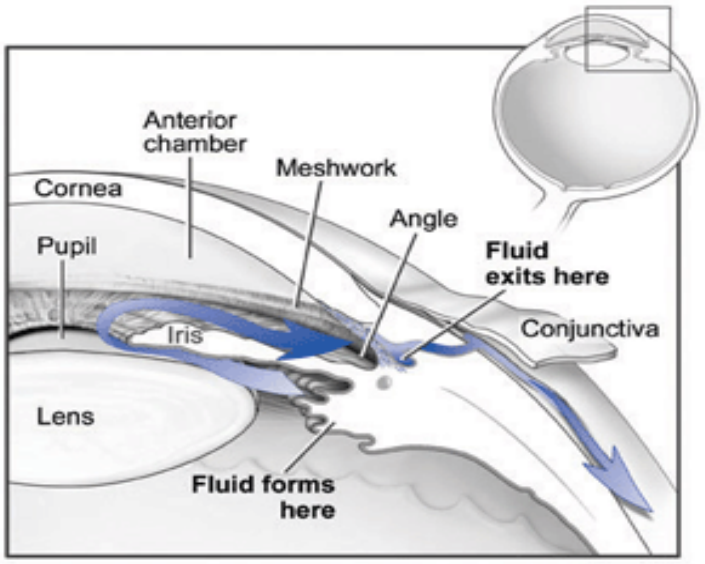
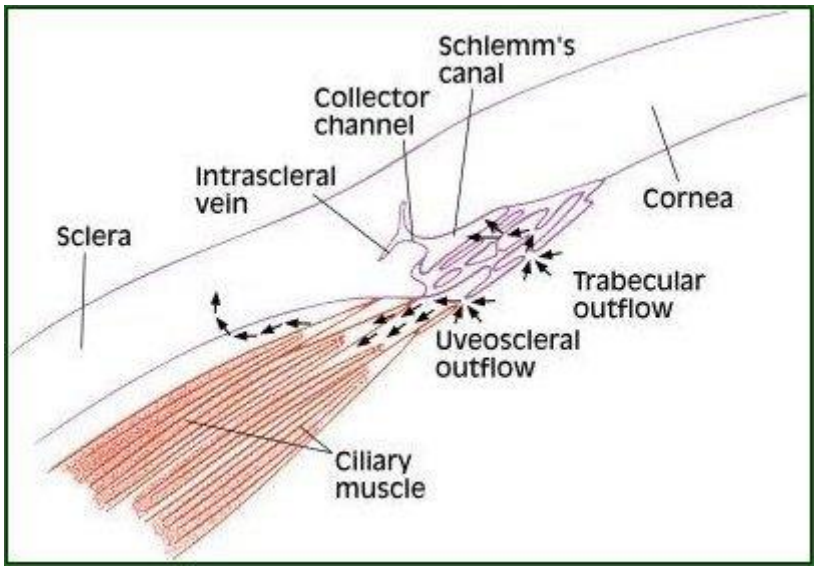


FIGURE 2: UVEOSCLERAL OUTFLOW SYSTEM



Formation of aqueous humour

The aqueous humour is primarily derived from the plasma within the capillary network of the ciliary processes[10]. The various constituents of the aqueous humour have to traverse the three tissue layers viz., the capillary wall, the stroma and the two layers of the epithelium; for reaching the posterior chamber from the plasma within the capillary network of the ciliary processes. The various substances appear to pass through these layers by the following processes[11]:

Diffusion

Diffusion is a biophysical process by which molecules of a gas or solution distribute themselves uniformly throughout the space in which they are contained, by motion of its particles. In this process, there occurs a net flux of the particles from areas of high concentration to areas of low concentration. In the process of aqueous production, the lipid soluble substances are transported by diffusion

through the lipid portions of the cell membrane of the ciliary processes[12], proportional to a concentration gradient across the membrane.

Ultrafiltration

When a solution of protein and salt is separated from plain water or a less concentrated salt solution by a membrane permeable to salt and water and not the protein, there will be a net movement of water on the protein side by diffusion and a movement of the salt away from the protein side. This process is called dialysis. Ultrafiltration refers to occurrence of dialysis under hydrostatic pressure. In the process of aqueous formation, water and water soluble substances (limited by size and charge) flow through the theoretical micropores in the protein part of the cell membrane in response to osmotic gradient or hydrostatic pressure[13].

Secretion

Secretion implies an active process that selectively transports some substances across the cell membrane. With the energy consumed, substances can be moved across a concentration gradient in a direction opposite to what would be expected by passive mechanism alone. In the process of aqueous formation, water soluble substances of larger size or greater charge are actively transported across the cell membrane[14]. This mechanism is probably mediated by globular proteins in the membrane and requires the expenditure of energy.

IDENTIFYING PATIENTS AT RISK

COAG has no associated symptoms or other warning signs before the development of advanced visual field loss. It is for this reason that public and family physician

awareness programs are needed to ensure that high-risk patients receive glaucoma assessment examinations by ophthalmologists and optometrists. Such programs must use the systemic and ocular risk factors which are commonly associated with the disease, to identify those segments of the population requiring the closest attention. In addition, once a patient has been found to have persistent IOP elevation (the most significant risk factor), but no apparent optic nerve head or visual field damage, the additional risk factors must be considered by the physician when trying to decide which of these individuals require closer observation or the initiation of therapy before definite damage occurs[15].

TABLE 2: DOCUMENTED RISK FACTORS WITH RELATIVE RISK[1]

GOOD EVIDENCE

RISK FACTOR	RELATIVE RISK
Age (per decade over 40)	2
Blacks v/s whites	4
Family history (first-degree relative)	2 – 4
Myopia	1.5 – 3
Pseudoexfoliation	5 – 10
Diastolic perfusion pressure (<55 mm Hg)	3

FAIR EVIDENCE

- Large C/D ratio
- Diabetes mellitus
- Optic disc hemorrhage

WEAK EVIDENCE

- Systolic blood pressure
- peripapillary atrophy
- migraine (for NTG)
- hypothyroidism
- sleep apnea
- autoimmune

OPEN-ANGLE GLAUCOMA MECHANISMS

The open-angle mechanisms are those in which the anterior chamber angle structures (i.e., trabecular meshwork, scleral spur, and ciliary body band) are visible by gonioscopy. The elements obstructing aqueous outflow may be located on the anterior chamber side of the trabecular meshwork (pretrabecular mechanisms), within the trabeculum (trabecular mechanisms), or distal to the meshwork, in Schlemm's canal, or further along the aqueous drainage system (posttrabecular mechanisms).

TABLE 3: CLASSIFICATION OF OPEN ANGLE GLAUCOMAS BASED ON OUTFLOW MECHANISMS[1]

A. Pretrabecular (membrane overgrowth)

1. Fibrovascular membrane (neovascular glaucoma)
2. Endothelial layer, often with Descemet-like membrane
3. Epithelial downgrowth
4. Fibrous ingrowth
5. Inflammatory membrane

B. Trabecular (occlusion of intertrabecular spaces)

1. Idiopathic
2. Clogging of the trabecular meshwork
3. Alterations of the trabecular meshwork

C. Posttrabecular

1. Obstruction of Schlemm's canal
2. Elevated episcleral venous pressure.

CLINICAL FEATURES

- *Cornea*

The cornea is typically normal in COAG. In one study, patients with cornea guttata were reported to frequently have abnormal tonographic values[16], and preliminary specular microscopic studies of patients with chronic glaucoma suggested abnormal corneal endothelium. However, a subsequent study comparing individuals with normal IOP, untreated ocular hypertension, treated ocular hypertension, or COAG revealed no significant difference in the central corneal endothelial density or central corneal thickness[17]. Most studies, however, suggest that patients diagnosed with ocular hypertension have a higher incidence of increased central corneal thickness than glaucoma or control subjects, which may cause an artifactual elevation of the IOP measurements[18]. Of greater significance, thinner central corneal thickness, implying artifactually lower IOP measurements, was shown to be a significant risk factor for development of COAG in the Ocular Hypertension Treatment Study[19].

- *Pupil*

Open-angle glaucomas may occasionally manifest as an acute attack, especially when associated with events such as inflammation, hemorrhage, or rubeosis iridis. These cases are usually readily distinguished from acute angle-closure glaucoma on the basis of the gonioscopic appearance and associated findings. Topical thymoxamine (0.5%) can often open a narrow or appositionally closed angle and lower the IOP in angle-closure glaucoma, but it cannot alter the pressure in an eye with open-angle glaucoma[20]; hence it can be used to differentiate between the two entities. Alternatively, dapiprazole, a commercially available adrenergic blocker, can be used to produce miosis. Another approach to distinguishing between closed- and open-angle glaucoma is to perform a laser iridectomy, which relieves the pressure elevation in a pure angle-closure case, but additional measures will be required if an open-angle component is present.

- *Optic Nerve Head*

The appearance of the optic nerve head and peripapillary retina is the single most important clinical feature in establishing the presence of glaucomatous damage. A helpful early finding is defects in the retinal nerve fiber layer, which may be a sign of glaucomatous optic atrophy before apparent changes are seen in the nerve head. Other early findings include enlargement of the optic dose cup, thinning or saucerizing of the neural rim, disc hemorrhages, and parapapillary atrophy.

- *Visual Abnormalities*

Central visual acuity, as measured by standard clinical tests, typically remains normal until peripheral visual field loss is advanced and therefore, is of no value

in the early detection of COAG. Preliminary evidence, however, suggests that more subtle measures of vision dysfunction, such as contrast sensitivity, color vision, and motion perception may one day be useful as early indicators of visual dysfunction before the development of typical visual field loss. Once typical glaucomatous damage to the visual field has been documented in one eye, there is a high incidence of subsequent field loss in the fellow eye[21]. The latter was reported to be 29% in 31 patients followed up for 3 to 7 years and 25% of 104 individuals after 5 years of follow-up in another series[22].

INVESTIGATIONS

- *Gonioscopy*

By traditional definition, the anterior chamber angle in eyes with COAG is open and grossly normal[23]. Preliminary studies, however, suggest that these patients may have more iris processes, a higher insertion of the iris root, more trabecular meshwork pigmentation, and a greater than normal degree of segmentation in the pigmentation of the meshwork[24].

- *Intraocular Pressure*

As previously noted, part of the definition of COAG is an IOP greater than 21 mm Hg before treatment. Even though an elevated IOP is only one of several risk factors for the development of COAG, it is a causative risk factor and most studies agree that it is the single most important risk factor.

- *Visual Field Test*

The current generation of computerized perimeters allows placement of stimuli of varying sizes, intensities, and colors into backgrounds of varying intensities, and they accurately chart the patient's responses. A wide variety of test and interpretation protocols are in use, and more are being developed continually. A few disease-specific protocols have also been standardized against groups of patients with the target condition.

AIMS AND OBJECTIVES:

To evaluate correlation of optic nerve damage using disc damage likelihood scale to visual field defects in Chronic Open Angle Glaucoma.

REVIEW OF LITERATURE

HISTORY OF GLAUCOMA

In the Hippocratic Aphorisms the term glaucoma was used to describe blindness coming on in advanced years associated with a glazed appearance of the pupil.

The first suggestion of a disease associated with a rise in intraocular pressure, corresponding to what is now known as glaucoma, seems to occur in the Arabian writings of At-Tabari (tenth century) who wrote in the "Book of Hippocratic treatment" of a chronic inflammatory condition of the eye with raised tension, and of Sams-ad-Din (1348) of Cairo, who, among the one hundred and fifty three diseases of the eye and its adnexa, described with the ophthalmias a "migraine of the eye" or "headache of the pupil", an illness associated with pain in the eye, hemicrania and dullness of the humours, and followed by dilatation of the pupil and cataract, if it became chronic, tenseness of the eye and blindness supervened.[25]

It was not until the beginning of the nineteenth century that Antoinne-Pierre Demours (1818) gave the first excellent description of glaucoma with a raised ocular tension in a treatise. The clinical picture was fully detailed and he described for the first time the appearance of the colours of a rainbow around the lights. In London, Guthrie GJ recognized hardness of the eye as a characteristic of a disease, which he termed 'Glaucoma'.

The next epoch in the history of glaucoma followed the introduction of the ophthalmoscope, when clinical observation on the glaucomatous cup began to accumulate. The disease was divided into three categories - acute, chronic and secondary by Von Graefe (1857). For some decades thereafter the general concept

prevailed that primary glaucoma of all types was due to an obstruction to the drainage of aqueous humour, most commonly due to formation of peripheral anterior synechiae.

With the advent of the gonioscope, various others pointed out that glaucoma could be divided into two types, one with an open angle and other with closed angle.

EPIDEMIOLOGY

FREQUENCY AMONG THE GLAUCOMAS

COAG is clearly the most common single form of glaucoma, although it is difficult to precisely establish the proportion of individuals with this disorder to the total number of patients with all forms of glaucoma. In a British survey of 4,231 individuals between the ages of 40 and 75 years, one third of the glaucoma population or 0.28% of the general population had COAG[26]. However, in a study of 8,126 subjects in Japan who were at least 40 years of age, open-angle glaucomas accounted for 73% of the glaucomas detected (exclusive of ocular hypertensives), of which the majority were NTG[27]. In another selective population based survey conducted in Andhra Pradesh, India in 2000, 1399 subjects over the age of 40 years were examined and the overall incidence of glaucoma was found to be 3.7%, out of which 2.6% were COAG[28]. In a 2003 study of 5150 patients in Tamil Nadu, 2.5% was the total prevalence of glaucoma, out of which 1.7% had COAG. These epidemiologic surveys will obviously be influenced by the population being studied, as well as the methods and criteria used to identify patients with glaucoma.

PREVALENCE WITHIN GENERAL POPULATIONS

Glaucoma afflicts more than 67 million people worldwide, of whom about 10% or 6.6 million are estimated to be blind. It is the leading cause of irreversible blindness worldwide and is second only to cataracts as the most common cause of blindness overall[29]. Glaucoma is responsible for 14% of all blindness[30]. In the United States, COAG affects more than 2.2 million persons and this number is projected to increase to 3.4 million persons by 2020[31]. Over the same time period in the developing world, the percentage increase in numbers of individuals with glaucoma is expected to be even more dramatic as the older-than-60-year-old population more than doubles. Several large surveys have been conducted to determine the number of patients with ocular hypertension and COAG within a population at a given time[32]. The prevalence of glaucoma in persons older than 40 years is between 1% and 2% in most studies, although reports again vary considerably according to the population being studied, the diagnostic criteria, and the screening techniques.

CLINICAL SPECTRUM

One group of investigators has described two conditions: (a) senile sclerotic glaucoma, which is seen in the elderly, with relatively low IOPs and normal-appearing anterior chamber angles, and (b) high-tension glaucoma, which occurs in a younger population, with high pressures and signs of developmental abnormalities of the angle. A third variation may be normal-tension glaucoma (NTG), in which untreated IOP never exceeds the statistical norm[33]. It is in the latter patients that the pressure-independent causative factors, such as vascular or structural defects of the

optic nerve head, or factors promoting ganglion cell apoptosis most likely play their biggest role[34]. However, even in NTG, a relative IOP elevation appears to play a role in its pathogenesis. As our understanding of the molecular genetic basis of the glaucomas continues to expand, it is likely that a large number of separate conditions will eventually be recognized, conditions that are now included in the chronic open-angle glaucoma category.

It is likely that COAG represents a spectrum of disorders in which several causative factors, of which IOP is one, have varying degrees of influence. One group of investigators has described two subgroups of COAG[35]. The first of these, which they refer to as senile sclerotic glaucoma, is seen in older adults with relatively low IOP and normal anterior chamber angles, whereas the second, COAG glaucoma, occurs in a younger age group with high IOP and which, in some cases, may have signs of developmental abnormalities of the angle. The two groups are also distinguished by the nature of the optic atrophy and the appearance of the peripapillary retina and choroid. In another study, a population of COAG patients revealed two statistically distinct groups: a smaller group with evidence of vasospastic abnormalities and a high correlation between mean deviation index of visual field severity and the highest IOP, and a larger group with evidence of coagulation and biochemical abnormalities, but no correlation between the field index and highest IOP[36].

SIGNIFICANCE OF INTRAOCULAR PRESSURE

The commonly used IOP level of 21 mm Hg is based on the concept that 2 standard deviations (SD) above the mean within a gaussian distribution for the Caucasian

population represents the upper limit of normal for that biologic parameter. However, because the distribution of IOP in the general population is skewed to the right, or to higher pressures, this principle provides only a rough approximation of the normal limits. More importantly, many eyes will not develop glaucomatous optic atrophy or visual field loss, at least not for long periods of time, despite having IOP well above 21 mm Hg, whereas others will suffer progressive glaucomatous damage at pressures that are never recorded to exceed this level. These latter observations have brought into question the role of IOP in the mechanism of COAG. Even though many studies have confirmed a correlation between the level of IOP and the rate of visual field loss in some groups of patients with COAG, this correlation is not seen in all cases[37]. Leske in 2001 and Le in 2003 found that the relative risk of glaucoma increased from 3 times in IOP 19-21 mm Hg to 13 times in IOP 22-29 mm Hg and 40 times above 30 mmHg. Other causative factors figure into the formula for glaucomatous damage, which appears to explain the lack of absolute correlation between IOP and the development of COAG[38]. In any case, this discrepancy between IOP level and glaucomatous damage has led to the use of additional terms within the general category of COAG.

OCULAR HYPERTENSION OR GLAUCOMA SUSPECT

Patients who have the first two criteria for COAG (i.e., an IOP above 21 mm Hg for which there is no apparent cause), but whose optic nerve heads and visual fields are normal are commonly said to have ocular hypertension[39]. Chandler and Grant suggested the term early open-angle glaucoma without damage for this condition[40],

whereas Shaffer preferred the term glaucoma suspect[41]. The latter term may also include other risk factors for glaucoma, such as suspicious optic nerve heads.

NORMAL-TENSION GLAUCOMA

At the other end of the spectrum with regard to susceptibility to IOP are those patients with open, normal-appearing anterior chamber angles, who have glaucomatous optic nerve head and visual field damage despite pressures that have never been documented above 21 mm Hg. These patients are said to have normal-tension glaucoma[42] (NTG). The term low-tension glaucoma has also been used, although the IOP in these individuals is usually normal or high normal and is rarely below normal. The criteria used to define NTG over the past 25 years have been highly variable. Some investigators believe that NTG is a variant of COAG, whereas others believe that the mechanism of optic atrophy in the two conditions is different. Although a number of differences between the two disorders have been described, COAG and NTG appear to represent a continuum of glaucomas in which the mechanism of the glaucomatous optic neuropathy shifts from predominantly elevated IOP in the former to additional IOP- independent factors in the latter, with considerable overlap of causative factors[43].

NATURAL HISTORY OF VISUAL FIELD LOSS IN COAG

Leydhecker studied the distribution of IOP and glaucomatous visual field loss in a large population survey[44]. When persons with pressures higher than 20 mm Hg and those with definite glaucomatous field defects were plotted against their age, the

two slopes were parallel and separated horizontally by 18 years, which led to the notion that 10 to 20 years may elapse between the onset of ocular hypertension and the development of visual field loss. Lichter and Shaffer, however, found that field loss in a population of 378 ocular hypertensives, observed for a period averaging 12¾ years, occurred earlier than Leydhecker suggested, even though most were being treated during that time[45]. The level of IOP appears to influence the rate of visual field loss. In one study of 177 untreated COAG patients comparing the mean age of presentation with the degree of field loss, it was estimated that untreated disease is likely to progress from early to end-stage visual field loss in 14.4 years at pressures of 21 to 25 mm Hg, in 6.5 years at 25 to 30 mm Hg, and in 2.9 years at pressures over 30 mm Hg[46]. Furthermore, once field loss has occurred, further damage tends to progress more rapidly than in the fellow undamaged eye exposed to the same IOP, which appears to reflect the increased susceptibility of the damaged eye[47,48].

The natural course of NTG was evaluated in the Collaborative Normal Tension Glaucoma Study during the time interval before randomization and in those patients assigned not to receive treatment[49]. About one third of patients showed confirmed localized visual field progression at 3 years, and about one half showed further deterioration at 7 years. The change was typically small and slow, often insufficient to measurably affect the mean deviation index, and there was tremendous variability in progression rates, with women and individuals with migraine having a greater risk for progression.

CLINICAL APPEARANCE OF OPTIC NERVE HEAD

MORPHOLOGY OF THE NORMAL OPTIC NERVE HEAD

To recognize pathologic alterations of the optic nerve head, one must first be familiar with the wide range of normal variations.

1. General Features

The ophthalmoscopic appearance of the optic nerve head is generally that of a vertical oval, although there is considerable variation in size and shape[50]. The central portion of the disc usually contains a depression, the cup, and an area of pallor, which represents a partial or complete absence of axons, with exposure of the lamina cribrosa. Even though the size and location of cup and pallor are normally the same, this is not always the case, especially in disease states and these two parameters should not be thought of as being synonymous[51]. The tissue between the cup and disc margins is referred to as the neural rim. It represents the location of the bulk of the axons and normally has an orange-red color because of the associated capillaries. Retinal vessels ride up the nasal wall of the cup, often kinking at the cup margin before crossing the neural rim to the retina.

2. Physiologic Neural Rim

By tradition, more is said about the cup than the neural rim of both normal and glaucomatous optic nerve heads. However, it is actually alterations in the neural rim of an eye with glaucoma that leads to changes in the cup as well as to loss of visual field[52]. The cup/disc ratio (C/D) is only an indirect measure of the amount of neural tissue in the optic nerve head and may be misleading, because a larger diameter of

the nerve head may be associated with a thinner neural rim width and larger cup size, despite a stable number of axons[53]. It is important, therefore, to pay close attention to the appearance of the neural rim.

The neural rim of the normal optic nerve head is typically broadest in the inferior quadrant, followed by the superior and then the nasal rims, with the temporal rim being the thinnest[54,55]. Several studies have attempted to correlate the area of the neural rim with that of the disc, and there is general agreement that the two are positively correlated, that is larger discs have larger neural rim areas[56]. However, the contour of the cup influences this correlation, in that the relative rim area is typically larger in discs with flat temporal sloping than in those with circular steep cups. The increase in neural rim area with increasing disc area appears partly to be due to a greater number of ganglion cell axons.

There are several factors that can interfere with the interpretation of the neural rim width. A slate gray crescent in the optic nerve head has been described and located in the temporal or inferotemporal periphery of the neural rim[57]. It is more common in blacks and apparently represents a variation of the normal anatomy. However, mistaking the gray crescent for a peripapillary pigmented crescent could result in the physiologic neural rim being misinterpreted as pathologically thin in that area.

Another source of error in interpreting the neural rim is the optic nerve head in myopia, in which the oblique insertion of the nerve may lead to distortion of the temporal neural rim from ophthalmoscopic view, suggesting pathologic thinning of this tissue[58]. Other features of highly myopic discs that may interfere with interpretation include a larger disc area, a shallower than usual cup, which may mask the deepening of the cup in glaucoma, and a temporal peripapillary crescent, which may be confused with peripapillary pigmentary changes that are seen more

frequently around some glaucomatous discs. The rim area appears to decline with age and with increasing IOP[59]. It has also been observed that patients with diabetes mellitus may have an increase in the neural rim over time, which the authors thought could be due to nerve swelling[60].

PATHOPHYSIOLOGY OF GLAUCOMATOUS DAMAGE OF OPTIC NERVE

THEORIES

The pathogenesis of glaucomatous optic atrophy has remained a matter of controversy since the mid-19th century when two concepts were introduced in the same year. In 1858, Muller proposed that the elevated IOP led to direct compression and death of the neurons (the mechanical theory); while von Jaeger suggested that a vascular abnormality was the underlying cause of the optic atrophy (the vascular theory). In 1892, Schnabel proposed another concept in the pathogenesis of glaucomatous optic atrophy, suggesting that atrophy of neural elements created empty spaces, which pulled the nerve head posteriorly (Schnabel's cavernous atrophy).

Initially, the mechanical theory received the greatest support. This concept held sway through the first quarter of the 20th century until LaGrange and Beauvieux popularized the vascular theory in 1925. In general, this belief held that glaucomatous optic atrophy was secondary to ischemia, whether as the primary result of the elevated IOP or an unrelated vascular lesion. In 1968, however, the role of axoplasmic flow in glaucomatous optic atrophy was introduced, which revived support for the mechanical theory, but did not exclude the possible influence of ischemia.

EVIDENCE

Continued investigation into the pathogenesis of glaucomatous optic atrophy has led to the following bodies of information:

A. ANATOMIC AND HISTOPATHOLOGIC STUDIES

Histopathologic observations of human eyes with glaucoma provide the most direct method of studying the alterations associated with glaucomatous optic atrophy, although they do not fully explain the mechanisms that caused the damage. More recent studies, which have attempted to correlate clinical observations with histopathologic changes in optic nerve heads from eyes with varying stages of glaucoma, appear to clarify many of these points.

a. Glial alterations

It was once suggested that loss of astroglial supportive tissue precedes neuronal loss[61], which was thought to explain the early and reversible cupping in infants[62]. However, subsequent studies have shown that glial cells are not selectively lost in early glaucoma and are actually the only remaining cells after loss of axons in advanced cases.

b. Vascular alterations

It was also once proposed that loss of small vessels in the optic nerve head accompanies atrophy of axons, and one histologic study suggested a selective loss of retinal radial peripapillary capillaries in eyes with chronic glaucoma[63]. However, subsequent investigations revealed neither

a correlation between atrophy of this vascular system and visual field loss nor a major selective loss of optic nerve head capillaries in human eyes with glaucoma. In animal models of optic atrophy, the resulting disc pallor was not associated with a decrease in the ratio of capillaries to neural tissue, although the caliber of the vessels diminished[64,65]. Instead, these studies showed a proliferation or reorganization of glial tissue, which obscures ophthalmoscopic visualization of the vessels.

c. Alterations of lamina cribrosa

Backward bowing of the lamina cribrosa has long been recognized as a characteristic feature of late glaucomatous optic atrophy, as well as an early change in the infant eye with glaucoma[66]. Further study, however, has suggested that alterations in the lamina may actually be a primary event in the pathogenesis of glaucomatous optic atrophy. In enucleated human eyes, acute IOP elevation caused a backward bowing of the lamina, and similar changes have been observed in primate glaucoma models. Most of the posterior displacement occurred in the peripheral lamina cribrosa, corresponding to the region of early axonal loss. In a histopathologic evaluation of 25 glaucomatous human eyes, compression of successive lamina cribrosa sheets was the earliest detected abnormality, and backward bowing of the entire lamina occurred later and involved primarily the upper and lower poles. In the early stages of adult glaucoma, the magnitude of backward bowing may be enough to produce a pressure gradient along the axoplasm of exiting optic nerve axons, challenge the circulation, and cause compression of the axons[67]. It has

been suggested that the structure of the lamina cribrosa may be an important determinant in the susceptibility of the optic nerve head to damage from elevated IOP.

The extracellular matrix of the lamina cribrosa may play an important role in the progression of glaucomatous damage[68]. Elastin, which is the major protein of elastic fibers and responsible for elastic recoil, appeared curled instead of straight and seemed disconnected from other elements of the connective tissue matrix in glaucomatous eyes of humans and monkeys. These changes may be secondary to long-standing elevation of IOP and may modify the course of glaucomatous optic atrophy[69].

d. Axonal alterations

The actual cause of early optic nerve head cupping in glaucoma is loss of axonal tissue. Experimental models of primate eyes exposed to chronic IOP elevation suggest that the damage is associated with a posterior and lateral displacement of the lamina cribrosa, which compresses the axons. The damage first involves axonal bundles throughout the nerve with somewhat greater involvement of the inferior and superior poles. With continued nerve damage, the susceptibility of the polar zones becomes more prominent. Histologic studies of both monkey and human optic nerves indicate that nerve fibers larger than the normal mean diameter atrophy more rapidly in glaucomatous eyes, although no fiber size is spared from damage. This preferential loss of large fibers appears to be due to a higher proportion of the fibers in the inferior and superior poles, as well as an inherent susceptibility to injury by glaucoma. In the retina

of glaucomatous monkey eyes, there is also a selective loss of the larger ganglion cells in both the mid-periphery and fovea. The same animal studies suggest that RGCs in glaucoma die by apoptosis, characterized histologically by chromatin condensation and intracellular fragmentation and a significant decrease of corpora amylacea, (which are homogeneous oval bodies believed to correlate with axonal degeneration), in RGCs and the optic nerve of human eyes with advancing stages of glaucoma.

B. BLOOD FLOW STUDIES

Blood flow measurements in the optic nerve head of human eyes using laser Doppler demonstrated autoregulatory compensation to reduced perfusion pressure secondary to elevated IOP[70]. In glaucomatous eyes, Doppler studies show reduced flow velocity in the nerve head[71]. Blood flow of the optic nerve head lamina and rim area is decreased with increasing glaucomatous damage.

A technique of continuously monitoring disc brightness during and after an abrupt artificial elevation of IOP also showed that the extent to which a glaucomatous eye can adjust to the pressure changes is significantly reduced from that of nonglaucomatous eyes. Age may influence the vascular responses to IOP. One study showed that major retinal vessels at the disc border increased in caliber in response to IOP reduction in patients with open-angle glaucoma who were 55 years or younger, but not after that age. It may be, therefore, that ischemia of the optic nerve head in glaucoma involves faulty autoregulation, which may worsen with age.

C. FLUORESCEIN ANGIOGRAPHY

The normal fluorescein pattern[72,73] of the optic nerve head is usually described as having three phases:

- An initial filling, or preretinal arterial, phase is thought to represent filling of the prelaminar and lamina cribrosa regions by the posterior ciliary arteries. Fluorescein in the retrobulbar vessels may also contribute to this phase.
- The peak fluorescence, or retinal arteriovenous phase, is primarily due to filling of the dense capillary plexus on the nerve head surface from retinal arterioles. With increasing age, there is a decrease in the filling time of both the retinal and choroidal circulations.
- A late phase consists of 10 to 15 minutes of delayed staining of the nerve head, which is probably due to fluorescein in the connective tissue of the lamina cribrosa. Tracer studies in monkeys suggest the leakage may come from the adjacent choroid.

i. Effect of artificially elevated intraocular pressure

The effect of artificially elevated IOP on the fluorescein angiographic pattern has provided an understanding of the relative vulnerability of ocular vessels to elevated pressure in the normal and glaucomatous eye[74]. There is a general delay in the entire ocular circulation in response to an elevation of the IOP. The vasculature of prelaminar portion of the nerve head appears to be the most vulnerable portion.

Studies regarding the vulnerability of the peripapillary choroid to IOP elevation have provided conflicting results. Fluorescein angiography human eyes with

glaucoma have shown delays in peripapillary choroidal filling which appear to be sensitive to elevated IOP. However, histopathologic observations in most studies of monkey and normal human eyes have shown the choroidal circulation in general to be more vulnerable than that of the retina to elevated IOP, although one study found the two systems to fill at the same level of increased pressure. Regional differences in circulation of the optic nerve head, retina, and peripapillary choroid have been reported.

ii. Studies of glaucomatous eyes

Fluorescein angiographic studies of glaucomatous and nonglaucomatous eyes have revealed two types of filling defects[75] of the optic nerve head: (a) persisting hypoperfusion and (b) transient hypoperfusion.

Persisting hypoperfusion, or absolute filling defects, are more common in eyes with glaucoma, especially low- tension glaucoma, and are said to correlate with visual field loss. The characteristics of a filling defect include decreased blood flow, a smaller vascular bed, narrower vessels, and increased permeability of the vessels. The filling defect may be either focal or diffuse. The former is thought to reflect susceptible vasculature with or without elevated IOP and is the typical defect in low-tension glaucoma. *Focal defects* occur primarily in the inferior and superior poles of the optic nerve head. In glaucomatous eyes, they are most often seen in the wall of the cup, whereas in normal eyes they occur more commonly in the floor of the cup. The *diffuse defect* is thought to represent prolonged pressure elevation[76].

The nature of the defect in open-angle glaucoma is thought to be specific, and it has been suggested that fluorescein angiography of the optic nerve head may help to differentiate open-angle glaucoma from other conditions that have similar clinical changes in the optic disc. Computed image analysis has been used to objectively quantify fluorescein angiograms of the optic disc and has shown that increases in fluorescein-filling defect areas correlate with glaucomatous progression.

D. AXOPLASMIC FLOW

a) Physiology of axoplasmic flow

Axoplasmic flow, or axonal transport, refers to the movement of material (axoplasm) along the axon of a nerve (the dendrite may also have transport) in a predictable, energy-dependent manner[77]. This movement has been characterized as having fast and slow components, although numerous intermediate rates may also exist. The fast phase moves approximately 410 mm/day in various species and may supply material to synaptic vesicles, the axolemma, and agranular endoplasmic reticulum of the axon; the slow phase moves at 1 to 3 mm/day and is believed to subserve growth and maintenance of axons. The flow of axoplasm may be orthograde (from retina to lateral geniculate body) or retrograde (lateral geniculate body to retina).

b) Experimental models of axoplasmic flow

Animal models (usually in monkeys) have been developed for studying axoplasmic flow by injecting radioactive amino acids, such as tritiated leucine, into the vitreous. The amino acid is incorporated into the protein synthesis of RGCs and then moves down the ganglion cell axon into the optic nerve, allowing histologic study of the orthograde movement of radioactively labeled protein[78]. In addition, retrograde flow can be studied by observing the accumulation of certain unlabeled neuronal components such as mitochondria by electron microscopy or by injecting tracer elements such as horseradish peroxidase into the lateral geniculate body and studying its movement toward the retina[79]. These models can be used to study factors that cause abnormal blockade of axoplasmic flow, which may relate to glaucomatous optic atrophy in the human eye.

c) Influence of intraocular pressure on axoplasmic flow

Elevated IOP in monkey eyes causes obstruction of axoplasmic flow at the lamina cribrosa and the edge of the posterior scleral foramen. It is also preferentially decreased in the magnocellular layers of the dorsal lateral geniculate nucleus, to which the large RGCs project. The obstruction in general involves both the fast and slow phases, as well as the orthograde and retrograde components. In monkey eyes, the obstruction to fast axonal transport preferentially involves the superior, temporal, and inferior portions of the optic nerve head. The height and duration of pressure elevation influence the onset,

distribution, and degree of axoplasmic obstruction in the optic nerve head. The mechanism by which elevated IOP leads to obstruction of axoplasmic flow is uncertain, but there are two popular theories: mechanical and vascular[80].

The *mechanical theory* suggests that physical alterations in the optic nerve head, such as a misalignment of the fenestrae in the lamina cribrosa due to its back bowing, may lead to the axoplasmic flow obstruction. In support of this hypothesis is the observation that elevated IOP leads to blockage of axonal transport despite an intact nerve head capillary circulation and an elevated arterial $Po_{2.}$ Furthermore, obstruction of axoplasmic flow has also been reported in response to ocular hypotony leading some investigators to suggest that a pressure differential across the optic nerve head, whether due to a relative increase or decrease in IOP, causes mechanical changes with compression of the axonal bundles.

In conflict with the mechanical theory is the observation that elevated intracranial pressure in monkeys neither caused obstruction of rapid axoplasmic flow nor prevented it in response to elevated IOP, despite reduction in the pressure gradient across the lamina. This suggests that more than a simple mechanical or hydrostatic mechanism may be involved. It has been observed that axon damage is diffuse within bundles, rather than focal as might be expected with a kinking effect, and the location of transport interruption does not correlate with the cross-sectional area of fiber bundles, the shape of the laminar pores, or the density of interbundle septa.

The *vascular theory* suggests that ischemia at least plays a role in the obstruction of axoplasmic flow in response to elevated IOP. Interruption of the short posterior ciliary arteries in monkeys has been reported to block both slow

and fast axoplasmic flow, although it did not cause glaucomatous cupping. Central retinal artery occlusion has been associated with obstruction of both rapid orthograde and retrograde axonal transport. It has also been noted in monkey eyes with elevated IOP that leakage from microvasculature of the nerve head was associated with blockade of axonal transport at the lamina cribrosa.

Against a vascular mechanism for pressure-induced obstruction of axoplasmic flow is the observation that ligation of the right common carotid artery in monkeys, which reduced the estimated ophthalmic artery pressure by 10 to 20 mm Hg below the left side, did not significantly affect the extent to which IOP elevation interrupted axonal transport. When obstruction to retrograde axoplasmic flow was studied in rat eyes, a direct relationship with IOP was still found, even though the influence of the blood circulation was removed and the lamina cribrosa is only a single laminar sheet.

It may be, therefore, that factors other than, or in addition to, ischemia and kinking of axons by a multilayered lamina cribrosa are involved in the IOP-induced obstruction to axoplasmic flow. One study has found that partial constriction of axoplasmic flow may be present at the lamina cribrosa in both orthograde and retrograde directions, and that accumulations of mitochondria at that level were more common in unmyelinated axons than in adjacent, myelinated axons[81]. The authors suggested that the constriction may be a factor in glaucoma wherein IOP is not elevated.

E. ELECTROPHYSIOLOGIC STUDIES

When the IOP is artificially elevated in normal human eyes, a significant reduction in the amplitudes of electroretinographic (ERG) components and visual-evoked potentials occurs only when the pressure approaches or exceeds the ophthalmic blood pressure[82]. However, the perfusion-pressure amplitude curve of the visual-evoked potential in normal eyes showed a kink, suggestive of vascular autoregulation, which was not observed in glaucoma patients again pointing to a possible deficiency in autoregulation in glaucoma.

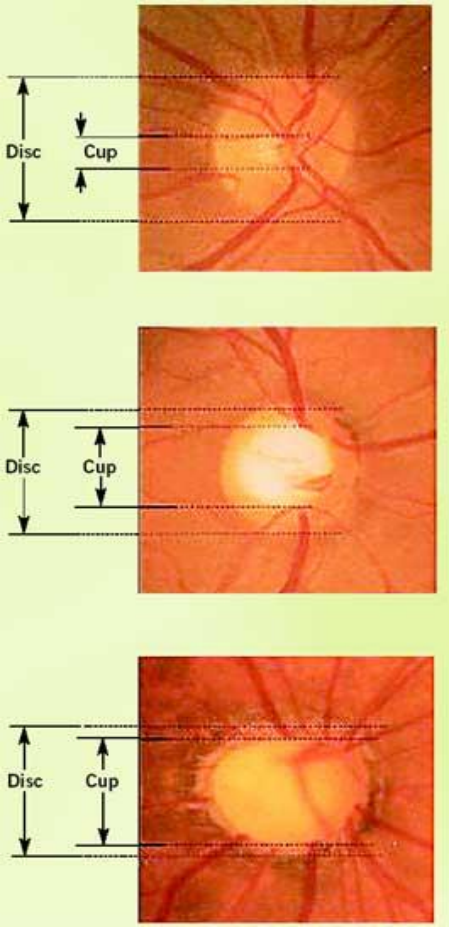
The pattern ERG is believed to originate in the RGCs and is expected to be reduced in glaucoma. Therefore, it might be used to detect ganglion cell loss, but it failed to separate glaucoma patients from healthy individuals when used alone. A study of patients with ocular hypertension showed that pattern ERG amplitude correlates with various optic disc morphometric parameters, particularly in sectors considered to be at risk for early glaucomatous damage[83].

CONCLUSIONS REGARDING PATHOPHYSIOLOGY

The present evidence suggests that obstruction to axoplasmic flow may be involved in the pathogenesis of glaucomatous optic atrophy. However, it is still not clear whether mechanical or vascular factors are primarily responsible for this obstruction, or whether other alterations are also important in the ultimate loss of axons. It may be that all of these factors are involved to some degree or (as Spaeth has suggested), that there is more than one mechanism of optic atrophy in eyes with glaucoma. For example, the observed differences in glaucomatous visual field

defects between patients with low-tension and high-tension glaucomas has led to the suggestion that ischemia may be the predominant factor in those glaucomas at the lower end of the IOP scale, whereas a more direct mechanical effect of the pressure may prevail in cases with higher IOP.

FIGURE 3: NORMAL CUP VERSUS GLAUCOMATOUS CUPPING



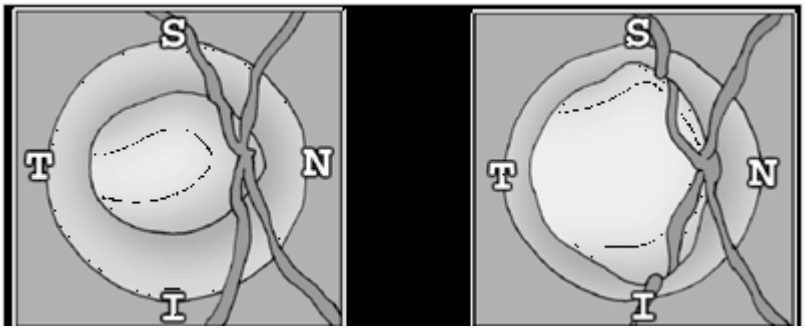
DISC DAMAGE LIKELIHOOD SCALE

The Disc Damage Likelihood Scale (DDLS) was developed by Spaeth et al to facilitate the diagnosis and management of glaucoma. The DDLS relies on the optic nerve as a direct indicator of disease[34,84].

FIGURE 4: DISC DAMAGE LIKELIHOOD SCALE

	Narrowest width of rim (rim/disc ratio)				Examples		
DDLS Stage	For Small Disc <1.50 mm	For Average Size Disc 1.50-2.00 mm	For Large Disc >2.00 mm	DDLS Stage	1.25 mm optic nerve	1.75 mm optic nerve	2.25 mm optic nerve
1	.5 or more	.4 or more	.3 or more	0a			
2	.4 to .49	.3 to .39	.2 to .29	0b			
3	.3 to .39	.2 to .29	.1 to .19	1			
4	.2 to .29	.1 to .19	less than .1	2			
5	.1 to .19	less than .1	0 for less than 45°	3			
6	less than .1	0 for less than 45°	0 for 46° to 90°	4			
7	0 for less than 45°	0 for 46° to 90°	0 for 91° to 180°	5			
8	0 for 46° to 90°	0 for 91° to 180°	0 for 181° to 270°	6			
9	0 for 91° to 180°	0 for 181° to 270°	0 for more than 270°	7a			
10	0 for more than 180°	0 for more than 270°		7b			

FIGURE 5: SCHEMATIC DIAGRAM OF NORMAL AND ABNORMAL NRR



Diagnosis

Any disc graded stage 5 or higher is unhealthy. It will almost always be pathologic, although it may not be glaucomatous. Damage from glaucoma will usually be infero- or superotemporal. DDLS scores of 1 through 3 are rarely associated with

glaucomatous visual field loss. Some individuals are born with DDLS 3 optic discs, whereas others begin with DDLS 1 discs. For this reason, noting that a person has a DDLS 3 optic disc indicates that it is reasonably healthy and that there is no visual field loss. However, this score is not proof that the disc's health has not worsened because it could have been a stage 1 or 2 in the past.

Categorization

The DDLS allows quantification of the amount of damage that the optic nerve has sustained. Visual field loss usually will not occur before stage 5. The differentiation between very early and no damage are important, because a neuroretinal rim that has already narrowed is likely to become narrower still, whereas an undamaged rim is far more likely to remain stable. An ophthalmologist may choose to defer treatment and observe closely patients with optic nerves of stages 0 through 5, because the consequences of treatment may outweigh those of non-treatment. Unless glaucomatous progression has stabilized (eg, in cases of inactive glaucoma secondary to trauma or corticosteroids), a DDLS score of 6 and above strongly supports treatment.

Monitoring

The stability of a patient's glaucoma is often best determined by evaluating the optic disc. DDLS scores on patients' charts must be noted at every examination of the fundus to assess whether their glaucoma is stable, improving, or deteriorating except when judging an intervention's effect on IOP (eg, a follow-up visit 3 weeks after the patient began using glaucoma drops).

ASSESSMENT OF VISUAL FIELDS

Advances in the technology of visual field testing have changed our clinical perception of normal and abnormal fields of vision. The two-dimensional presentation of concentric lines around the point of fixation has given way to three-dimensional displays in symbols and numerical values[85]. However, the normal field of vision and the changes created by glaucoma are just the same as they were 100 years ago when Bjerrum discovered the arcuate scotoma using the back of his consulting room door as a background for his field testing.

NORMAL VISUAL FIELD

A helpful way to begin the study of visual fields and the methods by which they are measured is to consider Traquair's classic analogy of an island of vision surrounded by a sea of blindness. This three-dimensional concept can be reduced to quantitative values by plotting lines (isopters) at various levels around the island, or by measuring the height (sensitivity) at different points within the island of vision.

a) BOUNDARIES

The shoreline of the island corresponds to the peripheral limits of the visual field, which normally measure, with maximum target stimulation, approximately 60 degrees above and nasal, 70 to 75 degrees below, and 100 to 110 degrees temporal to fixation. The typical configuration of the normal visual field, therefore, is a horizontal oval, often with a shallow inferonasal depression. The shape is usually of

greater diagnostic significance than the absolute size of the visual field, because the latter is influenced by many physiologic and testing variables.

b) CONTOUR

The peaks and valleys on the island correspond to areas of increased or decreased vision within the peripheral limits of the visual field. These contours can by mapped by recording the weakest light stimulus that can be seen at specific locations in the field of vision or by using test objects with reduced stimulus value to plot smaller isopters within the absolute boundaries. The area of maximum visual sensitivity in the normal field at photopic condition is at the point of fixation, corresponding to the foveola of the retina, and appears as a smoothly rising peak surrounded by a high plateau. The visual sensitivity then tapers down more gradually until it again falls abruptly at the peripheral limits.

c) BLIND SPOT

Nerve fibers, collecting visual information from the retina, come together approximately 10 to 15 degrees nasally from the fovea. This region corresponds to the optic nerve head and creates a deep depression within the boundaries of the normal visual field, (which is called the blind spot)[86]. As the image formed on the retina is upside down and backward, the blind spot is located temporal to fixation. The blind spot has two portions: (a) an absolute scotoma and (b) a relative scotoma. The *absolute scotoma* corresponds to the actual optic nerve head and is seen as a vertical oval. Because there are no photoreceptors in the nerve head, this portion of the blind spot is independent of the test object stimulus value. The *relative scotoma* surrounds the absolute portion and corresponds to peripapillary retina, which has

reduced visual sensitivity, especially inferiorly and superiorly. In a study correlating the blind spot size to the area of the optic disc and peripapillary atrophy, the absolute scotoma included the peripapillary scleral ring and the peripapillary zone beta whereas zone alpha was attributed to the relative scotoma.

PHYSIOLOGIC FACTORS THAT INFLUENCE VISUAL FIELDS

The following factors should be compensated for, if possible, or otherwise should be considered when interpreting the fields.

1) PUPIL SIZE

Significant miosis may depress central and peripheral threshold sensitivities and exaggerate field defects, even after correction of induced myopia. One study used neutral density filters to reduce the retinal illumination the equivalent of halving the pupillary diameter, which reduced the mean threshold with two automated perimeters by 1.1 to 1.7 dB. Another study has also shown that pilocarpine significantly worsened the visual field global indices, such as mean deviation and pattern standard deviation. Mydriasis has less influence on the visual field, although pupillary dilatation with tropicamide 1% in healthy subjects or no ocular medication was shown in one study to significantly reduce threshold sensitivity with automated perimetry.

2) AGE

Increasing age is also associated with a reduction in retinal threshold sensitivity. This effect starts as early as 20 years of age, progresses linearly throughout life,

and involves the peripheral and superior areas more than the pericentric and inferior portions of the field[87]. This age-related visual field sensitivity appears to be primarily due to neural loss rather than preretinal factors. Standard automated perimetry protocols compensate for age influence by using age-bracketed databases.

3) CLARITY OF OCULAR MEDIA

Cataracts produce glare and change the intensity of the stimulus and can cause or exaggerate central or peripheral field defects. Even minimal light scattering, caused by an early cataract may influence threshold measurements. Eyes with open-angle glaucoma and cataracts may have improvement of foveal sensitivity, and sometimes even a reversal of a scotoma, after cataract extraction[88]. However cataract surgery can also reveal mild and moderate field defects masked by cataracts. Nuclear cataracts depress central perimetric sensitivity more than peripheral sensitivity with both large and small targets, whereas nonnuclear cataracts influence central sensitivity more for small targets and peripheral sensitivity more for large targets. Attempts have been made to correlate visual field damage with lens opacity and visual acuity to aid clinicians in determining the significance of field change in patients with glaucoma and cataracts.

Reduced clarity of the ocular media from other causes, such as a corneal disturbance, a cloudy posterior lens capsule after cataract surgery, or vitreous opacities, also affect the visual fields.

4) REFRACTIVE ERROR

When the projected stimulus is not focused on the retina, the edge of the stimulus is blurred, contrast is decreased, and the stimulus may not be detected by the patient.

Refractive errors primarily influence the central field. When a size III stimulus is used, refractive errors of 1 diopter or less may not need to be corrected, as it usually causes about 1 dB of general reduction of sensitivity[89]. Mild *myopia* does not require correction, unless the refractive error exceeds 3 diopters. Posterior staphylomas can create areas of relative myopia, called refraction scotomas, which may be confused with glaucomatous field defects, but can usually be eliminated with an appropriate refractive correction. *Hyperopia* has a greater influence on perimetric results, and even small hyperopic refractive errors can significantly alter threshold sensitivity. Age tables are available to aid in determining the appropriate correction for presbyopia. A contact lens provides the best correction for the aphakic and highly myopic eyes, although spectacle correction can be used for the central 24 to 30 degrees with no correction for the peripheral field. Astigmatism should be corrected unless the cylinder is less than 1 diopter, in which case it can be included as the spherical equivalent.

5) PSYCHOLOGIC FACTORS AND FATIGUE

The patient's understanding of the test and his or her alertness, concentration, fixation, and cooperation all influence the results of visual field testing. One study found that patients with refractive errors, especially myopes, revealed a larger learning effect than did emmetropes. Another study found that moderate alcohol intake did not influence differential light sensitivity as tested by automated perimetry.

Full threshold protocols take a long time to complete, and patients usually find visual field testing exhausting. Fatigue causes artificially decreased sensitivity in the areas of existent glaucomatous defect, decreased performance in patients with

glaucoma within central 10 degrees, as well as increased deterioration of the mean defect and localized loss in the periphery.

VISUAL FIELD LOSS IN GLAUCOMA

a) PERIPHERAL LOSS

Defects along the peripheral boundaries of the visual field (i.e., peripheral nasal steps, vertical steps, and temporal sector defects) are most often found in association with scotomas in the more central arcuate area, although in some patients with early glaucomatous visual field loss, peripheral defects may be the only detectable abnormality[90,91]. With automated static perimetry, it has become common practice to measure only the central 24 to 30 degrees of the visual field, because of the increased time requirement with this technique. The question arises, therefore, as to how much information is being missed by ignoring the more peripheral portions of the field[92]. In the presence of paracentral scotomas, peripheral measurements do not appear to add significant information regarding the progression of visual field damage. In the initial diagnosis, however, a peripheral field defect, usually a nasal step, may be the only abnormality detected by automated perimetry in 3% to 11% of patients, depending on the testing method[93]. To be clinically useful, the time required to obtain this information must not add excessively to the overall testing time and further study is needed to determine whether this can be achieved with newer programs for automated perimetry.

b) LOCALIZED NERVE FIBER LAYER DEFECTS

In glaucoma, structural damage to ganglion cells and their axons causes partial or complete functional loss in the area of damaged cells. The glaucomatous process typically causes initial damage to one or more axon bundles, creating a localized visual field defect. Focal defects, due to loss or impairment of retinal nerve fiber bundles, constitute the most definitive early evidence of visual field loss from glaucoma. The nature of the nerve fiber bundle defects relates to the retinal topography of these fibers.

i. Arcuate Defects

Bjerrum described an arcuate visual defect, which he showed is strongly suggestive of glaucoma. This *arcuate scotoma* starts from the blind spot and arches above or below fixation, or both, to the horizontal median raphe, corresponding to the arcuate retinal nerve fibers. The nasal extreme of the arcuate area along the median raphe may come within 1 degree of fixation and extends nasally for 10 to 20 degrees. Early visual loss in glaucoma commonly occurs within this arcuate area, especially in the superior half, which correlates with the predilection of the inferior and superior temporal poles of the optic nerve head for early glaucomatous damage[94]. As field defects develop within the arcuate area, they most often appear first as one or more localized defects, or paracentral scotomas. The typical pattern of progression of glaucomatous visual field defects is for a shallow paracentral depression to become denser and larger, eventually forming a central absolute defect, surrounded by a relative scotoma. The relative scotoma represents fluctuation that can be seen at the border of the physiologic blind spot and

glaucomatous defects, but is significantly larger and more sloping in the latter. Occasionally, the early arcuate defect may connect with the blind spot and taper to a point in a slightly curved course, which has been referred to as a *Seidel scotoma*. As the isolated defects enlarge and coalesce, they form an arching scotoma that eventually fills the entire arcuate area from the blind spot to the median raphe, which is called an arcuate or *Bjerrum scotoma*. With further progression, a *double arcuate (or ring) scotoma* develops. The rate of visual field loss correlates with the size of the scotoma, in that, the larger the scotoma, the more rapidly it is likely to enlarge[95].

Although the arcuate defect is probably the most reliable early form of glaucomatous field loss, it is not pathognomonic[96]. The following additional causes must be considered, especially when the field and disc changes do not seem to correlate: chorioretinal lesions, optic nerve head lesions, anterior optic nerve lesions, and posterior lesions of the visual pathway.

ii. Nasal Steps

The loss of retinal nerve fibers rarely proceeds at the same rate in the upper and lower portions of an eye. Consequently, a steplike defect is frequently created where the nerve fibers meet along the median raphe. Because the superior field is involved somewhat more frequently than the inferior portion in the early stages of glaucoma, the nasal step more often results from a greater defect above the horizontal midline, which is referred to as a *superior nasal step*. However, *inferior nasal steps* are not uncommon. Nasal steps are also distinguished by their central or peripheral location. A *central nasal step* is created at the side of an unequal double arcuate scotoma closest to fixation. Unequal contraction on the peripheral side of

the defect, due to loss of corresponding bundles of peripheral arcuate nerve fibers, produces a defect that has been called the *peripheral nasal step of Ronne*. Nasal step often begins as an isolated scotoma in the nasal periphery. The shape of the peripheral nasal step with kinetic testing differs according to its distance from fixation, and is not necessarily found in all isopters. Nasal step appears to be a common defect in acute and early chronic angle- closure glaucoma.

iii. Vertical Step

A stepwise defect along the vertical midline, referred to as a vertical step or *hemianopic offset*, is a less common feature of glaucomatous field loss than the nasal step, but has been reported to occur in approximately 20% of cases. The mechanism of this field defect is not fully understood, although it may relate to segregation within the optic nerve head of axons from either side of the vertical midline. The defect more often appears on the nasal side of the vertical midline. However, studies of normal subjects have also revealed greater sensitivity temporal to the hemianopic border, and it has been suggested that a small peripheral step at the vertical midline should arouse suspicion of glaucoma only if the defect is located temporally. It also has limited diagnostic value because most are associated with other glaucomatous field changes and the main significance of the observation is in distinguishing glaucomatous vertical midline defects from those caused by neurologic lesions.

c) GENERALIZED AND CENTRAL DEPRESSION OF THE VISUAL FIELD

The increased sensitivity with which newer instruments allow evaluation of vision is changing our understanding of the natural history of progressive visual field loss in glaucoma. Although defects related to loss of retinal nerve fiber bundles are the most familiar visual field changes induced by glaucoma, and central vision is typically one of the last regions to be totally lost, studies have shown mild central and diffuse reduction in the visual field even in the early stages of glaucoma[97]. The mechanism for this is uncertain, although it appears to represent pressure-induced damage with diffuse nerve fiber loss, as evidenced by abnormal light-sense and flicker perimetry, which have been shown to accompany diffuse retinal nerve fiber layer loss[98].

Central vision is typically preserved during the early course of glaucoma, but it may rarely be affected by a localized damage involving the fixation point. In these situations, other visual functions, such as visual acuity and color vision may become abnormal. These central defects should be differentiated from macular disorders[99].

Although most studies agree that some patients with early glaucoma can have purely diffuse loss in the absence of other causes other investigators have challenged this concept, suggesting that a generalized depression in glaucoma is rare and that these patients may have other causes for the diffuse loss of perimetric sensitivity, such as media opacity, miosis, or retinal dysfunction. In any case, the diagnostic value of this finding is currently limited by its nonspecific nature, but it should still be looked for and noted in the course of visual field testing and analysis. While the measures of generalized reduction in visual function may one

day be important in the early detection of glaucoma, they are too inconsistent and nonspecific at the present time to be of highly significant clinical value[100]. In the future, they may acquire greater diagnostic significance as our knowledge of glaucomatous visual dysfunction expands. The following are some of the perimetric and other measures that can be used to evaluate generalized visual impairment in glaucoma.

a. Concentric Contraction

Generalized reduction in the visual field may become manifest as a decrease in sensitivity for specific retinal locations or as a concentric constriction of the visual field, both of which have been noted to precede other detectable glaucomatous field defects in many patients. Isopter contraction, as an early field defect of glaucoma, is often more marked in the nasal field, which has been called crowding of the peripheral nasal isopters. •

b. Enlargement of the Blind Spot

Enlargement of the blind spot, due to depression of peripapillary retinal sensitivity, is also considered to be an early glaucomatous field change. However, it may be seen with other optic nerve or retinal disorders. One example has been called acute idiopathic blind spot enlargement and is related to multiple evanescent white dot syndrome and possible other retinal diseases. Enlargement of the blind spot can also be produced in normal individuals with threshold targets, so that it is not a pathognomonic sign of glaucoma. The relative portion of the blind spot is dependent on the stimulus value and varies with different testing methods. If the temporal margin of the relative blind spot comes close to the corresponding isopter

(in kinetic perimetry), the two boundaries may artifactually become confluent, creating false baring of the blind spot. In addition, because the reduced sensitivity of the peripapillary retina is greater in the upper and lower poles, test objects with small stimulus value may cause vertical elongation of the blind spot, which can break through the isopter causing true baring of the blind spot.

c. Angioscotomata

Angioscotomata are long, branching scotomas above and below the blind spot, which are presumed to result from shadows created by the large retinal vessels. One study has shown that retinal vessels may have corresponding representation of angioscotomata in the visual cortex. Angioscotomata may represent an early glaucomatous field defect (although it is technically difficult to demonstrate) and not highly diagnostic.

d) TEMPORAL SECTOR DEFECT

Because the retinal nerve fibers nasal to the optic nerve head converge on the disc by a direct route, a lesion involving these fiber bundles produces a sector defect temporal to the blind spot. This defect usually appears later in the course of glaucomatous field loss. With automated perimetry, glaucomatous defects temporal to the blind spot are not uncommon, but usually add significant information over central field testing only in patients with late visual field loss[101].

e) ADVANCED GLAUCOMATOUS FIELD DEFECTS

The natural history of progressive glaucomatous field loss is eventual development of a complete double arcuate scotoma, which coalesce nasally at the horizontal meridian and may extend to the peripheral limits in all areas except temporally. This results in a central island and a temporal island of vision in advanced glaucoma. With continued damage, these islands of vision progressively diminish in size until the tiny central island is totally extinguished, which may occur abruptly. Glaucoma surgery appears to accelerate the loss of the small central island in some patients, possibly due to the sudden change in IOP. The frequency with which this surgical complication occurs is not large enough to constitute a contraindication to surgery in these patients. The temporal island of vision is more resistant and may persist long after central vision is lost. However, it, too, will eventually be destroyed if the glaucoma is not controlled, leaving the patient with no light perception.

HODAPP-ANDERSON-PARISH VISUAL FIELD SEVERITY SCORE(SITA 30-2)

Minimum criteria for diagnosing glaucomatous damage:

- A Glaucoma Hemifield Test outside normal limits on atleast two fields; OR
- A cluster of 3 or more non-edge points, in a location typical for glaucoma, all of which are depressed at p<1% level on 2 consecutive fields; OR
- A corrected standard pattern deviation that occurs in less than 5% of normal fields on two consecutive fields.

Any one criterion is to be fulfilled to fall into a particular grade

1) Criteria for early defect

- Mean deviation less than −6 dB
- On pattern deviation plot, <25% of points depressed below the
- 5% level and <15% of points depressed below the 1% level
- No points within central 5° with sensitivity <15 dB

2) Criteria for moderate defect

- Mean deviation worse than −6 dB but no worse than −12 dB
- On pattern deviation plot, <50% of points depressed below the 5% level and <25% of points depressed below the 1% level
- No point within central 5° with sensitivity 0 dB
- Only 1 hemifield containing a point with sensitivity <15 dB within 5° of fixation.

3) Criteria for severe defect

- Mean deviation worse than −12 dB
- On pattern deviation plot, >50% of points depressed below the 5% level or >25% of points depressed below the 1% level
- Minimum 1 point within central 5° with sensitivity 0 dB
- Both hemifields containing point(s) with sensitivity <15 dB within 5° of fixation.

CORRELATION BETWEEN OPTIC NERVE HEAD AND VISUAL FIELD DEFECTS

In most patients with glaucoma, clinically recognizable disc changes precede detectable field loss and the presence or absence of glaucomatous field defects can usually, but not always, be predicted from the appearance of the optic nerve head. Quigley and co-workers attempted to correlate axon loss in the optic nerve head with visual field defects. Although limited by small sample size, their work did suggest that, not only does nerve fiber loss occur before reproducible field defects in some patients with elevated IOP, but that the extent of axonal loss may be much greater than the corresponding visual field change. With standard perimetric techniques, 25% to 35% of the retinal ganglion cells may be lost in an eye with a normal field by the time reproducible early field defects are found and 10% or fewer axons may remain by the stage of severe field loss[102]. When correlating retinal ganglion cell atrophy with automated perimetry in glaucoma patients, a 20% loss of cells, especially large ganglion cells in the central 30 degrees of the retina, correlated with a 5-dB sensitivity loss, while a 40% loss corresponded with a 10-dB decrease, and some ganglion cells remained in areas with 0-dB sensitivity[103].

The nature of optic nerve head cupping can also be used to predict the type (in addition to the presence) of field loss. Extensive or focal absence of neural rim tissue, especially at the inferior or superior poles, is the most reliable indicator of visual field disturbance and is usually associated with a field defect in the corresponding arcuate area. In some cases, field loss may occur before the pallor reaches the disc margin and unusual cases have been reported with field damage despite round, symmetric cups. Quantitative measures of the retinal nerve fiber

layer have also been shown to correlate with the visual field loss in glaucoma patients.

The ability to predict impending glaucomatous visual field loss by the appearance of the optic nerve head is less accurate than correlating disc damage with established field loss. No single parameter or combination of parameters in glaucomatous optic atrophy has been found to be totally satisfactory for this purpose.

The parameters that correlate best with visual field loss are magnification-corrected measurements of neuroretinal rim area and defects in the retinal nerve fiber layer. Diffuse structural changes in the optic nerve head or retinal nerve fiber layer are more often associated with diffuse depression of visual function, whereas localized changes correlate more with localized visual field changes. In some cases, the early field loss associated with retinal nerve fiber layer defects can be detected with automatic perimetry.

The correlation between optic nerve head and visual field defects in glaucoma is close enough to prompt a search for other underlying disease processes, such as neurologic disorders, if a correlation is not found. Nevertheless, the absence of a perfect correlation indicates that both disc and field examinations are essential in managing the glaucoma patient. (In general, optic nerve head and retinal nerve fiber layer changes have their greatest value in the early stages of glaucoma, whereas progressive visual field loss becomes the more useful guide to therapy in advanced cases).

MATERIALS AND METHODS

Total 100 eyes of 50 patients who attended the glaucoma clinic at R.L.J. HOSPITAL AND RESEARCH CENTRE, TAMAKA, KOLAR attached to SRI DEVARAJ URS MEDICAL COLLEGE, between November 2009 and May 2011 were prospectively analysed. Patients fulfilling the selection criteria were included in the study after taking informed consent.

Inclusion criteria:

a) Primary Open Angle Glaucoma patients

b) Glaucoma suspects

Exclusion criteria:

i. Eyes with refractive error >5D from emmetropia or 2.5D astigmatism

ii. Any corneal, retinal, neurological pathology causing visual field defects

iii. Primary or secondary narrow angle glaucoma

iv. Secondary open angle glaucoma

v. H/o intra/extraocular surgery or trauma

Method of collection of data:

Patients underwent detailed ophthalmic examination including

- Detailed Ocular History.
- Detailed Family history.
- Anterior segment examination including Pupils.

- Best Corrected Visual acuity using Snellen's chart.
- Intra Ocular Tension using Applanation Tonometry.
- Gonioscopy using 4-mirror gonioscope.
- Optic Nerve evaluation using Volk +90D lens, direct ophthalmoscopy and Disc Damage Likelihood Scale staging was done.
- Visual Field analysis using Humphrey field analyser (SITA 30-2) and HPA staging was done.

THE DDLS STEP BY STEP

The pupils were dilated to allow a clear view of the fundus. Both of the patient's optic nerves were briefly examined at the biomicroscope with a +90.00 D. The graticule on the slit lamp was used to measure the vertical size in millimeters, this figure was multiplied by 1.3. We examined the optic disc for an area where its outer edge is clearly distinguished with direct ophthalmoscope. The full circumference of the outer edge and the inside edge of the neuroretinal rim were defined. The rim-to-disc ratio was estimated by comparing the width of the neuroretinal rim with that of the disc diameter on the same axis at several clock positions especially noting the area at which the rim is narrowest. When sketching, the course of blood vessels and any pertinent features of the disc (eg, notches, pallor, hemorrhage) were noted. Determine the DDLS by using your drawing of the disc, the narrowest rim-to-disc ratio. If the nerve was smaller or larger than average, it was staged as if average size and then increased by one if the nerve is small or decreased by one if large.

The patients were divided into 4 groups depending on Visual Field defects (no damage, mild, moderate, severe). These groups were then correlated with Stages (0-8) on the DDLS scale.

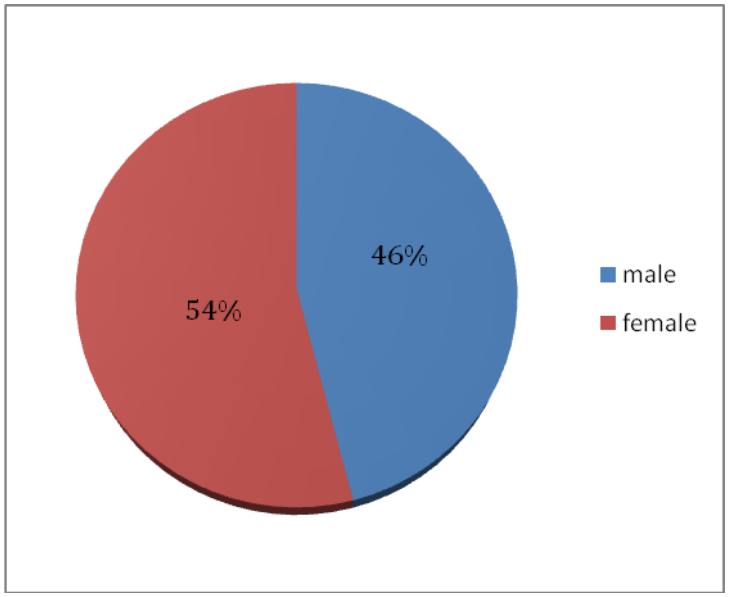
Statistical Methods: Pearson and Spearman linear analysis, Regression Analysis plots

RESULTS AND OBSERVATIONS

TABLE 4 – SEX DISTRIBUTION

Sex	No.
Male	23
Female	27

FIGURE 6 – SEX DISTRIBUTION

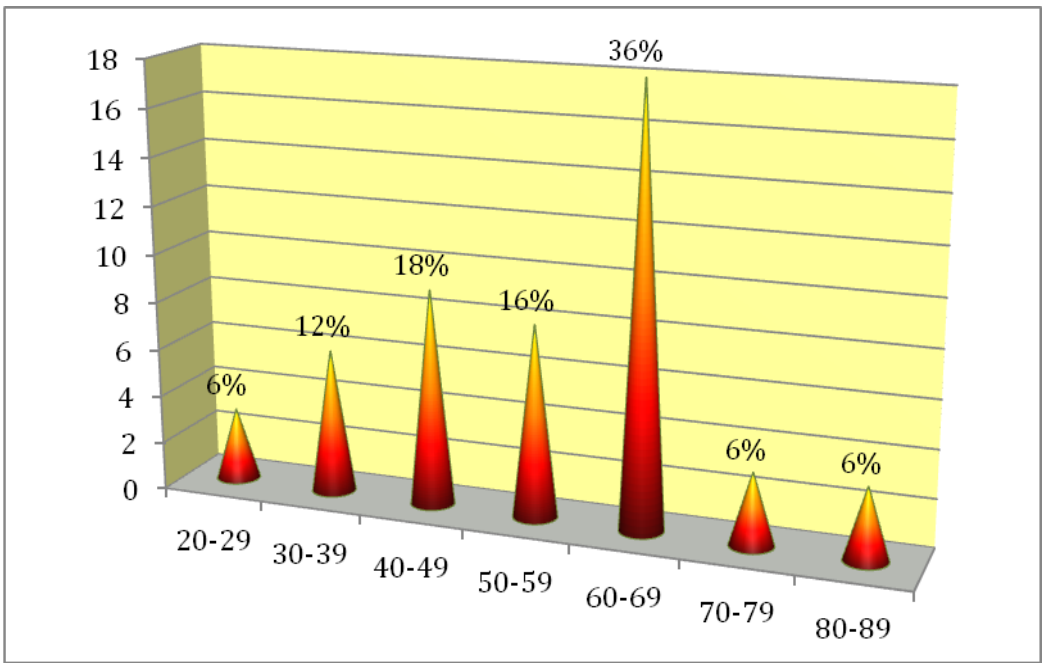


Out of a total of 50 patients, our study had 27 females and 23 males.

TABLE 5 – AGE DISTRIBUTION

Age	No. of patients
20-29	3
30-39	6
40-49	9
50-59	8
60-69	18
70-79	3
80-89	3

FIGURE 7 – AGE DISTRIBUTION

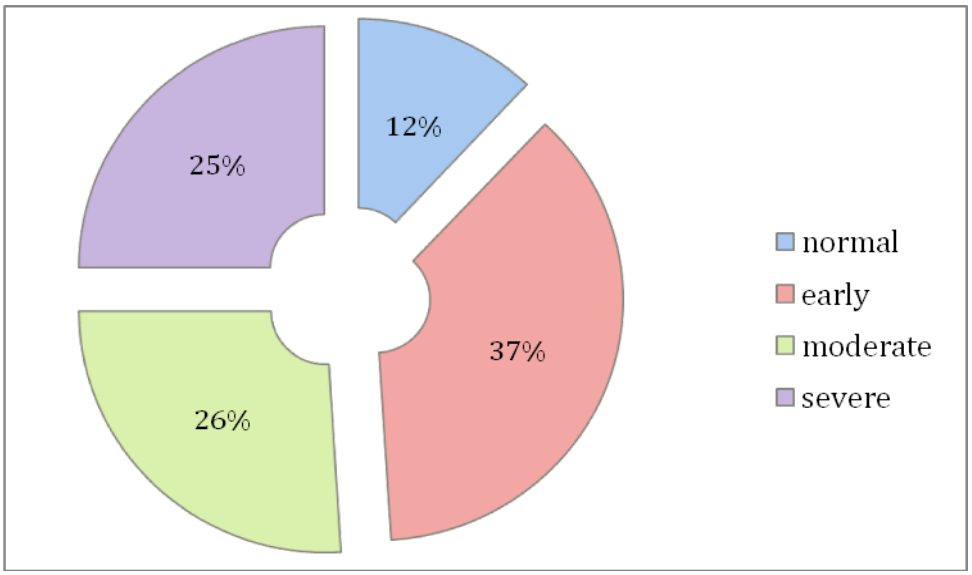


The mean age was 56.38 years, ranging from 25 years to 86 years, with 36% of patients between ages 60 - 69 years.

TABLE 6 – DISTRIBUTION OF H-P-A VISUAL FIELD DEFECT SEVERITY GRADES

HPA GRADE	No. of Eyes
normal	12
early	37
moderate	26
severe	25

FIGURE 8 – DISTRIBUTION OF H-P-A VISUAL FIELD DEFECT SEVERITY GRADES

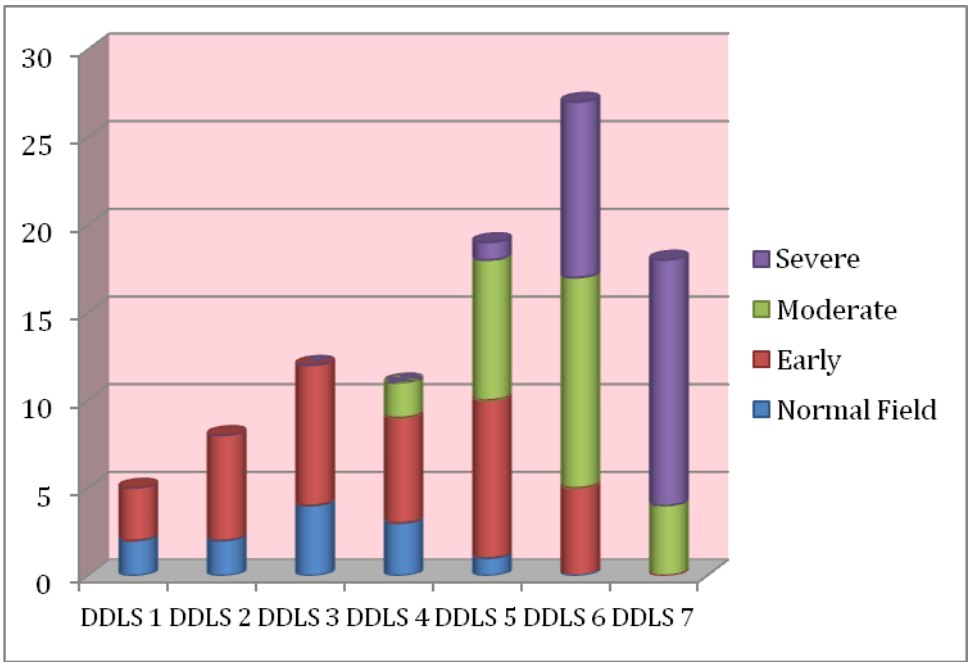


Thirty-seven eyes in our study showed Early Visual Field Defects, while Moderate and Severe were noticed almost equally (26 and 25 eyes respectively). Only 12 eyes had Normal Visual Fields at the time of examination. The grading was carried out according to the Hodapp-Parish-Anderson criteria explained previously.

TABLE 7 – CORRELATION OF DDLS STAGE TO VISUAL FIELD DEFECT

DDLS GRADE	Normal VF	Early FD	Moderate FD	Severe FD
DDLS 1	2	3	0	0
DDLS 2	2	**6**	0	0
DDLS 3	**4**	**8**	0	0
DDLS 4	**3**	**6**	2	0
DDLS 5	1	**9**	**8**	1
DDLS 6	0	5	**12**	**10**
DDLS 7	0	0	**4**	**14**

FIGURE 9 – CORRELATION OF DDLS STAGE TO VISUAL FIELD DEFECT

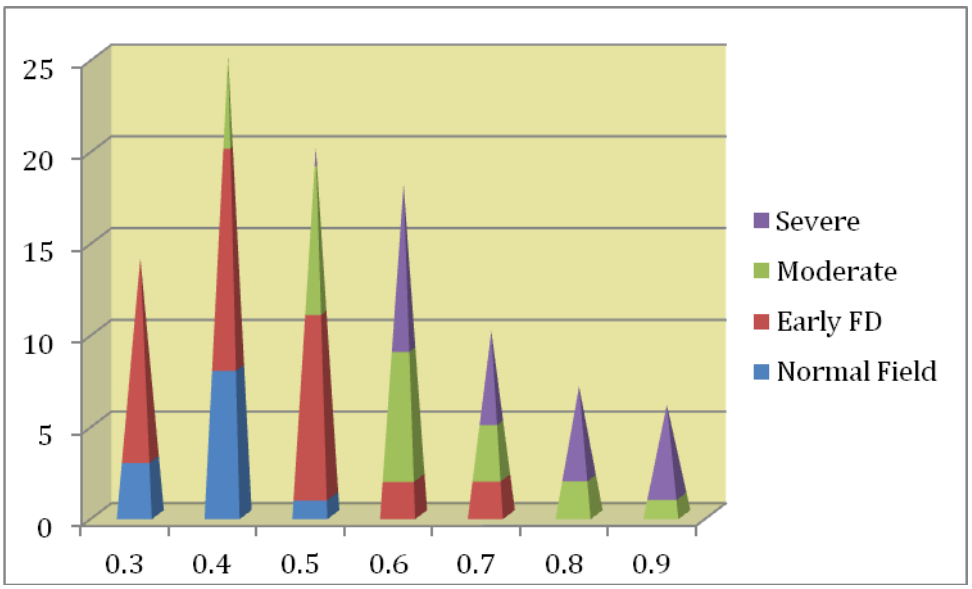


The table compares frequency of Visual Field Defect Grade at all Stages of Disc Damage Likelihood Scale. A definite correlation was found, i.e. the more severe the damage to the optic nerve head, the worse the field defects.

TABLE 8 – COMPARISON OF C/D RATIO TO VISUAL FIELD DEFECT

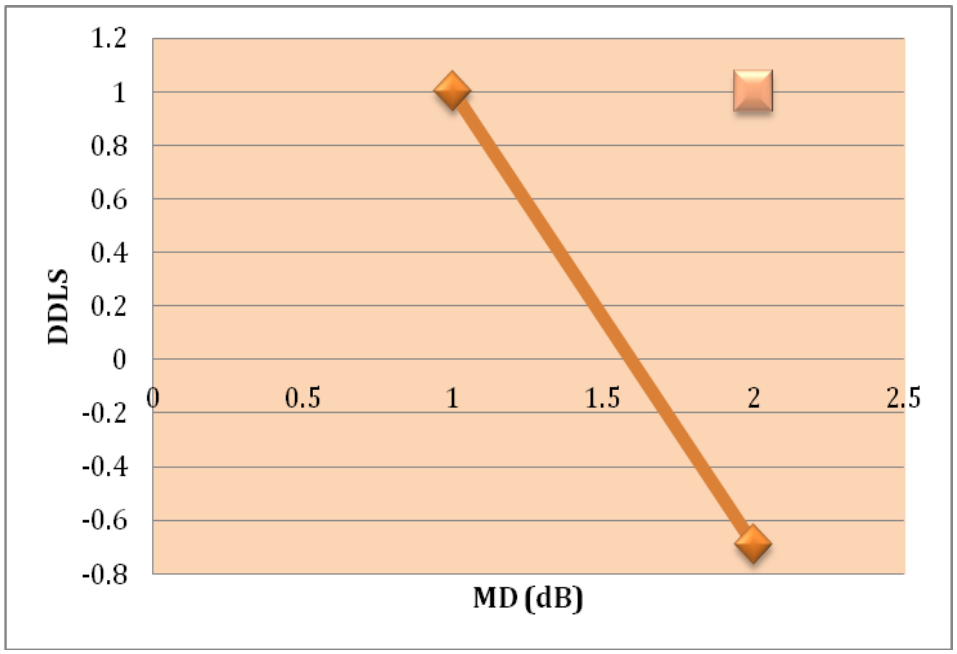
CDR	Normal	Early	Moderate	Severe
0.3	3	**11**	0	0
0.4	**8**	**12**	5	0
0.5	1	**10**	**8**	1
0.6	0	2	**7**	**9**
0.7	0	2	3	5
0.8	0	0	2	5
0.9	0	0	1	5

FIGURE 10 – COMPARISON OF C/D RATIO TO VISUAL FIELD DEFECT



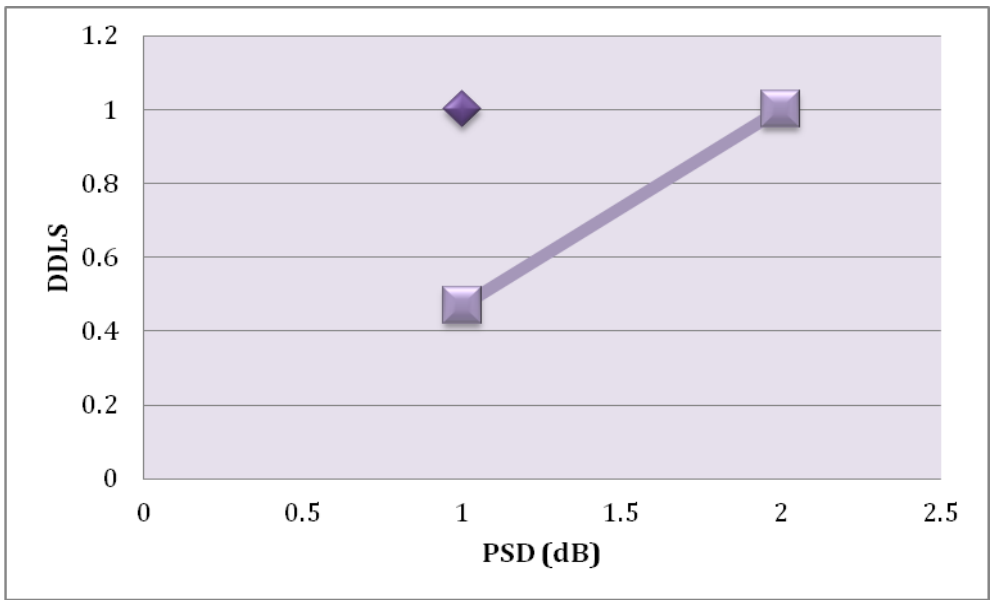
The correlation between Armaly Cup Disc Ratio and Visual Field Defect was plotted in order to compare it with DDLS.

FIGURE 11 – LINEAR CORRELATION PLOT BETWEEN MD AND DDLS



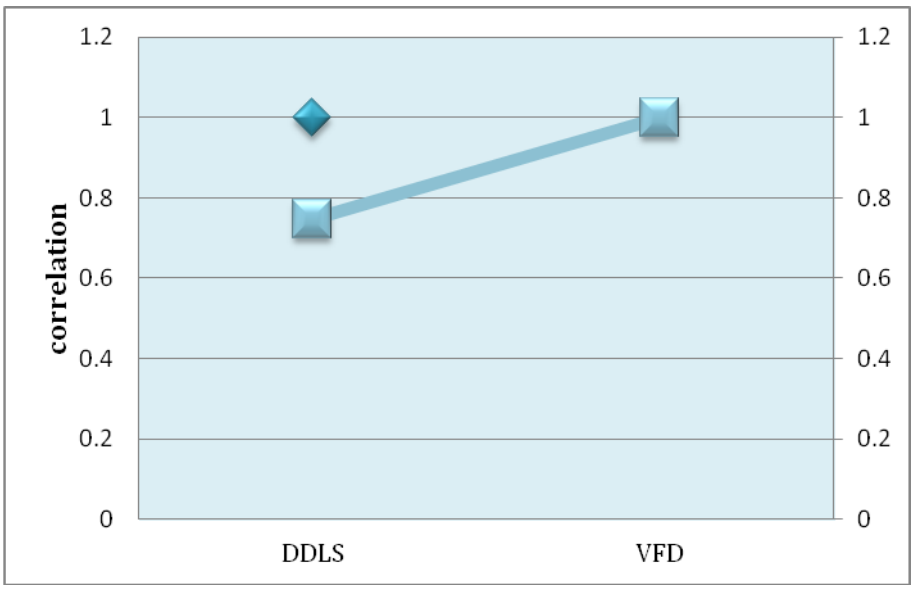
Scatter plot of relation between mean deviation of the visual field and disc damage likelihood scale (DDLS). Linear regression analysis showed correlation coefficient $r = -0.69$, $p<0.0001$. Mean value of MD was -8.88 dB (-31.25 to 1.12)

FIGURE 12 – LINEAR CORRELATION PLOT BETWEEN PSD AND DDLS



Scatter plot of relation between pattern standard deviation of the visual field and disc damage likelihood scale (DDLS). Linear regression analysis showed a correlation coefficient $r = 0.46$, $p<0.0001$. Mean PSD was 6.61 (1.34 to 14.48).

FIGURE 13 – LINEAR CORRELATION PLOT BETWEEN DDLS AND HPA-VFD



This is a scatter plot of relation between level of the visual field damage and disc damage likelihood scale (DDLS). Linear regression analysis showed a correlation coefficient $r = 0.75$, $p < 0.0001$.

FIGURE 14 – LINEAR CORRELATION PLOT BETWEEN CDR AND HPA-VFD

This is a scatter plot of relation between visual field damage and cup to disc ratio. Linear regression analysis showed a correlation coefficient $r = 0.72$, $p<0.0001$.

TABLE 9 – SUMMARY OUTPUT

Regression Statistics	
Multiple R	0.74824077
R Square	0.55986425
Adjusted R Square	0.51544312
Standard Error	0.118933365
Observations	100

FIGURE 15 – PREDICTION PLOT BETWEEN DDLS AND VFD

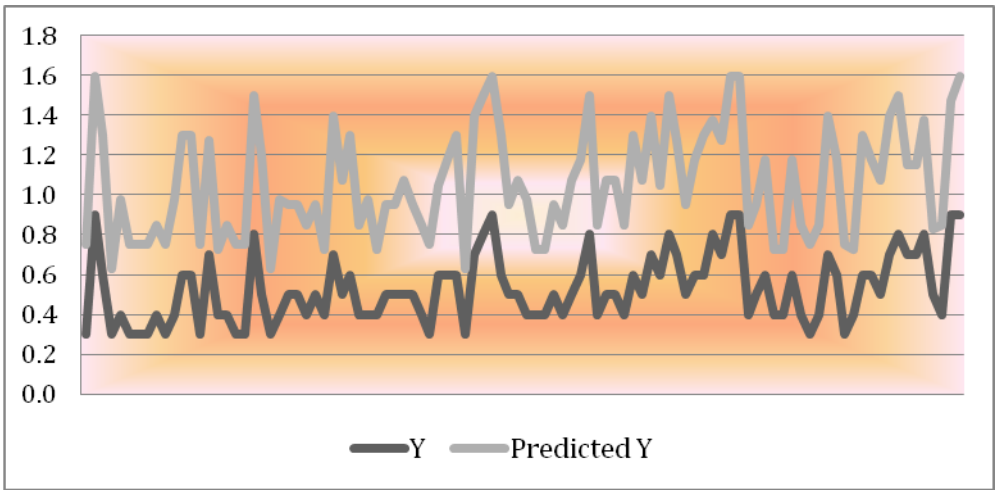
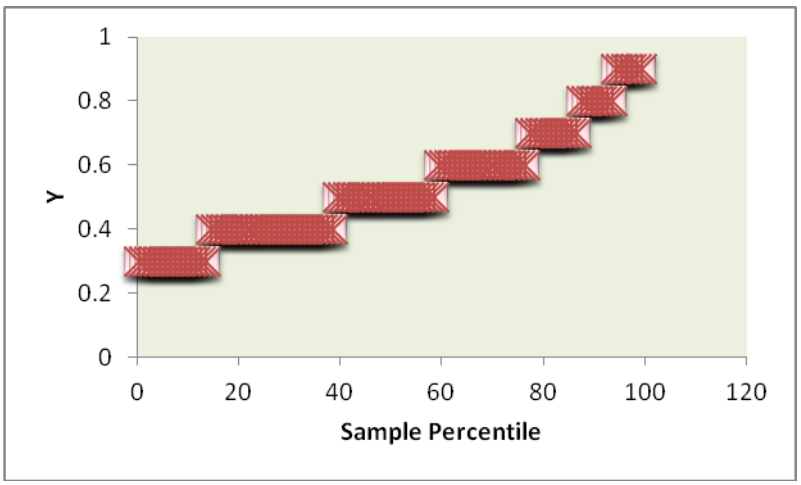


FIGURE 16 – NORMAL PROBABILITY PLOT



DISCUSSION

Table 4 gives the sex distribution of patients in our study. We examined a total of 50 patients with 27 females (54%) and 23 males (46%). As sex is not a major risk factor in incidence of POAG, almost equal predilection is seen in both sexes.

Table 5 gives the age distribution of patients in our study. Majority of patients (36%) in our study were between the ages of 60 and 70 years, while 18% and 16% of patients were in the 4^{th} and 5^{th} decades of life respectively. As a rule of thumb, prevalence tends to roughly double for each decade over 40 (i.e., relative risk of 2 per decade) and is about 10-fold higher in the 80+ group compared to the 40- to 49-year-old group[1,23]. In the clinically selected population of the Ocular Hypertension Treatment Study (OHTS), the relative risk of developing COAG was lower at 1.2 per decade of age, possibly as a result of excluding glaucoma suspects[19]. In the EMGT, the relative risk of progression of early glaucoma was 1.5 for those 68 years of age and older compared to those younger than 68 years[104]. In our study also we found an increased incidence as well as prevalence of glaucoma in patients above 60 years of age.

Table 6 provides a distribution of severity classification using the HAP severity scale. Twelve eyes showed Normal VF. Early VFD was seen in 37 out of 100 eyes in our study, followed by Moderate and Severe VFD in 26 and 25 eyes respectively.

Table 7 provides data depicting correlation between DDLS Grade and HPA Stage of Visual Field Defects. While Early VFD were found even uptil DDLS 6 (37 eyes

with almost equal distribution at different grades of DDLS); Moderate VFD were only seen after DDLS 4 (8 out of 26 at DDLS 5, 12 out of 26 at DDLS 6) and Severe VFD were almost exclusively noted in eyes with DDLS worse than 5 (10 out of 25 at DDLS 6 and 14 out of 25 at DDLS 7). As the bar graph in **Figure 9** depicts, a clear and strong correlation between DDLS and VFD grade is observed in our study. Especially as the grade worsens, the correlation with the stage improves which is useful in monitoring progression, response to treatment and prognosis of the disease.

Table 8 plots the correlation between CDR and HPA grading. As **Figure 10** shows clearly, a strong yet slightly inaccurate correlation has been seen in our study. Early VFD were found even in CDR 0.7 (37 eyes), Moderate VFD were seen in eyes with CDR 0.2 through 0.9, with 15 out of 26 falling in eyes with CDR 0.5 – 0.6. Severe VFD were noted with CDR more than 0.5 (9 eyes with CDR 0.6, 5 eyes each with CDR 0.7 to 0.9).

Traditionally we have relied on the Armaly cup/disc ratio to describe the disc. It has been shown that larger the C/D ratio more severe the field damage is likely to be. However, the C/D ratio has certain limitations, the first being that it does not take into consideration the diameter of the disc, hence is prone to give false positive and false negative impressions. The second limitation is that focal changes in the neuroretinal rim that are so characteristic of glaucoma are not readily detected by the C/D ratio[105]. Several investigators have pointed out that small discs have fewer nerve fibres and smaller C/D ratios than do larger discs.

The disc damage likelihood scale devised by Spaeth et al incorporates the evaluation of disc size and rim width in clinical grading of the disc[106]. It has a high inter-observer reproducibility as well.

Figures 13 and 14 are line graphs to depict linear correlation between DDLS and HPA; and CDR and HPA respectively. The former gives a correlation coefficient r = 0.75 ($p<0.0001$) while the latter gives a correlation of r = 0.72 ($p<0.0001$). Both are statistically significant values. H V Danesh-Meyer et al in their study found that DDLS outperformed the CDR in predicting VF damage and has been shown to be a reliable and reproducible method of estimating the amount of optic nerve damage caused by glaucoma[106]. This is also in agreement with a study done by Jeffrey D Henderer et al, where it was found that for the stereo optic disk photographs, the inter- and intra-observer agreement for the DDLS was greater than the Armaly cup/disk ratio. For the in vivo patient measurements, the level of agreement for the DDLS and the Armaly cup/disk ratio was similar[105].

We have also included linear correlation analysis of DDLS to MD in **Figure 11** and DDLS to PSD in **Figure 12**. Mean value of MD was -8.88 dB and the graph shows a strong inverse correlation (r = -0.62, $p<0.0001$). Mean PSD was 6.61 dB and the graph showed a positive correlation with DDLS (r = 0.46, $p<0.0001$). These values were found similar to the results of the study conducted by Danish Meyer et al. they also concluded that its systematic estimation of disc size and rim narrowing is apparently at least as sensitive and specific as laser imaging by HRT-II, at lower cost[106].

Table 9 is a summary of the output of Regression Analysis with standard error = 0.12. **Figure 15** shows the predictability plot between DDLS and HPA, compared to a normal predictability in a sample percentile **(Figure 16)**

In a study by Ritchings and Spaeth, examination of stereoscopic optic disc photographs allowed accurate prediction of glaucomatous and normal fields to be made in 82 and 95% of eyes respectively and for visual field loss to be correctly located in upper and lower half in 83 and 91% of cases respectively. The high correlation between the state of the visual field and the optic disc means that, in the evaluation of the visual functions of a glaucoma patient, the appearance of the optic disc and the visual field should be in agreement.

The two major advantages of DDLS are, firstly, that it considers the disc size and secondly that it focuses attention on how much neuroretinal rim tissue is present. By categorising discs as small, medium or large, the expectation of rim thickness is adjusted. This reduces the misclassification bias based on the disc size. It also takes into consideration the focal loss of rim tissue. Hence two eyes with same rim areas may have different DDLS stage if one has a focal rim tissue loss.

CONCLUSION

1. In our study, we found DDLS an easy, quick, inexpensive and accurate method to document ONH damage. It appears to be superior to C/D ratio for optic disc evaluation. The two major advantages of DDLS are, firstly, that it considers the disc size and secondly that it focuses attention on how much neuroretinal rim tissue is present. By categorising discs by size, the expectation of rim thickness is adjusted. It also takes into consideration the focal loss of rim tissue.
2. DDLS was shown to correlate more closely with visual field indices and the HPA staging system which is extremely useful in predicting visual field loss; thereby making it a formidable tool for an early diagnosis, monitoring progression, response to treatment and assessing prognosis of COAG.

SUMMARY

Glaucoma is a leading cause of irreversible blindness throughout the world. Worldwide, it has become the second most common cause of bilateral blindness. 100 eyes of 50 patients (27 females and 23 males, mean age 56.38 years) diagnosed with Primary Open Angle Glaucoma were examined in our study. Among the 100 eyes examined in our study, DDLS showed a coefficient correlation value of r = 0.75, r = -0.62 and r = 4.48 ($p<0.0001$) when plotted against HPA, MD and PSD respectively. In our study we also compared the predictability of DDLS at different grades of visual field defects and found that it had an excellent predictability compared to CDR.

Traditionally cup to disc ratio has been used as an indicator for ONH status. However, it does not take into consideration the diameter of the disc, is prone to give false positive and false negative impressions and focal changes in the neuroretinal rim characteristic of glaucoma are not readily detected by the C/D ratio.

The disc damage likelihood scale devised by Spaeth et al incorporates the evaluation of disc size and rim width in clinical grading of the disc. It has a high inter-observer reproducibility as well. Rim to disc ratio is a far more sensitive indicator of ON damage and superior predictor of VF defect.

In our study, DDLS was shown to correlate more closely with visual field indices and the HPA staging system which is extremely useful in predicting visual field loss; thereby making it an easy, quick, inexpensive and accurate method for documentation, early diagnosis, monitoring progression, response to treatment and assessing prognosis of COAG.

REFERENCES

1. Shields MB. Textbook of glaucoma, Ed:5th. Lippincott Williams and Williams;2005

2. Khurana AK, Khurana I. Anatomy and Physiology of Eye. New Delhi: CBS Publishers and Distributors; 2002.

3. Moses RA, Grodzki WJ Jr, Starcher BC, et al. Elastin content of the scleral spur, trabecular mesh, and sclera. Invest Ophthalmol Vis Sci 1978;17(8):817.

4. Ashton N. The exit pathway of the aqueous. Trans Ophthalmol Soc U K 1960;80:397.

5. Fine BS. Structure of the trabecular meshwork and the canal of Schlemm. Trans Am Acad Ophthalmol Otolaryngol 1966;70(5):777.

6. Spencer WH, Alvarado J, Hayes TL. Scanning electron microscopy of human ocular tissues: trabecular meshwork. Invest Ophthalmol 1968;7(6):651.

7. Moses RA, Grodzki WJ Jr. The scleral spur and scleral roll. Invest Ophthalmol Vis Sci 1977;16(10):925.

8. Raviola G, Raviola E. Paracellular route of aqueous outflow in the trabecular meshwork and canal of Schlemm: a freeze-fracture study of the endothelial junctions in the sclerocorneal angel of the macaque monkey eye. Invest

Ophthalmol Vis Sci 1981;21(1 Pt 1):52.

9. Gipson IK, Anderson RA. Actin filaments in cells of human trabecular meshwork and Schlemm's canal. Invest Ophthalmol Vis Sci 1979;18(6):547.

10. Morrison J, Van Buskirk EM. Ciliary process microvasculature of the primate eye. Am J Ophthalmol 1984;97:372.

11. Reddy VN. Dynamics of transport systems in the eye. Friedenwald Lecture. Invest Ophthalmol Vis Sci 1979; 18(10):1000.

12. Raviola G, Raviola E. Intercellular junctions in the ciliary epithelium. Invest Ophthalmol Vis Sci 1978;17(10):958.

13. Gabelt BT, Kaufman PL. Aqueous humor hydrodynamics. In: Kaufman PL, Alm A, eds. Adler's physiology of the eye. St. Louis: Mosby, 2003:237.

14. Bill A. The role of ciliary blood flow and ultrafiltration in aqueous humor formation. Exp Eye Res 1973;16(4):287.

15. Leske MC, Connell AMS, Wu S-Y, et al. Risk factors for open-angle glaucoma. Arch Ophthalmol 1995;113:918.

16. Buxton JN, Preston RW, Riechers R, et al. Tonography in cornea guttata: a preliminary report. Arch Ophthalmol 1967; 77:602.

17. Korey M, Gieser D, Kass MA, et al. Central corneal endothelial cell density and central corneal thickness in ocular hypertension and primary open-angle glaucoma. Am J Ophthalmol 1982;94:610.

18. Argus WA. Ocular hypertension and central corneal thickness. Ophthalmology 1995;102:1810.

19. Kass MA, Heuer DK, Higginbotham EJ, et al. The Ocular Hypertension Treatment Study. Arch Ophthalmol 2002; 120:701.

20. Wand M, Grant WM. Thymoxamine test: differentiating angle-closure glaucoma from open-angle glaucoma with narrow angles. Arch Ophthalmol 1978;96:1009.

21. Jay JL, Murdoch JR. The rate of visual field loss in untreated primary open-angle glaucoma. Br J Ophthalmol 1993;77:176.

22. Harbin TS Jr, Podos SM, Kolker AE, et al. Visual field progression in open-angle glaucoma patients presenting with monocular field loss. Trans Am Acad Ophthalmol Otol 1976;81:253.

23. Kimura R, Levene RZ. Gonioscopic differences between primary open-angle glaucoma and normal subjects over 40 years of age. Am J Ophthalmol 1975;80:56.

24. Campbell DG, Boys-Smith JW, Woods WD. Variation of pigmentation and segmentation of pigmentation in primary open-angle glaucoma. Invest Ophthalmol Vis Sci 1984;25[Suppl]:122.

25. Fronimopoulos J, Lascaratos J. The terms glaucoma and cataract in the ancient Greek and Byzantine writers. Doc Ophthal 1991;77:369.

26. Schulzer M, Drance SM, Carter CJ, et al. Biostatistical evidence for two distinct chronic open-angle glaucoma populations. Br J Ophthalmol 1990;74:196.

27. Shiose Y, Kitazawa Y, Tsukahara S, et al. Epidemiology of glaucoma in Japan: a nationwide glaucoma survey. Jpn J Ophthalmol 1991;35:133.

28. Mukesh BN, et al. Five-year incidence of open-angle glaucoma: the visual impairment project. Ophthalmology 2002; 109:1047.

29. Kahn HA, Leibowitz HM, Ganley JP, et al. The Framingham eye study. I. Outline and major prevalence findings. Am J Epidemiol 1977;106:17.

30. Leske MC, Rosenthal J. Epidemiologic aspects of open-angle glaucoma. Am J Epidemiol 1979;109:250.

31. Klein BEK, Klein R, Sponsel WE, et al. Prevalence of glaucoma: the Beaver Dam eye study. Ophthalmology 1992; 99:1499.

32. Dielemans I, Vingerling JR, Wolfs RCW, et al. The prevalence of primary open-angle glaucoma in a population-based study in The Netherlands: the Rotterdam study. Ophthalmology 1994;101:1851.

33. Wilensky JT, Gandhi N, Pan T. Racial influences in open-angle glaucoma. Ann Ophthalmol 1978;10:1398.

34. Shaeffer NR, Becker B. Diagnosis and Therapy of the Glucomas, Ed:8th. Mosby Elsevier;2009.

35. Geijssen HC, Greve EL. The spectrum of primary open-angle glaucoma. I: Senile sclerotic glaucoma versus COAG glaucoma. Ophthalmic Surg 1987;18:207.

36. Schulzer M, Drance SM, Carter CJ, et al. Biostatistical evidence for two distinct chronic open-angle glaucoma populations. Br J Ophthalmol 1990;74:196.

37. Chauhan BC, Drance SM. The relationship between intraocular pressure and visual field progression in glaucoma. Graefes Arch Clin Exp Ophthalmol 1992;230:521.

38. Anderson DR. Glaucoma: the damage caused by pressure. Am J Ophthalmol 1989;108:485.

39. Kolker AE, Becker B. Ocular hypertension vs. open-angle glaucoma: a different view. Arch Ophthalmol 1977;95:586.

40. Chandler PA, Grant WM. Ocular hypertension vs. open-angle glaucoma. Arch Ophthalmol 1977;95:585.

41. Shaffer R. Glaucoma suspect or ocular hypertension? Arch Ophthalmol 1977;95:588.

42. Lee BL, Bathija R, Weinreb R. The definition of NTG. J Glaucoma 1998;7:366

43. Drance SM, Sweeney VP, Morgan RW, et al. Studies of factors involved in the production of low tension glaucoma. Arch Ophthalmol 1973;89:457.

44. Hollows FC, Graham PA. Intra-ocular pressure, glaucoma, and glaucoma suspects in a defined population. Br J Ophthalmol 1966;50:570.

45. Lichter PR, Shaffer RN. Ocular hypertension and glaucoma. Trans Pacific Coast Oto-Ophthalmol Soc 1973;54:63.

46. Grant WM, Burke JF Jr. Why do some people go blind from glaucoma? Ophthalmology 1982;89:991.

47. Anderson DR, Drance SM, Schulzer M. Natural history of normal-tension glaucoma. Ophthalmology 2001;108:247.

48. Kass MA, Kolker AE, Becker B. Prognostic factors in glaucomatous visual field loss. Arch Ophthalmol 1976;94:1274.

49. Susanna R, Drance SM, Douglas GR. The visual prognosis of the fellow eye in uniocular chronic open-angle glaucoma. Br J Ophthalmol 1978;62:327.

50. Jonas JB, Gusek GC, Naumann GO. Optic disc, cup and neuroretinal rim size, configuration and correlations in normal eyes. Invest Ophthalmol Vis Sci 1988;29:1151.

51. Jonas JB, Gusek GC, Guggenmoos-Holzmann I, et al. Variability of the real dimensions of normal human optic discs. Graefes Arch Clin Exp Ophthalmol 1988;226:332.

52. Bengtsson B. The alteration and asymmetry of cup and disc diameters. Acta Ophthalmol (Copenh) 1980;58:726.

53. Balazsi AG, Drance SM, Schulzer M, et al. Neuroretinal rim area in suspected glaucoma and early chronic open-angle glaucoma: correlation with parameters of visual function. Arch Ophthalmol 1984;102:1011.

54. Caprioli J, Miller JM. Optic disc rim area is related to disc size in normal subjects. Arch Ophthalmol 1987;105:1683.

55. Britton RJ, Drance SM, Schulzer M, et al. The area of the neuroretinal rim of the optic nerve in normal eyes. Am J Ophthalmol 1987;103:497.

56. Jonas JB, Gusek GC, Guggenmoos-Holzmann I, et al. Correlations of the neuroretinal rim area with ocular and general parameters in normal eyes. Ophthalmic Res 1988; 20:298.

57. Shields MB. Gray crescent in the optic nerve head. Am J Ophthalmol 1980;89:238.

58. Jonas JB, Gusek GC, Naumann GO. Optic disk morphometry in high myopia. Graefes Arch Clin Exp Ophthalmol 1988; 226:587.

59. Tsai CS, Ritch R, Shin DH, et al. Age-related decline of disc rim area in visually normal subjects. Ophthalmology 1992;99:29.

60. Klein BE, Moss SE, Klein R, et al. Neuroretinal rim area in diabetes mellitus. Invest Ophthalmol Vis Sci 1990;31:805.

61. Shaffer RN. The role of the astroglial cells in glaucomatous disc cupping. Doc Ophthalmol 1969;26:516.

62. Shaffer RN, Hetherington J Jr. The glaucomatous disc in infants: a suggested hypothesis for disc cupping. Trans Am Acad Ophthalmol Otolaryngol 1969;73:923.

63. Kornzweig AL, Eliasoph I, Feldstein M. Selective atrophy of the radial peripapillary capillaries in chronic glaucoma. Arch Ophthalmol 1968;80:696.

64. Quigley HA, Hohman RM, Addicks EM, et al. Blood vessels of the glaucomatous optic disc in experimental primate and human eyes. Invest Ophthalmol Vis Sci 1984;25:918.

65. Quigley HA, Hohman RM, Addicks EM. Quantitative study of optic nerve head capillaries in experimental optic disk pallor. Am J Ophthalmol 1982;93:689.

66. Henkind P, Bellhorn R, Rabkin M, et al. Optic nerve transection in cats. II. Effect on vessels of optic nerve head and lamina cribrosa. Invest Ophthalmol Vis Sci 1977;16:442.

67. Hayreh SS. Pathogenesis of cupping of the optic disc. Br J Ophthalmol 1974;58:863.

68. Emery JM, Landis D, Paton D, et al. The lamina cribrosa in normal and glaucomatous human eyes. Trans Am Acad Ophthalmol Otolaryngol 1974;78:OP290.

69. Yan DB, Coloma FM, Metheetrairut A, et al. Deformation of the lamina cribrosa by elevated intraocular pressure. Br J Ophthalmol 1994;78:643.

70. Anderson DR. Introductory comments on blood flow autoregulation in the optic nerve head and vascular risk factors in glaucoma. Surv Ophthalmol 1999;43[Suppl 1]:S5.

71. Rankin SJ, Walman BE, Buckley AR, et al. Color Doppler imaging and spectral analysis of the optic nerve vasculature in glaucoma. Am J Ophthalmol 1995;119:685.

72. Evans PY, Shimizu K, Limaye S, et al. Fluorescein cineangiography of the optic nerve head. Trans Am Acad Ophthalmol Otolaryngol 1973;77:OP260.

73. Ernest JT, Archer D. Fluorescein angiography of the optic disk. Am J Ophthalmol 1973;75:973.

74. Schwartz B, Kern J. Age, increased ocular and blood pressures, and retinal and disc fluorescein angiogram. Arch Ophthalmol 1980;98:1980.

75. Raitta C, Sarmela T. Fluorescein angiography of the optic disc and the peripapillary area in chronic glaucoma. Acta Ophthalmol (Copenh) 1970;48:303.

76. Blumenthal M, Gitter KA, Best M, et al. Fluorescein angiography during induced ocular hypertension in man. Am J Ophthalmol 1970;69:39.

77. Minckler DS, Tso MO. A light microscopic, autoradiographic study of axoplasmic transport in the normal rhesus optic nerve head. Am J Ophthalmol 1976;82:1.

78. Taylor AC, Weiss P. Demonstration of axonal flow by the movement of tritium-labeled protein in mature optic nerve fibers. Proc Natl Acad Sci U S A 1965;54:1521.

79. Weiss P, Pillai A. Convection and fate of mitochondria in nerve fibers: axonal flow as vehicle. Proc Natl Acad Sci U S A 1965;54:48.

80. Minckler DS, Tso MO, Zimmerman LE. A light microscopic, autoradiographic study of axoplasmic transport in the optic nerve head during ocular hypotony, increased intraocular pressure, and papilledema. Am J Ophthalmol 1976;82:741.

81. Quigley H, Anderson DR. The dynamics and location of axonal transport blockade by acute intraocular pressure elevation in primate optic nerve. Invest Ophthalmol 1976;15:606.

82. Breidenbach K, Neppert B, Dannheim F, et al. (Pattern electroretinography in routine clinical diagnosis of open-angle glaucoma.)Ophthalmologe 1996;93:451.

83. Colotto A, Salgarello T, Falsini B, et al. Pattern electroretinogram and optic nerve topography in ocular hypertension. Acta Ophthalmol Scand 1998;227:27.

84. Spaeth GL, Henderer J, Steinmann W. The Disc Damage Likelihood Scale (DDLS): its use in the diagnosis and management of glaucoma. Highlights of Ophthalmology. 2003;31:4-19.

85. Anderson DR, Patella VM. Automated static perimetry. St. Louis: Mosby, 1999.

86. Armaly MF. The size and location of the normal blind spot. Arch Ophthalmol 1969;81:192.

87. Spry PG, Johnson CA. Senescent changes of the normal visual field: an age-old problem. Optom Vis Sci 2001;78:436.

88. The advanced glaucoma intervention study, 6: effect of cataract on visual field and visual acuity. The AGIS Investigators. Arch Ophthalmol 2000;118:1639.

89. Koller G, Haas A, Zulauf M, et al. Influence of refractive correction on peripheral visual field in static perimetry. Graefes Arch Clin Exp Ophthalmol 2001;239:759.

90. Werner EB, Beraskow J. Peripheral nasal field defects in glaucoma. Ophthalmology 1979;86:1875.

91. Armaly MF. Visual field defects in early open-angle glaucoma. Trans Am Ophthalmol Soc 1971;69:147.

92. Schulzer M, Mikelberg FS, Drance SM. A study of the value of the central and peripheral isoptres in assessing visual field progression in the presence of paracentral scotoma measurements. Br J Ophthalmol 1987;71:422.

93. Ballon BJ, Echelman DA, Shields MB, et al. Peripheral visual field testing in glaucoma by automated kinetic perimetry with the Humphrey Field Analyzer. Arch Ophthalmol 1992;110:1730.

94. Samuelson TW, Spaeth GL. Focal and diffuse visual field defects: their relationship to intraocular pressure. Ophthalmic Surg 1993;24:519.

95. Gramer E, Gerlach R, Krieglstein GK, et al. [Topography of early glaucomatous visual field defects in computerized perimetry.]Klin Monatsbl Augenheilkd

1982;180:515.

96. Haefliger IO, Flammer J. Fluctuation of the differential light threshold at the border of absolute scotomas: comparison between glaucomatous visual field defects and blind spots. Ophthalmology 1991;98:1529.

97. Lachenmayr BJ, Drance SM. Diffuse field loss and central visual function in glaucoma. Ger J Ophthalmol 1992;1:67.

98. Heijl A. Lack of diffuse loss of differential light sensitivity in early glaucoma. Acta Ophthalmol (Copenh) 1989;67:353.

99. Asman P, Heijl A. Diffuse visual field loss and glaucoma. Acta Ophthalmol (Copenh) 1994;72:303

100. Advanced Glaucoma Intervention Study. 2. Visual field test scoring and reliability. Ophthalmology 1994;101:1445.

101. Johnson CA, Sample PA, Cioffi GA, et al. Structure and function evaluation (SAFE): I. Criteria for glaucomatous visual field loss using standard automated perimetry (SAP) and short wavelength automated perimetry (SWAP) (1). Am J Ophthalmol 2002;134:177.

102. Musch DC, Lichter PR, Guire KE, et al. The Collaborative Initial Glaucoma Treatment Study: study design, methods, and baseline characteristics of enrolled patients. Ophthalmology 1999;106:653.

103. Boden C, Sample PA, Boehm AG, et al. The structure-function relationship

in eyes with glaucomatous visual field loss that crosses the horizontal meridian. Arch Ophthalmol 2002;120:90.

104. Heijl A, et al. Reduction of intraocular pressure and glaucoma progression: results from the Early Manifest Glaucoma Trial. Arch Ophthalmol 2002;120:1268.

105. Henderer J, Liu C, Bayer A, Kesen , Altangerel U Bayer A, Steinmann WC, Spaeth GL. Reliability of the Disc Damage Likelihood Scale. Am J Ophthalmol 2003;135:44-8.

106. Spaeth GL, Henderer J, Liu C, Kesen M Altangerel U, Bayer A, Katz LJ, Myers J, Rhee D, Steinmann W. The disc damage likelihood scale: reproducibility of a new method of estimating the amount of optic nerve damage caused by glaucoma. Trans Am Ophthalmol Soc. 2002;100:181-6.

107. Danesh-Meyer HV, Gaskin BJ, Jayusundera T, Donaldson M, Gamble GD. Comparison of disc damage likelihood scale, cup to disc ratio, and Heidelberg retina tomography in the diagnosis of glaucoma. Br J Ophthalmol 2006;90:437-41.

PROFORMA

Name:	IP no:
Age/Sex:	
Address:	
Chief Complaints:	
History of presenting illness:	

Past history:

Family history:

Personal history:

General physical examination:

Pallor	Icterus	Cyanosis
Edema	Clubbing	Lymphadenopathy
Pulse:	BP-	

Systemic Evaluation:

Cardiovascular System:	Respiratory System:
Per abdomen:	Central Nervous System:

OCULAR EXAMINATION

Head Posture:	RE	LE
Ocular Posture		

Eye Lids

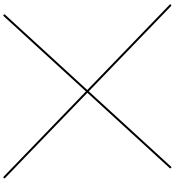
Conjunctiva

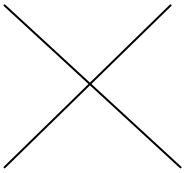
Cornea

Sclera

Anterior Chamber

Angles
(Gonioscopy)





Iris

Pupil- Size
Shape
Reaction

Lens

Visual Acuity

Distant vision-

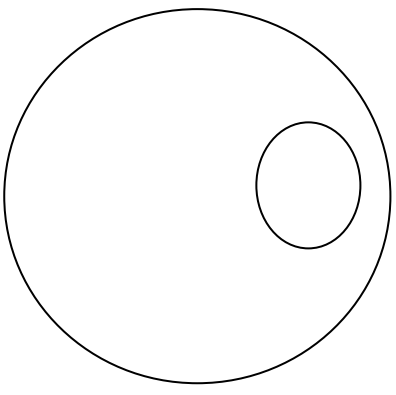
Near vision-

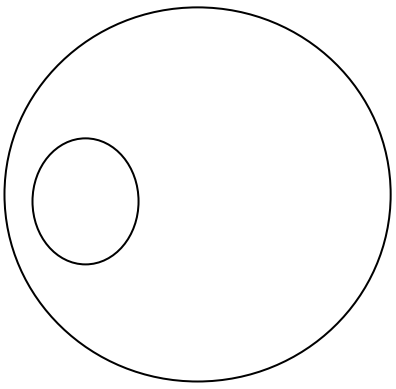
IOT

Fundus Examination

Optic Disc

CDR





Disc Damage Likelihood Scale

Narrowest width of Rim

Stage	1
	2
	3
	4
	5
	6
	7

Visual Field Defect Level

Mean Deviation

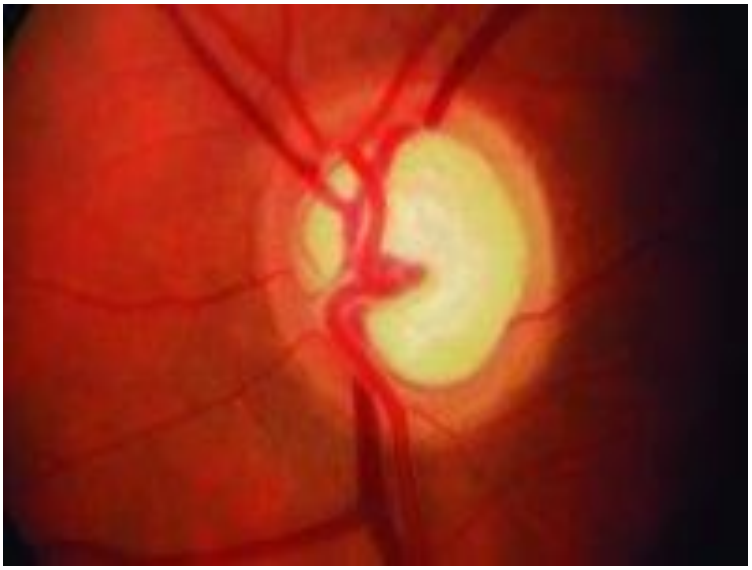
Pattern Standard Deviation

P value

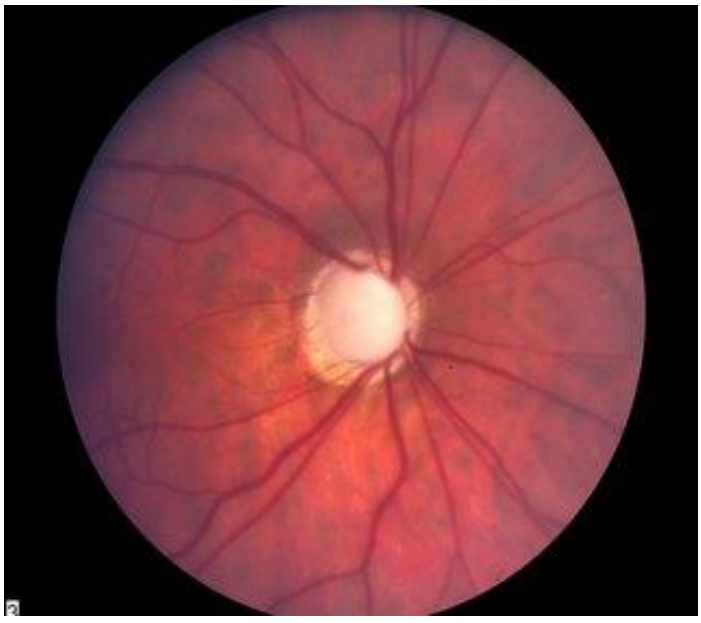
HPA Grade	Normal
	Early
	Moderate
	Severe

PHOTOGRAPHS

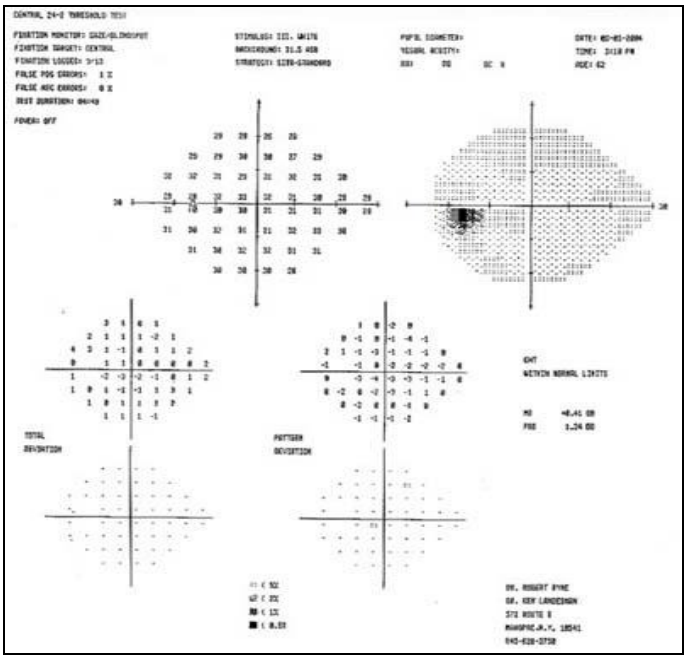
GLAUCOMATOUS DISC CUPPING



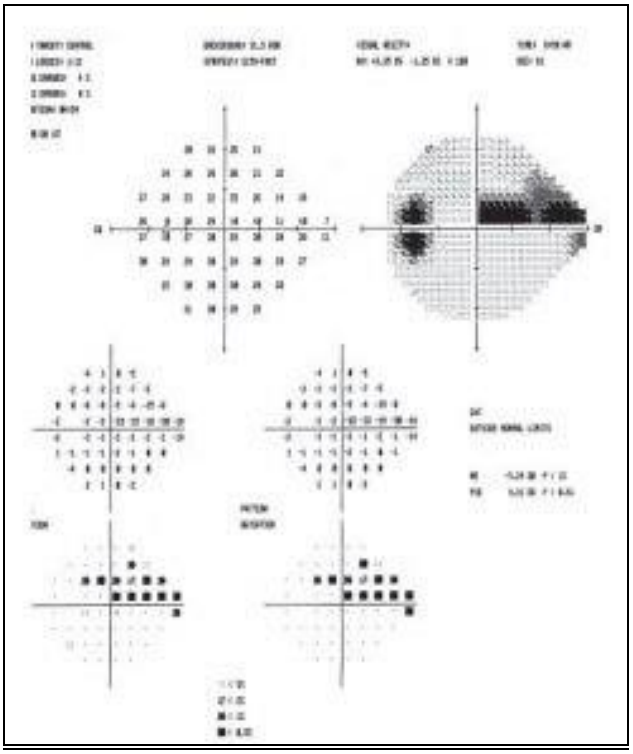
NEURO-RETINAL RIM THINNING WITH NERVE FIBRE LAYER DEFECT



NORMAL VISUAL FIELD



GLAUCOMATOUS VISUAL FIELD DEFECT



KEY TO MASTER CHART

- Sl. No. >> Serial Number
- CDR >> Cup Disc Ratio
- NRR >> Neuro Retinal Rim
- IOP >> Intra Ocular Pressure
- DDLS >> Disc Damage Likelihood Scale
- MD >> Mean Deviation
- PSD >> Pattern Standard Deviation
- P >> Probability
- HPA >> Hodapp-Parish-Anderson