

Glaucoma: Risk Factors and Prevalence: A Review

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Abstract

In recent time, the concept and definitions of glaucoma have changed from a single pathologic entity to a group of disorders with different clinical pictures. Glaucoma can be defined as a multifactorial optic neuropathy which may or may not be associated with angle abnormality in the presence or absence of any cause for the disease. Irrespective of the manifestation; glaucoma is the second leading cause of blindness worldwide, with preponderance in females, blacks and Asians. Various classifications have been proposed from time to time with the most basic classification system involves separation of angle-closure glaucoma from open-angle glaucoma. This review highlights the clinical features, classification and recent factors related to glaucoma.

Key Words: Aqueous humour; Glaucoma; Intraocular; Pressure; Classification

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INTRODUCTION

The concept and definitions of glaucoma have evolved over recent times from a single disease entity to a group of disorders different in their clinical profile, pathophysiology and management.¹ Glaucoma can be defined as a multifactorial optic neuropathy² with a characteristic accelerated degeneration of retinal ganglion³ cells presenting as classical optic nerve head features⁴ and correlating visual field changes, which may or may not be associated with angle abnormality in the presence or absence of any cause for the disease.^{5,6} These disorders share features of cupping and atrophy of the optic nerve head, with attendant visual field loss and are frequently (but not always) related to the level of intraocular pressure(IOP).¹ Because IOP presently the only factor that can be controlled to prevent progression of optic neuropathy, aqueous humour dynamics, closely related to ocular pressure are critical to glaucoma

management.^{7,8} IOP is determined by the equilibrium between rate of aqueous humour production by ciliary body, the resistance to aqueous outflow at the angle of the anterior chamber (AC), and the level of episcleral venous pressure. The resistance to damage of the optic nerve axons determines the optic nerve head and visual field changes.¹ current classifications of glaucoma are based on the initial events that in due course, lead to elevated IOP or the alterations in aqueous humour dynamics that are directly responsible for the increase. Continuous research, (including genetics) about the various risk factors lead to the ever changing concepts of glaucoma. However, three crucial parameters- IOP, the optic nerve, and the visual field are the core to our current understanding.⁹ classically, primary glaucomas do not have an association with known ocular or systemic disorders to account for the increased resistance to the aqueous outflow.¹⁰ on the other hand, the secondary glaucomas are

associated with ocular or systemic abnormalities responsible for elevated IOP. This dissection into primary and secondary reflects our incomplete understanding of the pathophysiology of the common final pathway of the glaucomatous optic nerve head damage and visual field loss.¹¹ Irrespective of the manifestation; glaucoma is the second leading cause of blindness worldwide, with preponderance in females, blacks and asians.¹²⁻¹⁵

CLASSIFICATION

The most basic classification system is the separation of angle-closure glaucoma from open-angle glaucoma. Moving beyond the historical definition of angle-closure glaucoma, the present-day proposal emphasizes on the ultimate pathogenic pathway mechanism of irido-trabecular impediment which results in functional angle closure.¹⁶ The current classification scheme is a mix of both the natural history of disease depicting the progressive stages, and a mechanistic scheme describing the sites of dysfunction. Clinico-etiological classification¹⁷:

- I. **Open Angle Glaucoma:** In open-angle glaucoma, there is relative impairment of flow of aqueous humour through the trabecular meshwork (TM)-schlemm's canal-venous system with an open angle and normal-looking AC.
- II. **Angle Closure Glaucoma:** In angle closure glaucoma resistance to outflow is increased because peripheral iris obstructs the TM.
- III. **Combined Mechanism Glaucoma:** Combination of two or more forms of glaucoma, sequentially or coincidentally.
- IV. **Childhood Glaucomas:** In childhood or developmental glaucomas, anterior segment dysgenesis either presents at birth or appear in the first decades of life.

Globally, primary open-angle glaucoma affects more people than angle-closure with an approximate ratio of 3:1, with wide variations among populations and an almost reversal of the global trend in south Asia. However, the symptomatology of angle-closure glaucoma warrants more clinical consult by patients than patients with the chronic benign open-angle glaucoma.^{14,18} Classification Based On Pathogenesis And Treatment:¹

Classification of open angle glaucoma:

- 1) **Primary open angle glaucoma**
- 2) **Normal tension glaucoma**
- 3) **Secondary open angle glaucoma**
 - a. Increased resistance to tm outflow associated with other conditions:
 - (i) pigment dispersion
 - (ii) pseudoexfoliation
 - (iii) phacolytic (lens induced) glaucoma
 - (iv) steroids
 - b. Increased resistance posterior to tm secondary to elevated episcleral venous pressure (e.g. Carotid cavernous sinus fistula, superior vena cava obstruction, sturge –weber syndrome).
 - c. Iatrogenic
 - (i) Glaucoma after cataract surgery
 - (ii) Glaucoma after vitrectomy (intraocular gas/silicone oil)
 - d. Glaucoma after trauma (chemical burns, electric shock, radiation, penetrating injury, contusion injury)
 - e. Glaucoma associated with intraocular haemorrhage
 - f. Glaucoma associated with retinal detachment
 - i. Glaucoma associated with uveitis (e.g. Fuchs's heterochromic iridocyclitis, trabeculitis, herpes simplex and zoster, sarcoidosis, juvenile rheumatoid arthritis, syphilis, and hiv).
 - j. Glaucoma with intraocular tumours

Classification of Angle Closure Glaucoma:

1. Primary angle closure disease

Irido-trabecular apposition obstructs aqueous outflow as the final pathology.

- a) Natural history
 - i. Primary angle closure suspect
 - ii. Primary angle closure
 - iii. Primary angle-closure glaucoma
- b) Anterior segment mechanisms of closure
 - i. Iris-pupil obstruction(e.g. 'Pupillary block')
 - ii. Ciliary body anomalies(e.g. 'plateau iris syndrome')
 - iii. Lens-pupil block (e.g. 'phacomorphic block')

2. Secondary angle closure

- a) Anterior 'pulling mechanism'
The iris is pulled forward by angle pathology, such as the contraction of a

membrane or peripheral anterior synechiae.

- i. Neovascular glaucoma
 - ii. Epithelial downgrowth
 - iii. Fibrous ingrowth
 - iv. Flat AC
 - v. Inflammation
- b) Posterior ‘pushing mechanism’
The iris is pushed forward by some pathology in the posterior segment.
- i. Ciliary block glaucoma
 - ii. Intraocular tumours
 - iii. Nanophthalmos
 - iv. Suprachoroidal haemorrhage
 - v. Intravitreal air injection
 - vi. Retrolental fibroplasias

Classification of Developmental glaucoma:

1. Primary congenital (infantile) glaucoma

- a. Congenital glaucoma
- b. Autosomal dominant juvenile glaucoma
- c. Glaucoma associated with systemic abnormalities
- d. Glaucoma associated with ocular abnormalities

2. Secondary glaucoma

- a. Traumatic glaucoma
- b. Glaucoma with intraocular neoplasm
- c. Uveitic glaucoma
- d. Lens-induced glaucoma
- e. Glaucoma after congenital cataract surgery
- f. Steroid induced glaucoma
- g. Neovascular glaucoma
- h. Secondary angle-closure glaucoma
- i. Glaucoma with elevated episcleral pressure
- j. Glaucoma secondary to intraocular infection

Specific diseases have been sub-classified, such as POAG types, based on various appearances of the damaged optic nerve¹⁹, or classification of disease stages by visual field damage²⁰; or the angle closure glaucomas based on IOP levels and gonioscopic configurations as correlated with ultrasonic biomicroscopy.²¹

Primary Open Angle Glaucoma

Primary open angle glaucoma (PAOG) is a chronic progressive optic neuropathy characterised by an

open, normal-looking ac and increased intraocular pressure (IOP) without any apparent ocular or systemic abnormality that might account for the raised IOP. Typical optic nerve head damage (ONH) or glaucomatous visual field abnormalities.⁹ Intraocular pressure is the major risk factor and is elevated above the statistical ‘normal’ range in a majority of cases. It is also the only modifiable risk factor.

Risk factors

Intraocular pressure: “normal” intraocular pressure may be defined as that pressure which does not lead to glaucomatous damage of the ONH. The commonly used IOP level of 21 mm hg is based on the observation of two standard deviations (SDS) above the mean of a gaussian distribution curve, and a clinically measured IOP greater than this level is considered elevated.⁹ Evidence from animal studies indicates that elevated IOP can cause glaucomatous ONH changes.^{22,23} Population surveys also corroborate the increase in prevalence of open angle glaucoma with increasing iop.²⁴⁻²⁶ Normal tension glaucoma and ocular hypertension are entities that complete the spectrum of open angle glaucoma disease and have been shown to be associated with a greater severity of disease with intraocular pressures on the higher side in control studies.²⁷⁻²⁹

Age of the patient: The prevalence increases with age. Age is also a risk factor for the conversion from ocular hypertension to open-angle glaucoma.^{24, 25, 30-32}

Sex: males have a higher prevalence of poag.^{33, 34}

Race: African descent is known to be a risk factor for the development of POAG.³⁰

Refractive error: Myopia is a risk factor.^{35,36}

Corneal thickness: Apart from causing erroneous low reading with applanation tonometry, a risk factor for the conversion of ocular hypertension to POAG, thin corneas may also be, independently, a direct marker for increased vulnerability of the optic nerve.³⁷

Systemic factors: Diabetes mellitus, thyroid eye disease, systemic hypertension, cardiovascular disease, peripheral vasospasm, migraine, sleep apnoea and systemic causes of low perfusion pressure have all been suggested as possible causes.¹

Clinical features

Optic nerve head: The appearance of the ONH and peripapillary retina is the single most

important clinical feature in establishing glaucomatous damage.

Visual abnormalities: Central visual acuity typically remains normal until there is marked visual field loss. Preliminary evidence, on Humphrey visual field analyser perimetry suggests that more subtle measures of visual dysfunction, such as contrast sensitivity, colour vision, and motion perception are early indicators of visual dysfunction before the typical visual field loss develops.⁹ In addition to those with consistently elevated IOP, there are individuals who exhibit optic nerve features suggestive of early glaucoma or who have suspicious field defects. To include these categories and identify a subpopulation of individuals or eyes at increased risk for POAG, the term glaucoma suspect was advocated by Shaffer.⁹

Definition of glaucoma suspect³⁸

Open angle by gonioscopy and one of the following in at least one eye:

- IOP consistently > 21 mm hg by applanation tonometry
- Appearance of the optic disc or RNFL suggestive of glaucomatous damage
- Abnormalities of the nerve fibre layer especially at the superior or inferior poles
- Disc haemorrhages
- Asymmetric appearance of the disc or rim between fellow eyes (e.g. Cup-to-disc ratio difference > 0.2) suggesting loss of neural tissue
- Visual fields suspicious for early damage

Ocular hypertension: Patients with an 'elevated' IOP but without the signs of glaucomatous damage in the ONH or any visual defects are referred to as having ocular hypertension.³⁹

Normal tension glaucoma: A clinical subset of PAOG, it has similar disc and field changes but pressures remain in the statistical 'normal' range without treatment.⁹

Angle closure glaucoma:

Angle closure is defined as the opposition of the peripheral iris against the tm, resulting in obstruction of aqueous outflow. The presence of angle closure with evident optic nerve damage is termed angle closure glaucoma.⁹ On the basis of signs and symptoms and the time course of the disease three types can be distinguished:

- I) Acute angle-closure,
- ii) Sub acute angle-closure glaucoma and
- lii) Chronic angle-closure glaucoma.⁴⁰

This classification is however, an oversimplification, as it neither depicts the natural history of disease progression, nor does it contribute to stage-specific management and interventions. The new classification takes into account the assessment of IOP, gonioscopy, and disc and visual field evaluation. Therefore, it depends on the presenting patients' clinical profile rather than the time course and symptom history for staging.

- 1) Primary angle closure suspect (PACS): greater than 270° of irido-trabecular contact plus absence of peripheral anterior synechiae (pas) plus 'normal IOP', disc, and visual field.
- 2) Primary angle closure (PAC): greater than 270° of irido-trabecular contact with elevated IOP and/or pas plus normal disc and visual field examinations.
- 3) Primary angle-closure glaucoma (PACG): greater than 270° of irido-trabecular contact plus elevated IOP plus optic nerve and visual field damage.

Acute primary angle closure remains a specific observable presentation of the disease, requiring emergent intervention.¹ Acute angle-closure glaucoma is characterised by severe pain in the distribution of the trigeminal nerve, redness and blurred vision. On examination, there is conjunctival hyperaemia, cloudy cornea and a mid-dilated fixed pupil. There is marked IOP elevation in the range of 40 mm hg to greater than 60 mm hg, with a severe reduction in central visual acuity. Sub acute angle-closure glaucoma is intermittent, self limited, IOP elevations accompanied by prodromal symptoms of headache, haloes and blurred vision but with normal IOP in the interparoxysmal period, in patients with an occludable angle. Chronic angle-closure glaucoma is typically asymptomatic until advanced visual field loss. Patients present with occludable angles having pas of more than 180 degrees and a chronically elevated IOP.^{41,42}

Risk factors:

Primary angle-closure mechanisms can present with three site-specific disturbances in the anterior segment i.e. the pupillary block mechanism, ciliary body anomalies (e.g. Plateau iris syndrome) and lens induced. Demographic risk factors are as follows:

- 1) Age of the patient: Incidence increases with age. Age associated changes cause an

increased tendency towards pupillary block, (especially 6th-7th decades).. However, it can present at any age.^{43,44}

- 2) Sex: Female predominance (2-3 times) possibly because of shallower ACS.⁴⁵
- 3) Heredity of the patient: Because configuration of the ac is under polygenic influence. Inuit population have the highest known prevalence.^{46,47}
- 4) Refractive error: smaller dimensions of depth and volume of ac predispose hyperopes to primary angle-closure glaucoma.^{45,48}

Ocular risk factors and mechanisms: these include reduced axial ac depth and volume, short axial length, steeper radii of corneal curvature, and thicker lens in particular.^{49,50} Based on an increased iop \geq 21 mm hg on two or more occasions and/or optic disc changes suggestive of glaucoma, patients should undergo a comprehensive evaluation using slit lamp, funduscopy, gonioscopy, applanation tonometry and perimetry to determine and classify the various subtypes of glaucoma presenting in clinic. The risk factors, clinical history, signs, symptoms and clinical profile of each patient should be recorded.⁵¹

CONCLUSION

One of the leading causes of blindness is glaucoma. It can be prevented by early diagnosis and treatment. Patients with a family history of the disease should be referred by the primary care physicians for a complete ophthalmologic examination. Many severity classification methods have been proposed, although none have had widespread use in clinical practice. Further, assessment of the optic nerve by direct ophthalmoscopy may rule out suspicious signs of optic nerve damage so that prompt referral to an eye care specialist can be done.

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