Frontiers in Health Informatics
ISSN-Online: 2676-7104
www.healthinformaticsjournal.com
2024; Vol 13: Issue 8
Open Access

Evaluation of Intraocular Pressure Fluctuations in Primary Open-Angle Glaucoma

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Cite this paper as: Prof. Dr. Md. Sanwar Hossain, Dr. Md. Arifuzzaman, Dr. Mohammad Mazaharul Islam, Dr. Md. Golam Faruk Hossain, Dr. Muktar Ali, Dr. Tasnim Khanom (2024). Evaluation of Intraocular Pressure Fluctuations in Primary Open-Angle Glaucoma. *Frontiers in Health Informatics*, *Vol.13, No.8*, 6941-6949

ABSTRACT

Background: Intraocular pressure (IOP) fluctuation is a known risk factor for glaucoma progression. This study aimed to evaluate diurnal IOP fluctuations and their association with treatment regimens in patients with primary open-angle glaucoma (POAG). ***Methods:*** This cross-sectional study was conducted in the Department of Ophthalmology, Dr. Sirajul Islam Medical College & Hospital Ltd, Dhaka and Bangladesh Eye Hospital, Malibagh, Dhaka, Bangladesh, from July 2022 to June 2023. A total of 120 patients with diagnosed POAG were enrolled. Baseline demographic and clinical characteristics were recorded, including visual acuity, visual field parameters, and ocular biometric measurements. IOP was measured at four fixed time points (08:00 AM, 12:00 PM, 04:00 PM, and 08:00 PM) in a single day to assess diurnal variation. ***Results:*** The mean age of participants was 58.4 ± 9.3 years, with a slight male predominance (53.33%). The average IOP was highest at 08:00 AM (20.76 ± 3.08 mmHg) and lowest at 04:00 PM (18.87 ± 2.86 mmHg). The overall mean daily IOP fluctuation was 3.41 ± 1.64 mmHg. Most patients (43.33%) had moderate fluctuations between 3–4 mmHg. IOP fluctuation was significantly associated with the type of medical therapy. Patients on monotherapy had the highest mean fluctuation (4.1 ± 1.2 mmHg), while those on triple therapy had the lowest (3.2 ± 1.3 mmHg) ($p = 0.045$). ***Conclusion:*** Diurnal IOP fluctuation is common among POAG patients and varies with the intensity of medical therapy. More aggressive treatment regimens may be beneficial in minimizing IOP variability, potentially reducing the risk of disease progression.

Keywords: Primary open-angle glaucoma, Intraocular pressure, IOP fluctuation, Glaucoma therapy.

INTRODUCTION

Glaucoma is the second leading cause of blindness globally, posing a significant public health challenge [1]. The worldwide prevalence of glaucoma is projected to reach 111.8 million by

the year 2040 [2]. Among various risk factors, intraocular pressure (IOP) is recognized as the most critical and currently the only clinically modifiable risk factor for the development and progression of glaucoma [3]. IOP, however, is not a static parameter; it fluctuates throughout the day and night [4]. Previous investigations have demonstrated that nighttime IOP levels often increase in patients with primary open-angle glaucoma (POAG) [5].

POAG and myopia are two prevalent ocular conditions with considerable global impact [6,7]. Epidemiological data have revealed a strong association between POAG and myopia, particularly high myopia [8]. Both high myopia and increased axial length are considered significant risk factors for the development of POAG [9,10]. Recent studies have also explored the possibility of a more rapid rate of glaucomatous progression in patients with POAG combined with high myopia (POAG-HM), although definitive conclusions remain elusive due to inconsistent findings in the literature [8]. The underlying causes of this suspected accelerated progression remain unclear. In addition to structural risk factors, IOP levels and their fluctuations are believed to play a central role in glaucoma progression. Elevated IOP remains a well-established risk factor [10,11].

IOP fluctuations can be classified into various types, notably short-term (24-hour diurnal) and long-term fluctuations [11,12]. Short-term IOP fluctuation refers to variations within a single day and is typically calculated as the difference between peak and trough IOP values. In contrast, long-term fluctuations are often defined by the standard deviation of IOP readings over multiple visits. While the contribution of IOP variability to glaucoma progression remains a topic of ongoing debate, multiple studies suggest a potential link between IOP fluctuations and disease advancement [4,13]. Therefore, understanding the patterns and magnitude of IOP fluctuations is clinically important in glaucoma management.

Seasonal variations in IOP have also been documented. Qureshi et al. reported significant seasonal IOP changes in both healthy individuals and patients with ocular hypertension (OHT) [14,15]. Furthermore, Asrani et al. found that 24-hour IOP fluctuation was a significant predictor of glaucomatous progression, whereas Liu et al. reported conflicting results [16,17]. Several studies have confirmed that patients with or suspected of having open-angle glaucoma exhibit greater 24-hour IOP fluctuation compared to healthy controls [18,19]. Fluctuations occurring during and beyond regular clinic hours have been identified as independent risk factors for glaucoma progression [16,20].

Similar to blood pressure, IOP is influenced by various physiological and environmental factors such as time of day, body position, fluid intake, physical activity, and medication adherence [21,22]. As a result, single IOP measurements obtained during routine office visits may fail to capture the full extent of IOP variability. Findings from the Advanced Glaucoma Intervention Study emphasized this point, demonstrating that IOP fluctuation was an independent predictor of visual field (VF) deterioration, even in patients with a well-controlled mean IOP. This suggests that significant undetected IOP variations could contribute to continued visual field loss despite seemingly adequate treatment [23].

Therefore, in the present study, we aimed to evaluate diurnal IOP fluctuations and their association with treatment regimens in patients with primary open-angle glaucoma (POAG).

METHODOLOGY & MATERIALS

This cross-sectional study was conducted in the Department of Ophthalmology, Dr. Sirajul Islam Medical College & Hospital Ltd, Dhaka and Bangladesh Eye Hospital Malibagh, Dhaka,

Bangladesh, from July 2022 to June 2023. In this study, we included 120 eyes of 120 patients diagnosed with primary open-angle glaucoma attending the OPD of the Ophthalmology department of Dr. Sirajul Islam Medical College & Hospital Ltd, Dhaka and Bangladesh Eye Hospital Malibagh Ltd, Dhaka, Bangladesh.

These were the following criteria for eligibility as study participants:

Inclusion Criteria

- Patients aged 40 years and above.
- Diagnosed with primary open-angle glaucoma based on clinical findings and investigations.
- Willing and able to comply with scheduled IOP measurements throughout the day.
- Provided informed written consent to participate.

Exclusion Criteria

- Patients with secondary glaucoma (e.g., pseudoexfoliation, pigmentary, neovascular).
- History of intraocular surgery or laser procedures within the past 6 months.
- Presence of corneal pathology that could affect accurate IOP measurement.
- Advanced cataract or media opacities interfering with optic disc or visual field evaluation.
- Uncontrolled systemic illnesses (e.g., diabetes mellitus, hypertension).
- Use of systemic medications known to influence IOP (e.g., corticosteroids).

Data Collection Procedure: After obtaining informed consent, all participants underwent a detailed ophthalmic examination. Baseline data collected included demographic information, duration of glaucoma, systemic comorbidities, family history of glaucoma, and current antiglaucoma medications. Visual acuity was measured using a LogMAR chart. IOP was measured using Goldmann applanation tonometry at four time points during the day: 08:00 AM, 12:00 PM, 04:00 PM, and 08:00 PM. The same calibrated tonometer and examiner were used throughout to ensure consistency. Daily IOP fluctuation was calculated as the difference between the maximum and minimum IOP values recorded within the day. Optic nerve head assessment was performed using slit-lamp biomicroscopy with a +90D lens. Visual field testing was conducted with standard automated perimetry (Humphrey Field Analyzer), and mean deviation (MD) values were recorded. Additional measurements included central corneal thickness (via pachymetry), axial length and anterior chamber depth (via A-scan biometry), and average circumpapillary retinal nerve fiber layer (cpRNFL) thickness using optical coherence tomography (OCT).

Statistical Analysis: All data were recorded systematically in a pre-formatted data collection form. Quantitative data was expressed as mean and standard deviation, and qualitative data was expressed as frequency distribution and percentage. Differences in IOP fluctuation across medication groups were analyzed using one-way analysis of variance (ANOVA). A p-value <0.05 was considered significant. Statistical analysis was performed by using SPSS 20 (Statistical Package for Social Sciences) for Windows version 10.

RESULTS

Table 1. Baseline Characteristics of Study Participants (N = 120)

Variable	Number	Percentage (%)
Age (years), mean ± SD	58.4 ± 9.3	
Gender		

Male	64	53.33
Female	56	46.67
Duration of Glaucoma (years)	6.2 ± 3.8	
Family History of Glaucoma	41	34.17
Systemic Hypertension	48	40.00
Corrected visual acuity, LogMAR	−0.08±0.11	
Mean deviation (dB)	−3.71±2.72	
CpRNFL thickness (μ)	87.89±17.10	
Central corneal thickness (μm)	536.93±40.33	
Axial length (mm)	24.43±1.47	
Anterior chamber depth (mm)	3.25±0.29	

(cpRNFL=circumpapillary retinal nerve fiber layer)

Table 1 presents the baseline characteristics of the 120 patients included in the study. The mean age of participants was 58.4 ± 9.3 years. Males comprised 53.33% (n=64) of the study population, while females accounted for 46.67% (n=56). The average duration of glaucoma was 6.2 ± 3.8 years, with 34.17% (n=41) of patients reporting a positive family history. The mean corrected visual acuity, expressed in LogMAR units, was −0.08 ± 0.11. The mean deviation (MD) on visual field testing was −3.71 ± 2.72 dB. The average cpRNFL thickness was 87.89 ± 17.10 μm. Central corneal thickness and axial length were 536.93 ± 40.33 μm and 24.43 ± 1.47 mm, respectively. The mean anterior chamber depth was measured at 3.25 ± 0.29 mm.

Table 2. Mean Intraocular Pressure (IOP) and Daily Fluctuations

Measurement Time	Mean IOP (mmHg) ± SD	Range (mmHg)
08:00 AM	20.76 ± 3.08	14–28
12:00 PM	19.62 ± 2.74	13–26
04:00 PM	18.87 ± 2.86	12–27
08:00 PM	19.07 ± 2.69	12–26
Daily Fluctuation	3.41 ± 1.64	1–8

Table 2 summarizes the mean intraocular pressure (IOP) measurements at four time points throughout the day. The highest mean IOP was recorded in the early morning at 08:00 AM (20.76 ± 3.08 mmHg), with a gradual decrease noted by the afternoon (18.87 ± 2.86 mmHg at 04:00 PM). A slight increase was observed again in the evening (19.07 ± 2.69 mmHg at 08:00 PM). The overall mean daily IOP fluctuation was 3.41 ± 1.64 mmHg, with fluctuations ranging from 1 to 8 mmHg across the study population.

Table 3. Distribution of Patients by IOP Fluctuation Level (n=120)

IOP Fluctuation (mmHg)	Number	Percentage (%)
≤2 mmHg	18	15.00
3–4 mmHg	52	43.33
5–6 mmHg	30	25.00
>6 mmHg	20	16.67

Table 3 categorizes patients based on the extent of their IOP fluctuations. The largest proportion of participants (43.33%) experienced fluctuations between 3–4 mmHg, while 25.00% had fluctuations in the 5–6 mmHg range. A smaller subset (16.67%) demonstrated fluctuations greater than 6 mmHg, and only 15.00% had minimal fluctuations (≤2 mmHg).

These findings suggest that the majority of patients experienced moderate IOP variability, which may have implications for disease progression and management.

Table 4: Medication Use and IOP Fluctuation

Medication Regimen	Mean Fluctuation (mmHg) ± SD	N (%)	P-value
Monotherapy	4.1 ± 1.2	40 (33.33%)	0.045
Dual Therapy	3.6 ± 1.1	52 (43.33%)	
Triple Therapy	3.2 ± 1.3	28 (23.33%)	

Table 4 presents the relationship between the type of glaucoma medication regimen and IOP fluctuation among the study participants. Patients on monotherapy exhibited the highest mean IOP fluctuation (4.1 ± 1.2 mmHg), followed by those on dual therapy (3.6 ± 1.1 mmHg), and the lowest fluctuation was observed in patients receiving triple therapy (3.2 ± 1.3 mmHg). The distribution of patients across the treatment groups was 33.33% for monotherapy, 43.33% for dual therapy, and 23.33% for triple therapy. The difference in IOP fluctuations among the three medication groups was statistically significant ($p = 0.045$), suggesting that patients on more intensive medical regimens may achieve better IOP stability.

DISCUSSION

Intraocular pressure (IOP) is known to fluctuate based on the time of day and various individual factors such as physical activity, fluid intake, and posture. These fluctuations have been identified as potential contributors to disease progression in patients with both primary open-angle glaucoma (POAG) [16,22-24] and primary angle-closure glaucoma (PACG) [25,26]. Although there is currently no universal consensus regarding the definitive role of IOP fluctuations in glaucoma progression, they remain an important clinical consideration, particularly in patients who exhibit progressive visual field (VF) loss despite stable IOP readings during routine follow-up [22,23].

In our study, IOP levels were found to vary throughout the day, with the highest mean values occurring in the early morning and decreasing toward the afternoon. Most patients experienced moderate IOP fluctuations in the range of 3–4 mmHg, a pattern that could contribute to long-term optic nerve damage. The majority of prior studies support the concept that short-term (diurnal) and long-term IOP fluctuations are relevant in the context of disease progression, especially in patients with advanced disease or structural risk factors such as thin retinal nerve fiber layers or large optic disc cupping.

Yang et al. demonstrated that under resting conditions, 24-hour IOP fluctuations were not significantly different among study groups, consistent with Liu et al.'s findings in younger adults [10,27]. However, a significant increase in IOP fluctuation was observed in POAG patients with high myopia (POAG-HM) following an exercise stress test. Structural changes associated with high myopia, such as elongated axial length [9], optic disc tilt, peripapillary atrophy [28], retinal nerve fiber layer thinning [29], and impaired choroidal and retinal perfusion, may reduce ocular autoregulation, potentially increasing vulnerability to IOP variation [30,31]. Interestingly, Yang et al. noted that while IOP decreased following exercise in high myopia cases (possibly offering benefit), the implications of such a decrease remain uncertain and may depend on the duration and consistency of the effect [10].

Sihota et al. reported that diurnal IOP fluctuations were significantly higher in both PACG and POAG patients compared to normal controls [32]. Notably, the PACG group had undergone laser peripheral iridotomy (LPI), and untreated POAG patients also demonstrated higher

fluctuation patterns. However, Sihota's study did not include PACG eyes with <180° peripheral anterior synechiae (PAS), which may limit the generalizability of their findings. In another study by Baskaran et al. [24], the International Society for Geographical and Epidemiological Ophthalmology (ISGEO) classification was used to define angle-closure disease. Foster et al showed that patients with PAC or PACG were more than twice as likely to exhibit diurnal IOP fluctuation of more than 3 mmHg, compared with those classified as PACS or normals (odds ratio: 2.38). However, their use of a non-contact tonometer rather than the Goldmann applanation tonometer (GAT) may affect measurement accuracy [33]. Moreover, the effect of anti-glaucoma medications on IOP fluctuation was not evaluated in these studies.

Arora et al. conducted a water-drinking test (WDT) and found greater IOP fluctuations in ACG patients (6.00 mmHg) compared to POAG patients (4.25 mmHg, $P = 0.004$). However, approximately 40% of the POAG group were not on anti-glaucoma medications, raising the possibility that many were glaucoma suspects rather than diagnosed cases, potentially explaining the lower fluctuations observed [34]. In contrast, Poon et al. reported similar IOP curves in PACG and POAG patients after water intake, despite biometric differences. Their reported mean IOP fluctuations (3.61 ± 2.49 mmHg in PACG vs. 3.79 ± 1.91 mmHg in POAG) suggest that factors beyond anterior chamber anatomy contribute to these responses [22].

In the present study, patients on monotherapy had the highest mean fluctuation (4.1 ± 1.2 mmHg), while those on triple therapy had the lowest (3.2 ± 1.3 mmHg). Topical anti-glaucoma medications have been shown to reduce IOP variability, including diurnal fluctuations [35,36]. Gardiner et al. also suggested that these medications might attenuate seasonal fluctuations, although it remains unclear which specific classes or agents exert this effect most effectively [37]. Additionally, Terauchi et al. observed that patients with a family history of glaucoma experienced significantly less seasonal IOP variation compared to sporadic cases, based on multiple linear regression analysis [38]. Mabuchi et al. further demonstrated a relationship between certain non-IOP-related genetic variants and a family history of glaucoma, suggesting that genetic background may influence IOP behavior and its variability [39].

Overall, these findings underscore the complex interplay between anatomical, physiological, environmental, and genetic factors in influencing IOP fluctuation. Identifying patients at higher risk for significant fluctuation, particularly those with high myopia or structural optic nerve vulnerability, is essential in tailoring more aggressive treatment strategies. Regular diurnal IOP monitoring, beyond standard office-hour measurements, may be valuable in such cases to prevent disease progression.

Limitations of the Study

This study has several limitations. First, it was conducted at a single tertiary care center, which may limit how well the findings apply to broader populations. Second, IOP measurements were taken at four times during office hours, which might not fully reflect nocturnal fluctuations or peak pressures that happen outside these times. Lastly, the study's cross-sectional design restricts the ability to evaluate the long-term effects of IOP fluctuations on disease progression.

Conclusion and Recommendations

This study highlights that intraocular pressure in patients with primary open-angle glaucoma demonstrates measurable diurnal fluctuations, with the highest values typically recorded in the early morning. A significant proportion of patients experienced moderate to high fluctuations, which may have clinical relevance in the context of disease progression and treatment planning. Notably, patients on more intensive medical regimens, particularly those receiving triple

therapy, exhibited lower mean IOP fluctuations compared to those on monotherapy. These findings underscore the importance of considering both absolute IOP levels and their variability when managing glaucoma and support the need for individualized treatment approaches to minimize fluctuation and preserve visual function.

Further study with a prospective and longitudinal study design, including a larger sample size, needs to be done to validate the findings of the study.

Funding: *No funding sources*
Conflict of interest: *None declared*
Ethical approval: *This study was ethically approved*

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