Survival analysis of phacomorphic glaucoma at a tertiary hospital in North India

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Abstract:
PURPOSE: To report the intraocular pressure (IOP) and visual outcomes in patients operated for phacomorphic glaucoma in a developing country

METHODS: Patients undergone surgery for phacomorphic glaucoma between January 2015 and February 2018 with a minimum follow-up of 6 months were reviewed. Multinomial logistic regression was used to predict final visual acuity with different preoperative variables. A Kaplan-Meier analysis was done to calculate survival probabilities at different time points.

RESULTS: Presenting IOP of study eye was 38.3±13.4 mmHg with 97.91% (n=94/96) patients on AGMs (mean: 2.7±1.08). Mean duration of complaints was 7.7±6.3 days. The most common postoperative complication was severe anterior chamber inflammation with or without fibrin membrane (in 29.16% eyes). The mean follow-up period was 14.5±9.2 months. At the last visit, the CDVA was 20/30 or better in 54/96 (56.25%) eyes, the mean IOP was 13.6±2.6 mmHg and 30 (31.25%) eyes required additional AGM with the mean number being 1.5±0.6. Two eyes required trabeculectomies for IOP control. The mean survival time of complete and qualified success was 28.5±1.9 and 41.2±0.05 months respectively. The probability of complete and qualified success at month 42 was 11% and 98%. Duration of complaints and VCDR were found to be associated with final visual acuity.

CONCLUSIONS: There was a positive correlation between shorter duration of symptoms with post-operative visual gain, but the glaucomatous damage showed a plateau effect at the IOP of around 35 mmHg. It is not the level of IOP, rather its duration which determines the degree of visual loss.

Keywords: Phacomorphic glaucoma, intraocular pressure, survival analysis, India

Introduction

Cataract accounts for 62.6% of all blindness in India,[1] In the past two decades, globally, the number of blind and visually impaired due to cataract have decreased by 11.4% and 20.2%, respectively.[2] Although India has been successful in raising its cataract surgical rate[3,4] (the number of cataract operations performed per year per million people of an area),[5] the burden of cataract remains a major public health concern. Various economic and socio-cultural influencing factors such as decreased need for vision, misconceptions that a cataract needs to be removed only when mature, lack of awareness about the disease, and fear of surgical procedure have been identified as the contributors to the barriers for the uptake of cataract surgery.[5‑8]

Phacomorphic glaucoma is a sequelae of a neglected advanced cataract and is one of the most common cause of secondary angle closure glaucoma in developing countries like India, the incidence of which is reported to be as high as 3.91%.[9,10] It is caused by a
compressed and compromised aqueous drainage pathway due to a mature and swollen lens leading to a resultant intra-ocular pressure (IOP) rise and optic nerve damage.\textsuperscript{[10,12]} Cataract extraction is the only definitive treatment after initial IOP control, but despite the availability of modern medical and surgical management, the visual prognosis remains guarded and often poor.\textsuperscript{[13,14]}

The aim of our study was to evaluate the visual outcome and IOP control postcataract extraction in phacomorphic glaucoma and correlate them with the presenting IOP and symptom duration. The secondary outcome measures were postoperative vertical cup-disc ratio (VCDR), mean deviation on Humphrey’s automated perimetry, number of anti-glaucoma medications (AGM) required, and time from symptoms to surgery.

**Materials and Methods**

This retrospective study was conducted at a tertiary care eye center in North India from January 2015 to February 2018. The hospital’s database was searched for patients with the diagnosis of phacomorphic glaucoma, which was defined as narrowing of the angle by forward pushing of the iris by an intumescent cataractous lens leading to the obstruction of aqueous flow between the border of the pupil and the anterior capsule of the lens (pupillary block) and is characterized by subjective complaints of diminished vision with pain and redness and objective signs such as the presence of an intumescent cataract with high IOP (>21 mmHg), shallow central anterior chamber, corneal edema, mid-dilated fixed pupil, and conjunctival congestion.\textsuperscript{[15-17]}

Distinguishing between acute angle closure and phacomorphic glaucoma is not always straightforward as the signs and symptoms are largely overlapping, but a normal contralateral eye with the presence of an intumescent cataract in the affected eye should strongly suggest a phacomorphic process, whereas a shallow anterior chamber, high IOP, occludable angles, and glaucomatous changes in the optic disc in the fellow eye indicate an acute angle closure mechanism.

A total of 142 such patients attended our outpatient department and underwent a detailed clinical examination of both eyes including the visual acuity, status of the lens, IOP recording by Goldmann-applanation tonometry, gonioscopy and optic disc evaluation of the fellow eye, and 16 patients found to have either an evidence of angle closure in the contralateral eye were excluded from the study. The present study was approved by the Institutional Ethics Committee (IRB approval number is: 018/2020) and adhered to the tenets of the declaration of Helsinki.

A total of 126 consecutive eyes (of 126 patients) were identified with phacomorphic glaucoma based on the aforementioned features. All patients underwent B-scan for the posterior segment evaluation. Axial length and anterior chamber depth were assessed using immersion biometry (OcuScan RxP, Alcon, Forth Worth, TX, USA). IOL power was calculated with optical biometer (Lenstar LS 900, Haag Streit., AG). Prior ophthalmic consultation and any ocular hypotensive drugs taken by the patients were noted.

The present study was conducted in two parts. The first part included all 126 cases that presented to our OPD, irrespective of being operated upon or not. This was done to look at the demographic data representation of phacomorphic glaucoma in our region. The details included the presenting age, presenting IOP, symptoms, and gender predilection. For the second part, 30 patients who were not operated or had a follow-up period of less than 6 months were excluded. Ninety-six eyes of 96 patients which got operated at our center with at least 6 months of follow-up were included and were studied for postcataract extraction clinical outcomes such as corrected distance visual acuity (CDVA), IOP, VCDR, and visual field changes.

All patients were treated uniformly with initial systemic acetazolamide, ruling out any systemic contra-indications, with topical steroids and combinations of AGM including beta-blockers, alpha-agonists, and/or carbonic anhydrase inhibitors. After obtaining informed consent and explanation of relatively guarded prognosis, the patients were subjected to either extracapsular cataract extraction (ECCE) or manual small incision cataract surgery (MSICS) or phacoemulsification (PE) under peribulbar anesthesia as day care surgery. The choice of surgical technique was based on surgeon’s preference. Preoperatively, intravenous mannitol 20% (1–2 g/kg body weight) was given if IOP was >35 mmHg just before the surgery.

Decision of implanting an intraocular lens (IOL) was made after assessing the status of capsular bag intra-operatively. Postoperative medications included topical antibiotic and steroids for the next 6–8 weeks. All patients were followed up for at least 6 months. Clinical parameters were noted at postoperative day 1, 1 week, 6 weeks, 6 months, and then on a 6–12 monthly basis.

During each follow-up visit, visual acuity (using a Snellen’s chart), IOP with Goldmann applanation tonometry, and slit lamp bio-microscopy were performed. Complete success was defined as an IOP of ≥5 mmHg and ≤21 mmHg without any AGM while qualified success was defined as IOP ≤21 mmHg with AGM. All cases with an IOP of >21 mmHg and those requiring any
secondary IOP lowering procedure were considered as failure.

At 6 weeks, the patients underwent refraction, posterior pole evaluation, including the VCDR, using the V Computerized Static Threshold Algorithm (SITA) 24-2 test; Carl Zeiss Meditec, Dublin, CA). Glaucoma treatment was re-implemented if IOP was >21 mmHg on two or more follow-ups. Patients underwent glaucoma filtration surgeries if IOP was not controlled even on maximum tolerable medical treatment.

Statistical analysis
Statistical Package for the Social Sciences software version 23 (SPSS Inc., Chicago, IL, USA) was used for the statistical analysis. Mean and standard deviation was calculated for the continuous variables. Categorical variables were reported in percentages and compared using the Chi-square test. Fisher’s exact test and Monte Carlo simulation was used, in case expected frequency of cell was below five. Independent t-test was used to compare two independent continuous variables. The repeated measure analysis of variance was used to determine the differences between the means of identified parameters at different time points. Mauchly’s test of sphericity was used to test the assumption of sphericity. If the data violated the assumption of sphericity, Greenhouse-Geisser correction was used to test within subject effect. Post hoc tests using the Bonferroni correction were performed. Kaplan–Meier survival analysis was done to calculate the survival probabilities at different time points. A probability (P) of 0.05 or less was considered statistically significant.

Results
One hundred and twenty-six records of patients with the diagnosis of phacomorphic glaucoma were reviewed. Of them, 96 (n = 96/126; 76.2%) patients were operated for phacomorphic glaucoma and 30 (n = 30/126; 23.8%) were not operated at our institute. Comparison of demographic characteristics of operated and not operation is presented in Table 1.

Of operated patients, 58 (n = 58/96; 60.4%) were females. The right eye was involved in 49 (n = 49/96; 51%) patients. The mean age of these patients was 62.3 ± 10.2 years. Presenting IOP of study eye was 38.3 ± 13.4 mmHg with 97.91% (n = 94/96) patients already on AGMs, the mean number being 2.7 ± 1.08. The mean duration of complaints was 7.7 ± 6.3 days. Of all, 88 (n = 88/96; 91.7%) patients had presenting vision of less than or equal to hand movement.

Eighty-four patients underwent cataract extraction with posterior chamber IOL implantation (76 underwent MSICS, 5 underwent PE, and three patients underwent ECCE). Three patients had pre-existent zonular dialysis, out of which one patient underwent an intra-capsular cataract extraction and 2 needed an IOL implantation with capsular tension ring to stabilize the capsular bag. Eleven patients had a posterior capsular rent, out of which two patients received an iris claw lens, two patients had a polymethyl myth-acrylate IOL placed in the capsular bag and three in sulcus, one received an anterior chamber IOL, and rest of the three eyes were left aphakic. All these patients underwent a concurrent anterior vitrectomy. Two patients had superior iridodialysis intra-operatively, out of which one underwent iris repair.

The most common complication encountered on the postoperative day 1 was severe anterior chamber inflammation with or without fibrin membrane in 28 (29.16%) eyes, followed by corneal edema in 25 (26%) eyes, hyphema in 6 (6.25%) eyes, and wound leak in

Table 1: Comparison of clinical parameters between operated and not operated patients

| Surgery          | Operated at institute | Not operated at institute | P     |
|------------------|-----------------------|---------------------------|-------|
| Complains in days| 7.69±6.3              | 4.93±2.9                  | 0.02  |
| Age              | 62.38±10.2            | 65.43±10.2                | 0.15  |
| Presenting IOP (mmHg) | 38.3±13.3                 | 37.9±14.3                | 0.88  |
| Gender           |                        |                           |       |
| Male             | 38                     | 10                        | 0.66  |
| Female           | 58                     | 20                        |       |
| Visual acuity at presentation |                  |                           |       |
| >20/60          | 96                     | 28                        | 0.05* |
| 20/60-20/200    | 0                      | 1                         |       |
| <20/200         | 0                      | 1                         |       |

*4 cells (66.7%) have expected count <5. The minimum expected count is 24. Based on 10,000 sampled tables with starting seed 2,000,000.
IOP=Intra-ocular pressure

Table 2: Frequency distribution of early and late complications

| Category             | Complication                                      | n (%)                      |
|----------------------|---------------------------------------------------|----------------------------|
| Early complication   | Severe anterior chamber inflammation with or without fibrin membrane | 28 (29.16)                 |
|                      | Corneal edema                                     | 25 (26)                    |
|                      | Hyphema                                            | 6 (6.25)                   |
|                      | Eyes and wound leak                               | 2 (2.08)                   |
|                      | Total                                              | 61 (63.5)                  |
| Late complication    | Glaucomatous optic neuropathy                     | 15 (15.6)                  |
|                      | Aphakic bullous keratopathy                       | 3 (3.1)                    |
|                      | Non glaucomatous optic neuropathy                 | 3 (3.1)                    |
|                      | Macular scar                                       | 2 (2.1)                    |
|                      | Full-thickness macular hole                        | 1 (1)                      |
|                      | Epiretinal membrane                               | 1 (1)                      |
|                      | Choroidal/retinal detachment                      | 1 (1)                      |
|                      | Total                                              | 26 (27.1)                  |
The mean follow-up period was 14.5 ± 9.2 months. Improved visual acuity was noted in 74/96 (77%) patients at 1 week, 78/96 (81.2%) patients at 6 weeks, and 75/96 (78%) patients at final follow-up. At the last visit, the CDVA was 20/30 or better in 54/96 (56.25%) eyes, 20/40–20/200 in 19/96 (19.7%) eyes, and <20/200 in 23/96 (23.95%) eyes. The distribution of visual acuity at different follow-up is presented in Table 3.

The causes of decreased vision were glaucomatous optic neuropathy in 15 (15.6%) patients, a phakic bullous keratopathy in 3 (3.1%) patients, nonglaucomatous optic neuropathy in 3 (3.1%) patients, macular scar in 2 (2.1%) patients, and full thickness macular hole and epiretinal membrane in 1 (1%) patient each. One eye developed choroidal/retinal detachment after an eventful surgery and had eventually NPL vision [Table 2].

The mean IOP at 1 week, 6 weeks, and last follow-up was 14.8 ± 5.7, 14.14 ± 3.6, and 13.6 ± 2.6 mmHg, respectively. A repeated-measures ANOVA with a Greenhouse-Geisser correction determined that mean IOP differed significantly between different time points (F [1.25, 117.7] = 32886.9, P ≤ 0.01). Post hoc tests using the Bonferroni correction revealed that mean IOP changed significantly from the presentation to subsequent follow-ups, at 1 week (P = 0.035; Fisher’s exact test) [Table 5]. At the last visit, VCDR of 68 (70.8%) patients was less than 0.8 and of 28 (29.2%) patients was more than equal to 0.8. In Group A, 14% (n = 3/22) patients had VCDR of

Thirty (31.25%) eyes required additional AGM at the final visit, the mean number of which was 1.5 ± 0.6. This difference in pre-operative and number of AGM at final follow-up was significant (P ≤ 0.01, paired t-test). Two eyes required trabeculectomies for IOP control at 3 and 4.5 months, respectively.

For the statistical analysis, duration of complaints was divided into three groups (Group I: “<7 days,” Group II: “between 7 and 14 days,” and Group III: “more than 14 days”). In Group I, 39 patients (n = 39/47; 83%) achieved final visual acuity of better than 20/40, as compared to 21 (n = 21/34; 61.8%) in Group II and 4 (n = 4/15; 26.7%) in Group III (P ≤ 0.01, 95% confidence interval [CI]: 0.00–0.001; Fisher’s exact test) [Table 4].

Similarly, presenting IOP was also divided into three groups (Group A: “<35 mmHg,” Group B: “between 35 and 45 mmHg,” and Group C: “more than 45 mmHg”). In Group A, 18 (n = 18/22; 81.8%) patients achieved final visual acuity better than 20/40 as compared to 30 (n = 30/48; 62.5%) in Group B and 16 (n = 16/26; 61.5%) in Group C (P = 0.035; Fisher’s exact test) [Table 5].

### Table 3: Frequency distribution of visual acuity categories at different time points

| Visual acuity | Presentation | 1 week FU | 6 weeks FU | 6 months FU |
|---------------|-------------|-----------|------------|-------------|
| 20/20-20/30   | 0           | 18        | 41         | 54          |
| 20/40-20/200  | 0           | 50        | 34         | 19          |
| 20/200-CF     | 8           | 14        | 11         | 10          |
| HM/PL         | 88          | 14        | 10         | 13          |
| Total         | 96          | 96        | 96         | 96          |

FU = Follow-up, CF = Counting Finger, HM = Hand movement, PL = Perception of light

### Table 4: Comparison between duration of complains and final visual acuity

| Durations of complains (days) | Final visual acuity (%) | Total |
|-------------------------------|-------------------------|-------|
|                               | <20/40-20/400 | >20/40 | CF/HM/PL |
| <7                            | 4 (8.5)       | 39 (83.0) | 4 (8.5) | 47  |
| 7-14                          | 5 (14.7)      | 21 (61.8) | 8 (23.5) | 34  |
| >14                           | 2 (13.3)      | 4 (26.7)  | 9 (60.0) | 15  |
| Total                         | 11            | 64       | 21       | 96  |

CF = Counting Finger, HM = Hand Movement, PL = Perception of light

### Table 5: Comparison between presenting intraocular pressure and final visual acuity

| Presenting IOP (mmHg) | Final visual acuity (%) | Total |
|-----------------------|-------------------------|-------|
|                       | >20/40   | <20/40-20/400 | CF/HM/PL |
| <35                   | 18 (81.8) | 2 (9.1)   | 2 (9.1)  | 22  |
| >45                   | 16 (61.5) | 2 (7.7)   | 8 (30.8) | 26  |
| 36-45                 | 30 (62.5) | 7 (14.6)  | 11 (22.9) | 48  |
| Total                 | 64 (66.7) | 11 (11.5) | 21 (21.9) | 96  |

IOP = Intra-ocular pressure, CF = Counting Finger, HM = Hand Movement, PL = Perception of light
more than equal to 0.8 as compared to 35% \((n = 8/18)\) in Group B and 31% \((n = 17/48)\) in Group C \((P = 0.17;\) Fisher’s exact test).

The mean survival time of complete success was 28.5 ± 1.9 months \((95\% CI: 24.8–32.3)\). The mean survival time of qualified success was 41.2 ± 0.05 months \((95\% CI: 40.1–42.2)\). The probability of complete success at month 42 was 11%. The probability of qualified success at month 42 was 98% [Figure 2].

Field test was done for 77 patients at 6 weeks, out of which 21 showed field defects, most common being biarcuate defects in 6, followed by, incomplete arcuate defects in 4, nasal step in 3, complete arcuate defects superiorly in 2, and scattered defects in 2 eyes. Two patients showed altitudinal field defects, suggestive of NAION and two patients had a central scotoma secondary to macular scarring. The test could not be conducted in 19 eyes due to poor vision secondary to reasons discussed previously.

Multinomial logistic regression was used to predict a final visual acuity with age at presentation, duration of complaints, IOP at presentation, preoperative AGM, and VCDR as independent variables. Based on Chi-square goodness of fit measure \((P = 0.45)\), the model fits the data well. Duration of complaints \((P \leq 0.01)\) and VCDR \((P \leq 0.01)\) was found to be associated with final visual acuity [Table 6].

![Figure 2: Kaplan–Meier plot showing survival probability of patient with qualified and complete success](image)

**Table 6: Multinomial logistic regression analysis**

| Model fitting criteria                  | likelihood ratio tests | Likelihood ratio tests |
|-----------------------------------------|------------------------|------------------------|
| -2 log likelihood of reduced model     | \(\chi^2\)              | df                     | Significant   |
| Intercept                               | 113.05                 | 10.64                  | 2             | 0.005         |
| IOP                                     | 104.63                 | 2.23                   | 2             | 0.329         |
| Duration of complaints                  | 120.93                 | 18.52                  | 2             | 0.000         |
| Age of patient                          | 102.64                 | 0.23                   | 2             | 0.889         |
| Preoperative anti-glaucoma medication   | 104.22                 | 1.81                   | 2             | 0.404         |
| CD ratio                                | 124.51                 | 22.11                  | 2             | 0.000         |

IOP=Intra-ocular pressure, CD= Cup disc

**Discussion**

The incidence of lens induced glaucoma in India is as high as 3.91%,\(^9,10\) Limited visual need of the population, along with socioeconomic constraints and a general tendency to neglect the disease do not prompt the patients to report to hospitals early. Although the reported success in phacomorphic glaucoma following cataract extraction is lesser than that in eyes with uncomplicated cataract,\(^18,19\) the consecutive visual loss is avoidable and reversible to much extent. Female preponderance (of 61.9%) in our study is in conformity with previous literature,\(^9,14\) though, few authors such as Prajna et al.\(^19\) and Jain et al.\(^20\) did not find any gender predilection in their studies. The reason could be a possible dependency of females in this age group over other family members and lesser attention received by them. Furthermore, a more crowded anterior chamber predisposes these eyes to angle closure. Thirty (23.8%) patients out of 126 did not get operated at our institute. We cannot rule out the possibility of these patients getting treatment elsewhere.

In our study, 76 out of 96 patients underwent MSICS. With higher risks of intra-operative complications such as shallow anterior chamber, peripheral rhexis extension, zonular weakness, supra choroidal hemorrhage, and iris prolapse,\(^21,22\) it may be the more appropriate surgical treatment for advanced cataracts, especially...
in developing countries. Although theoretically, phacoemulsification renders smaller risk of expulsive hemorrhage, the procedure may be more challenging in eyes with phacomorphic glaucoma. Moreover, with an already compromised endothelial reserve, as is often seen in such eyes, the close proximity of the phacotip during nucleus emulsification may be detrimental to cornea clarity in future. Some authors have suggested other means to facilitate surgery in such eyes, namely performing a laser iridotomy or an argon laser peripheral iridoplasty as an initial presurgical management in phacomorphic glaucoma, doing a femtosecond-assisted capsulorhexis and lens fragmentation and using pars plana vitreous tap or a sutureless, small gauge, limited pars plana vitrectomy to expand, and deepen the anterior chamber.

We found a positive correlation between the shorter duration of symptoms with postoperative visual gain. Eighty-three percent of patients who presented within 7 days of developing symptoms gained visual acuity better than 20/40 as compared to 61.8% patients who presented in 7–14 days and 26.7% patients who presented more than 14 days after developing symptoms. This may be attributed to irreversible ischemic optic nerve damage and axonal flow disruption similar to primary acute angle closure. A similar correlation was seen with the IOP of <35 mmHg (Group A) and >35 mmHg (Group B + C), suggesting that the glaucomatous damage shows a plateau effect at the IOP of around 35 mmHg. Further increase in the IOP did not result in greater visual loss. Our results are consistent with a study by Lee et al., who demonstrated that it is not the level of IOP, rather its duration which determines the degree of visual loss.

Complete success was seen in 66 (68.75%) patients postoperatively. The remaining 30 patients required a mean of 1.5 ± 0.6 AGMs, out of which 2 needed trabeculectomies eventually. These eyes were found to have extensive peripheral anterior synechiae, reflecting longer duration of phacomorphic attack, and a delayed presentation to our institute. These data are in accordance with previous studies, where controlled IOP with AGM was noted to be 75% by Angra et al., 93% by Jain et al., and 80.5% by Lee et al. Out of the 30 (46.7%) eyes, which presented with inaccurate light projection, 19 (63.3%) had >20/200 vision with 14 eyes gaining a vision of 20/40 or better. Thus, we agree with Angra et al. that an initial faulty projection of rays does not necessarily mean a poor outcome.

Optic-disc changes in the form of disc cupping were directly related to the duration of attack as well as the presenting IOP. In our series, 77/96 patients could undergo field testing. Poor vision hindered testing in 19 eyes, out of which 15 (15.6%) patients were found to have glaucomatous optic atrophy. Twenty-one eyes recorded field defects, biarcuate defect being the most common (6 eyes). In their study, Angra et al., Pradhan et al., and Jain et al. found 30%, 34%, and 33.8% of cases having glaucomatous damage of the optic nerve, respectively.

We found the three eyes which developed sectoral disc pallor with altitudinal field defects having small crowded discs. One of the patients was hypertensive, and other two were both hypertensive and diabetic. We postulate that the anatomical predisposition of these eyes made them susceptible to nonarteritic ischemic optic neuropathy (NAION). This has been validated by previous studies where a rise in IOP was found to reduce the perfusion pressure of the ONH from compression of vessels in the prelaminar region leading to NAION.

Retrospective design of a study has its own limitations. We excluded patients with short postoperative follow-up, patients operated elsewhere, and eyes with a suspicion of primary angle closure. Furthermore, we apprehend that a long-term follow-up of ≥2 years would have been more conclusive of the clinical outcomes and detected any progression of optic neuropathy postcataract extraction in phacomorphic glaucoma.

This series highlights the significance of focused propagation of ocular health education and timely diagnosis of cataract to enhance the uptake of cataract surgeries, especially in developing countries.

**Conclusion**

It is imperative to enhance demand generation among the needy and provide low cost, but high quality, cataract surgery to them, to avoid the complications of lens-induced glaucoma and early restoration of vision. Furthermore, an initial inaccurate projection of rays does not always extrapolate to a poor postoperative vision.

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**Conflicts of interest**

The authors declare that there are no conflicts of interests of this article.

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