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Clinical characteristics of morning glory disc anomaly in South India

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Abstract:

PURPOSE: Reports of morning glory disc anomaly (MGDA) in India have mostly been case reports. The aim of this study was to describe the demographic and clinical profile of patients with MGDA in South India.

MATERIALS AND METHODS: A retrospective review of the medical records of patients with MGDA seen at a tertiary eye hospital in South India over a period of 8 years was carried out. The patients' demographic and clinical data were extracted from the case files and were entered into Epi Info reporting software version 7.2.3.0 and then analyzed.

RESULTS: There were 51 eyes of 44 patients with MGDA comprised 25 (56.8%) males and 19 (43.2%) females. Seven (15.9%) patients had bilateral MGDA. The mean age for females was 5.8 years (standard deviation [SD]: 5.8) and for males, 11.2 years (SD: 12.1). This difference was not statistically significant with a $P = 0.07$. The most common ocular associations were strabismus, refractive error, and retinal detachment, whereas the most common systemic associations were cleft lip and cleft palate. Fifty-one percent of eyes were blind at presentation.

CONCLUSION: Patients with MGDA in India tend to present late with poor visual prognosis. Early diagnosis and prompt treatment of blinding complications are crucial in reducing the risk of irreversible visual loss. Associated systemic abnormalities highlight the importance of a multidisciplinary approach in the management of patients with this condition.

Keywords:

Cleft lip, India, morning glory disc anomaly, retinal detachment, strabismus

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Introduction

Morning glory disc anomaly (MGDA) is a congenital optic disc anomaly characterized by an enlarged, funnel-shaped excavation of the optic disc with a central mass of glial tissue, surrounded by an elevated ring of chorioretinal pigmentary disruption.[1] It was first described by Kindler in 1970 who observed the resemblance of the optic disc malformation to the morning glory flower.[2] MGDA is a rare sporadic disorder with no gender predisposition and has a median age at the diagnosis of 2 years.[3,4] It is typically unilateral and bilateral cases are rarer still.[3,5] It has an estimated prevalence of 2.6/100,000.[6]

The pathogenesis of MGDA is not fully understood.[7] It has been hypothesized that the anomaly is a primary mesenchymal abnormality due to poor development of the lamina cribrosa and faulty closure of the posterior sclera wall.[8] Mutations in the *PAX6* gene have also been identified in these patients as well as in other patients with optic nerve malformations.[9] The PAX6 gene is involved in ocular morphogenesis and is expressed in numerous ocular tissues during development as well as in the developing central nervous system.[8] MGDA can be isolated or associated with other ocular or nonocular anomalies. The common

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ocular associations include retinal detachment (RD), strabismus, congenital cataract, persistent hyaloid remnants, lid hemangiomas, preretinal gliosis, lens coloboma, chronic simple glaucoma, Duane's retraction syndrome, and microphthalmia.[10] Associated systemic anomalies include midline craniofacial defects, agenesis of the corpus callosum, basal encephalocele, renal, and congenital forebrain abnormalities.[11]

Most reports on MGDA in India have primarily been case reports.[11-17] An earlier study in South India reported on the prevalence of RD and outcome of treatment in a small series of 15 patients with MGDA.[18] The aim of this study, therefore, was to describe the clinical characteristics of a larger series of patients with MGDA in South India.

Methods

This is a retrospective study of patients with MGDA seen at the retina clinic of a tertiary eye hospital in South India from January 2011 to December 2018. The study was approved by the Institutional Review Board of the hospital and conducted in accordance with the tenets of the declaration of Helsinki (approval number: RET201400194). The cases were first identified from the electronic medical records of the hospital and the case files retrieved. Only cases with a minimum duration of follow-up of 6 months were included in the study. The following data were then extracted from the case files: age, sex, symptoms, ocular examination findings, and abnormalities on systemic examination. All the patients had comprehensive ocular and systemic examination. Fundus photographs and reports of optical coherence tomography (OCT) scans (Spectralis HRA + OCT by Heidelberg Engineering, Heidelberg, Germany), B-scan ultrasonograms, fundus fluorescein angiograms, and magnetic resonance imaging or computer tomography scans were reviewed where available. Categorization of visual acuity (VA) was done using the International Classification of Diseases 11 (2018) categorization of vision impairment as follows; normal vision: ≥6/12, mild visual impairment <6/12–6/18, moderate visual impairment: <6/18–6/60, severe visual impairment: <6/60–3/60, blindness: <3/60 to no perception of light.[19]

Statistical analysis

Data entry and analysis were done using Epi Info reporting software version 7.2.3.0 developed by the Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia (US). Frequencies, means and standard deviations (SDs) were determined, and tests of significance were done using the Student's *t*-test and Pearson's Chi-squared test. $P < 0.05$ was considered statistically significant.

Results

A total of 51 eyes of 44 patients with MGDA [Figures 1-3] were seen during the period under review. There were 25 (56.8%) males and 19 (43.2%) females, giving a male: female ratio of 1.3:1. The mean age at presentation was 8.8 years (range; 0.25–46.0 years, median; 5 years, SD: 10.17). The mean age at presentation for females was 5.8 years (SD: 5.8), and for males, 11.2 years (SD: 12.1). This difference was not statistically significant using the Student's *t*-test with a $P = 0.07$. The most common

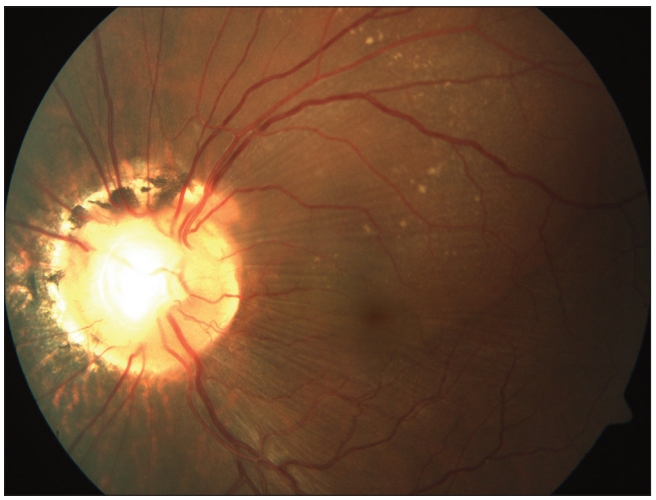


Figure 1: Fundus photograph of left morning glory disc anomaly

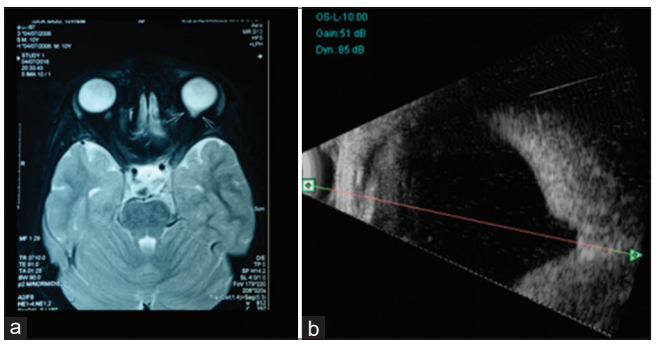


Figure 2: Magnetic resonance imaging scan of morning glory disc anomaly in right eye (a) along with B scan (left image) of the same eye showing funnel shaped excavation of the disc (b)

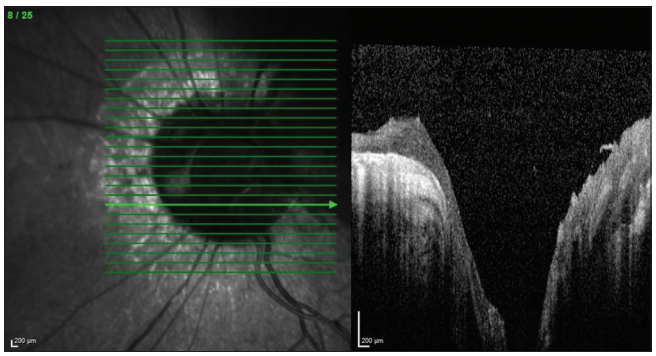


Figure 3: Optical coherence tomography showing excavated disc

complaints were defective vision, 31 (60.8%), deviation of the eye, 15 (29.4%), small size of the eye, three (5.9%), and white eye reflex, two (3.9%). Seven patients had more than one complaint.

Laterality could only be determined in 43 (97.7%) patients. Thirty-six (81.8%) patients had unilateral MGDA (20 left eyes and 16 right eyes), whereas seven (15.9%) patients had bilateral involvement. The most common ocular association was a squint which was present in 24 (47.1%) eyes followed by refractive error, 17 (33.3%). RD which was the most common retinal association was present in 12 (23.5%) eyes [Figure 4]. Most eyes had more than one associated anomaly [Table 1]. Among those with strabismus, there were 14 cases of esotropia and ten cases of exotropia. Bilateral lid abnormalities were seen in two patients. One patient had bilateral telecanthus and epicanthus with bilateral MGDA while the other had bilateral antimongoloid slant, but MGDA could only be confirmed in one eye. One patient had associated contractile movements of the disc and peripheral retinal nonperfusion.

Only seven (58.3%) of the 12 eyes with RD were operable. Six (50%) of these patients underwent surgery, while one patient declined surgical treatment. Surgery involved triamcinolone-assisted vitrectomy, trimming of preretinal glial tissue, internal limiting membrane peeling, retinal photocoagulation along the excavated disc, and internal tamponade with silicone oil or SF_6 gas. Silicone oil was used in four patients and SF_6 in two patients. An encircling band was used in combination with vitrectomy in two eyes. Anatomical success was achieved in four (57.1%) eyes, whereas visual improvement was recorded in two (28.5%) eyes and decrease in vision in one (14.2%) eye. The two patients with improvement in vision were boys aged 3 years and 12 years, respectively. The 3-year-old boy had a total RD, whereas in the 12-year-old boy, the RD was limited to the posterior pole.

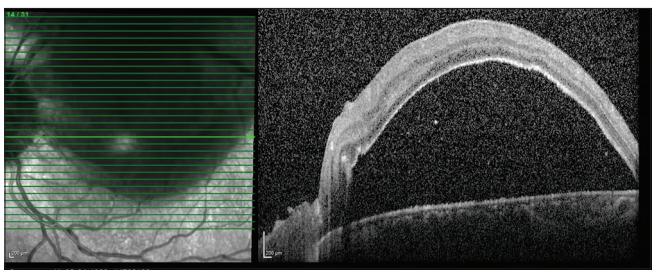
Twenty-six eyes (51%) were blind at presentation, and only four (7.8%) eyes had normal vision [Figure 5]. Four (7.8%) eyes had a VA of no perception of light. The most common ocular associations in blind eyes were strabismus, 11 (42.3%), RD, 10 (38.4%), and settled RD, seven (26.9%). Other findings in blind eyes included persistent fetal vasculature (PFV) (one eye), microcornea (two eyes), pulsatile disc (one eye), and peripheral retinal nonperfusion (one eye). Four eyes had MGDA alone. In eyes with a VA of 3/60 or better, 13 (52%) did not have an associated intraocular anomaly. The most common intraocular association in these eyes was cystoid macular oedema, three (12%). RD was documented in only two eyes.

Retinal complications were present in 19 (73.1%) eyes with a VA <3/60, and in five (20%) eyes with a VA ≥3/60 at presentation. This difference was statistically significant

Table 1: Ocular association in eyes with morning glory disc anomaly

Anomaly in affected eye	*n* (%)	Anomaly in fellow eye in unilateral MGDA	*n* (%)
Squint	24 (47.1)	RD	3 (50.0)
Refractive error	17 (33.3)	Retinochoroidal coloboma	1 (16.6)
RD	12 (23.5)	Microphthalmos	1 (16.6)
Nystagmus	8 (15.7)	Lid abnormality	1 (16.6)
Spontaneously settled RD	7 (13.7)	Phthisis bulbi	1 (16.6)
Posterior subcapsular cataract	4 (7.8)	Cataract	1 (16.6)
Microphthalmos	4 (7.8)	Anophthalmos	1 (16.6)
Lid abnormalities	5 (9.8)	Optic disc coloboma	1 (16.6)
Persistent fetal vasculature	3 (5.9)		
Relative afferent pupillary defect	3 (5.9)		
Cystoid macula oedema	3 (5.9)		
Microcornea	2 (4.5)		
Dermolipoma	1 (2.0)		
Epiretinal membrane	1 (2.0)		
Choroidal neovascular membrane	1 (2.0)		
Pulsatile disc	1 (2.0)		
Peripheral retinal nonperfusion	1 (2.0)		
Foveal hypoplasia	1 (2.0)		

RD=Retinal detachment, MGDA=Morning glory disc anomaly



Figures 4: Optical coherence tomography showing associated retinal detachment in same eye in Figure 3

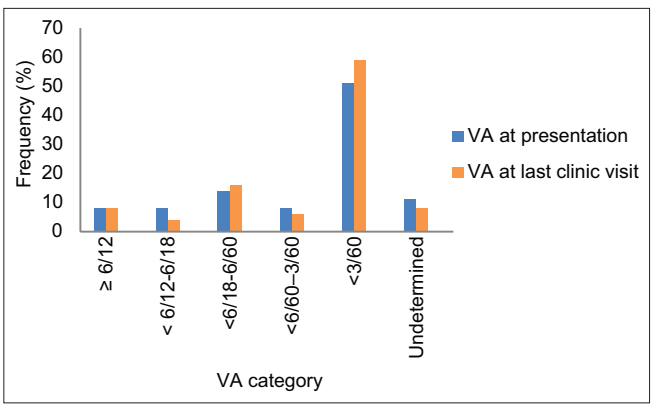


Figure 5: Visual acuity in eyes with morning glory disc anomaly

with a $P < 0.001$ using the Chi-square test. The mean age at presentation of patients with a VA <3/60 was 9.9 years (SD: 9.9), whereas the mean age of patients with VA ≥3/60 was 11.2 years (SD 11.4). This difference was not statistically significant with a $P = 0.7$. Four (28.6%) of 14 eyes with bilateral MGDA were blind, while 21 (58.3%) of 36 eyes with unilateral MGDA were blind. This difference was not statistically significant ($P = 0.11$). At the last, clinic visit 30 (58.8%) eyes were blind, and four (7.8%) eyes had normal vision [Figure 5].

Fellow eye anomalies were seen in six (16.7%) of the 36 patients with unilateral MGDA, and these included chronic RD, microphthalmos associated with retinochoroidal coloboma and closed funnel RD, phthisis bulbi, optic disc coloboma, antimongoloid slant with associated cataract and closed funnel RD, and anophthalmos [Table 1]. Five (83.3%) of these fellow eyes were blind at presentation.

The refraction results for 17 (33.3%) eyes were available, and using the spherical equivalent (SE), myopia was the most common error occurring in 9 (52.9%) eyes. The SE of myopic eyes ranged from −1 DS to −14 DS, and for hypermetropic eyes from + 2 DS to + 4.5 DS. In patients with unilateral MGDA, mean SE in affected eyes was 0.40 DS (range; −6.00 DS–+3.00 DS, SD: 3.3 DS), whereas mean SE in fellow eyes was 0.50 DS (range; −1.50 DS–+2.50 DS, SD: 1.50 DS). This difference was not statistically significant ($P = 0.77$). Systemic associations were documented in seven (15.9%) patients with two patients having more than one systemic disorder. The most common associated systemic anomalies were cleft lip and cleft palate [Table 2].

Discussion

This report presents the clinical characteristics of 51 eyes of 44 patients with MGDA seen at a tertiary hospital in South India over a period of 8 years. To our knowledge, this represents the largest cohort of patients with MGDA from India in the literature. The median age at the presentation in our report (5 years) is higher than the median age of 0.5 years and 2 years reported in similar studies in Sweden and China, respectively.[6,8] Late presentation in children with eye disorders is not unusual in India.[20,21] A study carried out among pediatric patients with retinoblastoma in Northern India observed that the average age at presentation was higher than findings in countries with very high human development index.[20] The authors attributed this disparity to the lack of education and awareness as most of their patients were from a rural population and of lower socioeconomic strata.[20] A lack of awareness on the part of the parents may have also been responsible for the late presentation in this current study. Studies on parents' awareness and perception of children's eye diseases and eye care need in South India revealed that most parents perceive squint as a sign of good luck and wearing of glasses before 4 years of age as a social stigma.[22,23] Strabismus and refractive errors are common in children and are also frequent associations of MGDA.[24,25] Developing strategies to increase parents' awareness of common eye diseases in children will, therefore, aid in the early diagnosis of MGDA in our environment. The age at diagnosis was lower in females in this report, and this compares favorably with the findings from the study in Sweden.[6] The association of MGDA with gender has been inconsistent from previous studies. In agreement with the report by Fei *et al*.[8] in China, there was a higher proportion of males in this study. On the contrary, Ceynowa *et al*. reported a slight female preponderance.[6]

Table 2: Systemic associations

Systemic condition	Frequency	Percentage of patients
Cleft lip	2	4.5
Cleft lip and palate	2	4.5
Corpus callosum dysgenesis	1	2.3
Periventricular leukomalacia	1	2.3
Midline cranial anomalies	1	2.3
Delayed developmental milestones	1	2.3
Asthma	1	2.3

The proportion of bilateral cases in our study (16%) compares favorably with 16% and 17% reported by Cennamo *et al*. and Ellika *et al*., respectively.[26,27] Ceynowa *et al*., however, did not report a bilateral case in their study.[6] MGDA is a sporadic condition and almost always unilateral.[6] It has been suggested that bilateral cases may be hereditary.[3] In this current report, there was a greater number of left eye involvement. This agrees with the observation by Ceynowa *et al*.,[6] but Cennamo *et al*.,[26] on the contrary, reported a slight right eye predominance.

MGDA may be associated with congenital ocular anomalies in the same eye as well as in the fellow eye.[8] Consistent with previous studies, strabismus was the most common ocular association in this present study.[4,6] Strabismus is commonly seen in MGDA as a result of impaired visual development.[28] The proportion of eyes with strabismus in our study (47%) is, however, lower than over 80% reported in earlier studies.[4,6] We found a higher proportion of esotropia in agreement with Cennamo *et al*.[26] In MGDA, esotropia has a higher incidence than exotropia as esotropia is considered to be a congenital ocular maldevelopment that forms during fetal development to 1½ years of age.[28] Other authors in contrast to our finding reported a higher prevalence of exotropia.[6] The frequent association of MGDA with strabismus is partly due to the presence of anisometropia.

Increasing degree of anisometropia is associated with a higher risk of developing strabismus.[29] Ceynowa *et al*. found a significant difference in refraction between the MGDA eye and the fellow eye with MGDA eyes being more myopic.[6] Similarly, most eyes with MGDA in this current study were myopic. There was, however, no significant difference between the mean SE of MGDA eyes and fellow eyes.

RD was the third most common ocular association of MGDA in this report. A prevalence of 23.5% in our study compares favorably with 22.7% reported by Cennamo *et al*.[26] Harasymowycz *et al*.,[4] however, reported a lower prevalence of 14%, whereas Haik *et al*.[30] reported a higher incidence of 37% in thirty patients followed up over a mean duration of 10 years. Postulated mechanisms of RD in MGDA include abnormal communication between the subarachnoid space and the subretinal space, tissue stretching around the peripapillary conus, and breaks at the margin of excavation or in the tissues lying within the optic disc.[26,31,32] RD s in MGDA have a variable course, including spontaneous reattachment and even redetachment.[30] Spontaneous reattachment is more likely to occur in the absence of vitreous or glial tissue causing traction on the retina within the defect or if a retinal break is absent.[10,33] In this study, approximately 12% of eyes had the features of spontaneously resolved RD which is at variance with 33% reported by Chang *et al*.[10] The recovery of visual function is, however, usually limited following such improvements primarily because of the retinal pigment epithelial alterations and possible outer-retinal damage associated with the long-standing detachments.[34] All the eyes with spontaneously settled RD in this study were blind.

PFV was reported in only 5.8% of eyes in this current study, in contrast to 25.8% reported by Fei *et al*.[8] PFV may be a fundamental condition in MGDA and may also have a genetic basis.[8] It usually presents in various forms, including anterior PFV, posterior PFV, and combined PFV.[35]

The visual prognosis in individuals with MGDA is poor.[36] In addition to the abnormal disc itself and the predilection for serous RDs, there is an added compounding variable of high refractive errors, amblyopia, and strabismus.[36] The proportion of eyes that were blind at presentation in this study (51%) is higher than the findings from previous studies which reported a range of 25%–45%.[4,6,26] This difference may be due to the greater number of eyes with RD in our study. Ceynowa *et al.*, for example, did not record any case of RD in their series.[6] RD along with retinal schisis are the most severe complications of MGDA that impair vision.[37] In this present study, the presence of an RD was associated with a poor visual prognosis. Late presentation in our patients may have also contributed to the higher proportion of blind eyes. Up to 81% of blind eyes could have been prevented from going blind with earlier diagnosis. There was, however, no statistically significant difference in the mean ages at the diagnosis of patients with blind eyes and those with eyes with a VA of 3/60 or better.

Fellow eye anomalies were present in 16.7% of patients in this study which contrasts with 25% reported by Ceynowa *et al.* in Sweden.[6] The fellow eye anomalies in this study were, however, more severe with 50% having RD, and 83% blind. Earlier presentation in these patients may have prevented visual loss in up to 67% of these eyes. A case each of Mittendorf's dot, cataract, and microphthalmos were the fellow eye anomalies reported by Ceynowa *et al*.[6] Close monitoring of the fellow eye in unilateral cases of MGDA is, therefore, important as retinal complications with irreversible visual loss may occur when an optic disc or retinochoroidal coloboma is present.

MGDA may be a part of other systemic abnormalities and syndromes, although it does not appear to be a specific genetic disorder.[36] Systemic associations were documented in 16% of patients in this study in contrast to 50% reported by Ellika *et al*.[27] Cleft lip and cleft palate were the most common associations in our study. On the contrary, extensive capillary hemangiomas was reported by Ceynowa *et al.* as the most common systemic association in their study.[6] The nature of the embryologic defect that leads to the MGDA remains the subject of debate. There is an overlap of the critical periods of development for the frontonasal process, midfacial structures, and primordium of the eyes, and MGDA is believed to emerge from a single insult occurring during induction of the forebrain.[27]

The limitations of our study are that it is retrospective in nature, and the data were collected through medical record review. This would have resulted in some missing data. It was also difficult to determine the association between disc morphology and ocular complications or VA from the case files. However, despite these limitations, the study provides important information on the clinical characteristics of MGDA in India and highlights the importance of early diagnosis and regular follow-up of patients with this disorder to prevent severe visual loss.

Conclusion

MGDA has a wide variety of ocular associations with strabismus and retinal complications being the most common associations in South India. Late

presentation is common and visual prognosis poor with half of affected eyes already blind at the time of diagnosis. RD is a major risk factor for poor visual outcome in affected eyes. Early diagnosis, prompt treatment of blinding complications, and correction of associated refractive errors are crucial in reducing the risk of irreversible visual loss. Associated systemic abnormalities highlight the importance of a multidisciplinary approach in the management of patients with this condition.

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Nil.

Conflicts of interest

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

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