Special Focus, Systemic Syndromes, Original Article

Clinical profile and outcome of ocular manifestation in Marfans syndrome in India

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Purpose: Marfan syndrome (MFS) is a genetic disorder associated with considerable morbidity and mortality. Presently, well-documented information on this condition is not available in India. **Methods:** In this retrospective cohort study, we recruited patients with clinically diagnosed MFS who presented to the outpatient department using revised Ghent nosology. We retrieved complete ophthalmic information, including vision, anterior and posterior segments, exported from electronic medical records, and relevant investigations, surgical details, and follow-up data were obtained in a specific, pretested format. **Results:** Our cohort consisted of 86 eyes of 43 patients and had a male preponderance. The prevalence was 20.5 per 100,000 individuals. The mean age of the patients was 23.9 years. All eyes were treated either optically with refraction or surgically using lensectomy and vitrectomy with suture supported scleral fixated intraocular lens (IOL), which significantly affected the visual outcome (P = 0.000). **Conclusion:** Although considered a rare disease, MFS is commonly found in the ophthalmological setting. Refraction and surgery (lensectomy with scleral fixated IOL) may improve the vision significantly.

Key words: Ectopia lentis, Marfan syndrome, scleral fixated lens, scleral tuck lens

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Marfan syndrome (MFS) and related disorders are a group of connective tissue disorders that can be inheritable and have many clinical features which involve cardiovascular, skeletal, craniofacial, ocular, and cutaneous abnormalities. The majority of the affected individuals have aortopathies linked to early mortality and morbidity. Targeted gene panel next-generation sequencing serves as a powerful tool for these individuals to obtain a genetic diagnosis.[1,2]

Since the first description of MFS, intense research on this topic[3] has contributed to our understanding of its genotype and phenotype. The definition of MFS proposed in 1986 according to the Berlin criteria[4] was based purely on the clinical phenotype. Subsequently, Dietz *et al*.[5] found a connection between MFS and FBN1, the fibrillin protein gene. The Ghent criteria put forth in 1996 (Ghent-I),[6] which were a revision of the Berlin criteria, used the newly discovered FBN1 mutation as a component in the diagnosis. The revised Ghent criteria (Ghent-II) formulated in 2010[7] highlighted FBN1 mutation, aortic dilatation, and ectopia lentis as cornerstones in the MFS diagnosis.[8] Generally reported prevalence of MFS is 20/100,000[8,9] by the textbook of Emery and Rimoins, Principles and Practice of Medical Genetics.[8] Still, the latest version refers to a calculation of 4–6/100,000 based on MFS patients found in the catchment area of Johns Hopkins Hospital in Baltimore. During the last 70 years, only five studies have reported MFS prevalence, and all but one are based on the Berlin criteria. This information, particularly on ocular manifestation, is not available in India.

Hence, this study aimed to describe the clinical profile, epidemiological findings, and incidence of MFS.

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Methods

Study approval

The study was approved by the Institutional Ethics Committee of xxxxx (xxEC No: 23/2019). Informed consent was obtained for clinical data, samples, and publication of photographs from the parents/legal guardians of the patients or the patients themselves. All interventions were performed following the relevant guidelines and regulations.

Patient cohort and data collection

This research was a retrospective cohort study**.** We recruited pediatric, adolescent, and adult patients who presented to the ophthalmology outpatient department of our hospital had features suggestive of MFS, aortopathy, or related clinical features over a period of 10 years and consented to participate in the study. Clinical data were retrieved from the electronic medical records in a specific format, exported to Excel sheets, and noted abnormalities or visual defects and cardiac surgeries. Physical examination was performed, and anthropometry was recorded for all patients. In addition, echocardiographic information, radiographic assessment, and other imaging data were collected whenever necessary. Revised Ghent criteria were used for the diagnosis of MFS.

Data analysis

Data analysis was done using descriptive analysis and cross-tabulation function; we analyzed information using

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SPSS-22 (no financial interest). *P* value < 0.05 was considered statistically significant.

Results

Our cohort consisted of 86 eyes of 43 patients, and all of them were bilateral with a mean presenting age of 23.9 ± 14.8 years. Out of the 43 patients, 13 (30.2%) were female and 30 (69.8%) were male. Furthermore, 23 patients (53.3%) belonged to the pediatric age group, while 40 (46.5%) had crossed the pediatric age group [Table 1]. All patients presented to the ophthalmology department as outpatients. All patients had ectopia lentis in both eyes, and the prevalence of the condition was found to be 20.5 per 100,000 individuals. The patients had varying systemic associations in the form of high arched palate, cardiac, pulmonary, and skeletal involvement [Table 2].

On examination, we found that the horizontal measurement exceeded the vertical height. Therefore, the results are presented in the form of a horizontal-vertical ratio [Table 3]. Our cohort had a mean axial length of 24.19 ± 1.96 mm and a mean k max of 42.06 ± 2.65 mm. When we explored other ocular manifestations, three patients (3.48%) presented with secondary glaucoma, two (2.36%) [Fig. 1] had a family history—a brother and sister [Fig. 2], and two (2.36%) had microspherophakia associated with MFS [Fig. 3]. When the axial length was compared between the pediatric and adult populations, the difference was not significant (*P* = 0.184).Forty-five eyes (52.3%) were treated using optical management to correct the aphakic/phakic zone. Of the patients who received optical management, 13 (28.8%) refracted through the aphakic part and 26 (57.7%) through the phakic part. On studying, we could not find a significant difference between the optical and surgical groups (*P* = 0.249). Various ranges of vision were observed on presentation [Table 4].

Table 1: Age sex distribution

Age Categories	Sex		Total
	Female	Male	
0-10	4	6	10
11-20	16	24	40
21-30	0	8	8
31-40	4	10	14
41-50	2	8	10
51-60	0	4	4
Total	26	60	86

Table 2: Systemic associations

No	Cardiac	Pulmonary	High arched palate	Other
No	11	2	17	5
Percent (%)	12.8	2.36	19.8	5.81

Table 3: Horizontal Vertical length Ratio

Ratio	No (*n*)	Percent (%)
1.00	7	8.1
1.10	61	70.9
1.20	16	18.6
1.30	2	2.3
Total	86	100.0

Table 4: Vision on presentation

Vision	Frequency	Percent
Nope	2	2.3
<1/60	15	17.4
1/60-3/60	35	40.7
6/60-6/36	12	14.0
6/24-6/18	18	20.9
6/12-6/9	1	1.2
6/6-6/5	3	3.5
Total	86	100.0

Discussion

Our cohort consisted of 86 eyes of 43 patients, all bilateral with a mean presenting age of 23.9 ± 14.8 years. According to Groth *et al*., the maximum global prevalence of MFS was 6.5/100,000 at the end of 2014. The median incidence was 0.19/100,000 (range: 0.0–0.7). Groth *et al*.[1] found a median age at diagnosis of 19.0 years (range: 0.0–74). We could not find information regarding the prevalence and incidence of the condition in India; however, we found 0.019% prevalence at our center in the current study. Jang *et al*.[10] reported that the overall prevalence of MFS was 2.27 per 100,000 individuals in Korea.

Wang *et al*. stated that the age of the patients ranged from 3 months to 56 years, with a median age of 14 years. The majority were males (51, 61.5%; 95% CI 51–71) and were either children or adolescents (53, 64% were less than 18 years of age; 95% CI 53–73).[2] Jang *et al*. documented that the mean age of the 103 included patients was 10.25 ± 9.67 (range: 3–48) years, and 66.02% were male.[10] The mean age at presentation was higher in the current study, probably because in poor tribal areas, several patients seek medical assistance only when they develop cataracts.

According to Groth *et al*.[1] the median age at diagnosis for the entire MFS group was 19.0 (0.0–74.5) years. The majority were males (51, 61.5%; 95% CI 51–71) and were either children or adolescents (53, 64% were less than 18 years of age; 95% CI 53–73). These data are similar to those obtained in the current study.

The revised Ghent nosology presents the classical features of MFS. However, MFS hides less prominent features behind its familiar face, and many ophthalmic clinical features are also not included.[3,11] Rahmani[12] noted that clinical examination revealed posterior segment pathology in 18% of the eyes, with an increased incidence of 70% in patients with a subluxated lens. We came across similar findings in the current study. Gehle *et al*.[13] opined that glaucoma was equally common. The current study reported 5.9% of eyes with secondary glaucoma. Nazarali *et al*.[14] documented childhood glaucoma in neonatal MFS. Dietz *et al*.[5] studied ocular findings, including myopia (the most common ocular feature), ectopia lentis (seen in approximately 60% of the affected individuals), and an increased risk for retinal detachment and glaucoma and early cataracts.[11] The current study also had similar findings except for retinal detachments.

Kuruvilla *et al*. reported microcornea with ectopia lentis with MFS, which was not seen in the current study.[15]

Bontzos *et al*.[16] reported ectopia lentis with microspherophakia in MFS. The current study reported two eyes with ectopia lentis with microspherophakia, of which one presented with secondary glaucoma and buphthalmos.

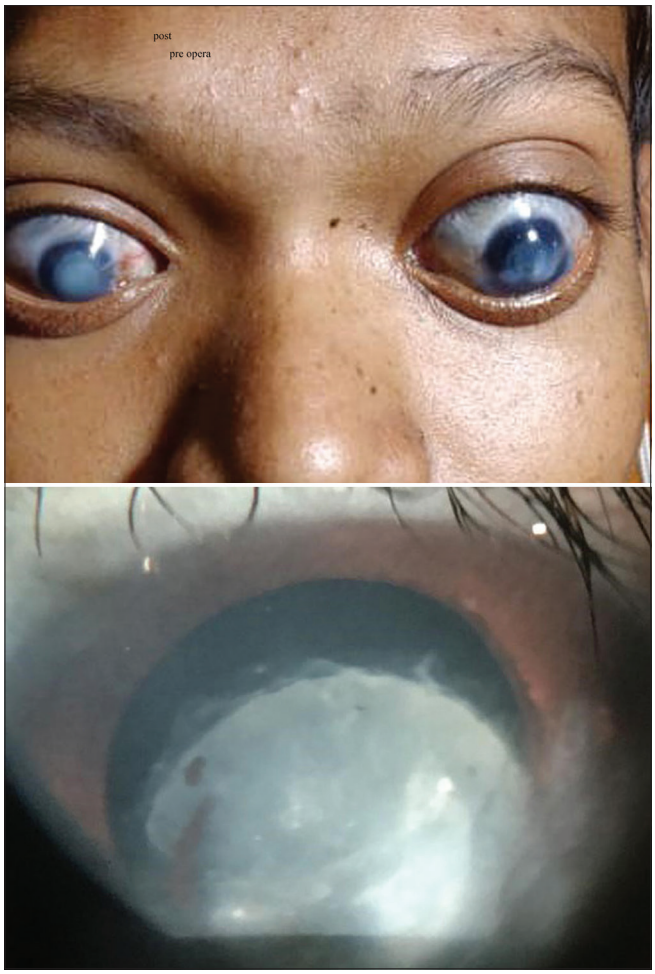

Figure 1: Preoperative postoperative images

Gehle *et al*.[13] observed that MFS eyes were longer (axial length 24.25 ± 1.74 mm versus 23.89 ± 1.31 mm, $P < 0.001$) and had a flatter cornea. Kinori *et al*.[17] reported that the axial length was longer (25.25 ± 0.32 mm vs. 24.24 ± 0.33 mm, $P = 0.03$).

Luebke *et al*.[11] reported that although both k-values differ significantly, k max is a better marker to identify MFS. A k max of >8.16 mm (41.36 d) seems to be a reasonable cut-off. Wang *et al*.[18] reported a k max of 41.36 d as the cut off OF Kinori *et al*.[17] and mentioned that the adult and pediatric groups had flat corneas (average keratometry [kmed] of 41.59 (0.35 diopters [d] in adults vs. 40.89 (0.36 d in children, $P = 0.17$).

Esfandiari *et al*. stated that the management of a subluxated lens starts with the correction of refractive error using eyeglasses in mild cases.[19] Chen *et al*.[20] reported that the visual improvement is significant in the eyes of MFS undergoing capsular tension ring transscleral fixation and intraocular lens (IOL) in-the-bag implantation. Erdogan *et al*.[21] studied three techniques and compared the results of intrascleral fixation, suture fixated scleral lens, and Cionni capsular tension ring with in-the-bag implants and did not find significant differences among the three surgical approaches in terms of the postoperative results and complications. In the current study, we did a lensectomy with suture fixated scleral lenses, and the vision improved significantly.

Zech *et al*.[22] studied predictive values and found that high positive predictive values were associated with ≥ grade 2 of the

Figure 2: Marfan family

five-grade classification of ectopia lentis. Rezar-dreindl *et al*. reported significant improvement in visual acuity following lensectomy.[23] Sen *et al*.[24] reported that scleral suture fixated IOL provides good visual outcomes in eyes with ectopia lentis associated with MFS. The present study also had similar findings, and there was no significant difference between the pediatric and adult populations ($P = 0.284$). Manning *et al*.[25] did not observe any significant hike in the rate of retinal detachment following lensectomy. The current study also came up with similar findings.

Rabie *et al*. reported that Artisan-iris fixated lens following lensectomy has a good outcome.[26]

Conclusion

MFS is a rare disease, and many patients have ocular involvement in various manifestations and complications. However, clinical diagnosis and early intervention can improve the vision and augment the patients' quality of life.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have

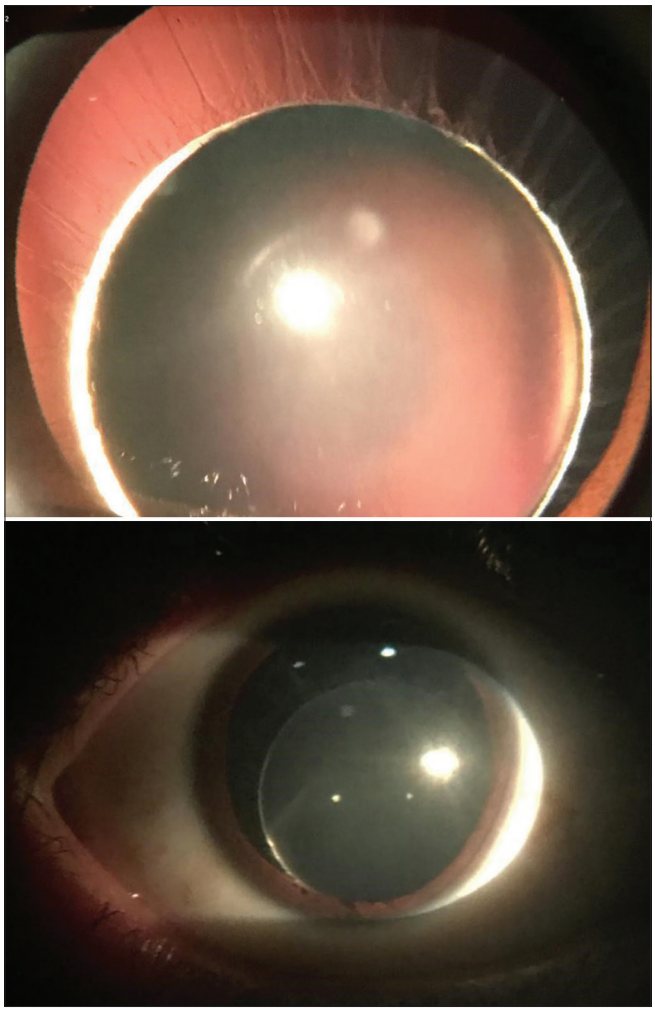

Figure 3: Microspherophakia

given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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