

Impact of COVID-19 on follow-up and medication adherence in patients with glaucoma in a tertiary eye care centre in south India

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Purpose: COVID-19 pandemic has affected the healthcare system worldwide hindering the continuum of treatment of chronic disease patients. The objective of the study is to analyze the barriers encountered by the glaucoma patients for the follow-up visit and medication adherence during the pandemic. **Methods:** This cross-sectional study included glaucoma patients who did not attend the scheduled appointment from April 1, 2020 to July 31, 2020 in a tertiary eye care center (88.21%). Eligible patients of age >18 years and advised antiglaucoma medication in Madurai Zone were interviewed with validated questionnaire through telephonic call. **Results:** 363 patients answered the questionnaire through telephonic interview. 57.3% of the patients were found to be non-adherent to medication. The main barriers for glaucoma follow-up visit during the pandemic were lockdown restriction, transport problem, and financial difficulties. The top barriers for medication adherence were non availability of medication (54.81%), financial difficulties (30.29%), did not feel much improvement with eye drops (20.19%). On multiple regression analysis, longer distance to hospital, low socioeconomic status, more than one antiglaucoma medication use, lack of awareness of glaucoma, non-complaint before COVID-19 and stress due to the pandemic were found to be significant factors for medication non adherence. **Conclusion:** COVID-19 pandemic has emphasized the need for reformation in health care system for accessibility of medical care to patients in rural areas. Decentralization of health system to primary care level and utilization of teleophthalmology should be considered by health care planners in future.

Key words: Adherence, antiglaucoma medication, COVID-19 pandemic, follow-up, lockdown

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic continues to have an unprecedented global impact, imposing a huge strain on healthcare system.^[1] In order to assuage the virus spread and to curtail the fatality spike, mass quarantines and travel restrictions were implemented throughout the world and India is no exception.^[2,3] The nationwide lockdown in multiple phases were imposed beginning from March 25, 2020, with initial phases of strict restrictions to transport, social distancing and curbing nonemergency services in the hospitals to restrain the spread of virus.^[4,5] These uncertain circumstances had posed extreme challenges for patients with chronic disease, with difficulty for access to the hospital visit and to procure medications.^[6,7] Thus the continuity in medical treatment is interrupted due to the pandemic which can lead to progression of the disease, and further magnifying the treatment difficulties.^[8]

Glaucoma is the leading cause of irreversible blindness, as in India 4% to 10% of bilateral blindness was attributable to glaucoma.^[9-11] As Glaucoma is a chronic progressive disease, it requires life-long management to delay disease progression, with regular follow-up and medication to prevent severe visual field (VF) loss later in life.^[12] Even before COVID pandemic,

poor medication adherence and failure of periodic glaucoma follow-up visit posed an obstacle for the proper disease management.^[13-15] The implementation of strict social distancing and travel restriction during COVID pandemic had further intensified the problem for routine follow-up visits affecting the continuum of glaucoma management. The fear of infection, restriction in movement and self-isolation during pandemic has increased the stress level of many.^[16] Psychosocial factors like anxiety and depression which were already known barriers to medication adherence in glaucoma patients must have perpetuated in many during the lockdown.^[17,18]

Thus, prompted the present study, tracing patients with glaucoma who had been lost to follow-up at a tertiary referral teaching hospital due to COVID pandemic from April 1, 2020 to July 31, 2020 and to assess the impediment for follow-up and medication adherence during this period. This will help us to plan incumbent steps to design effective disease management programs in future for uninterrupted glaucoma treatment for the patients.

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Methods

A cross-sectional study was conducted at the tertiary eye care center in Madurai district of South India between August 2020 and October 2020. The state had imposed lockdown in a phased manner starting from March 25, 2020 with prohibition of interdistrict/interstate transport in the initial phases. In later phases, travel passes were introduced and the use of public transport was permitted within the neighboring districts. To regulate the transportation in various districts during the lockdown period, the Tamil Nadu state was classified into eight zones for resumption of public transport within the zones.^[19] The study patients were selected from Madurai zone comprising of five nearby districts for the ease of monitoring and follow-up of the patient at one of the primary or secondary centers of Aravind Eye institute in the future.

The list of patients diagnosed with glaucoma who had been given appointments for follow-up from April 1, 2020 to July 31, 2020 in the glaucoma clinic of Aravind Eye Institute, Madurai were scrutinized. At Aravind eye hospital, patients diagnosed with glaucoma were advised for routine follow-up visits at regular intervals based on disease severity with mild glaucoma every 5–6 months, moderate glaucoma every 4–5 months and severe glaucoma every 3–4 months according to American Academy of Ophthalmology preferred practice pattern guidelines.^[20]

The study population was drawn from patients who could not attend the follow-up appointment scheduled from April 1, 2020 to July 31, 2020 in glaucoma clinic, Aravind eye hospital, Madurai. Out of 13,732 patients scheduled for follow-up from April 1, 2020 to July 31, 2020, 12113 patients (88.21%) missed their scheduled appointment during this period. The patients were selected from this population by computer generated random numbers with eligibility criteria of 1) age 18 years or older 2) diagnosed with glaucoma, both primary and secondary, who are on antiglaucoma medications 3) patients from Madurai zone comprising five nearby districts. The study protocol was approved by the institutional ethical committee and followed the Declaration of Helsinki guidelines.

The questionnaire was designed with the concept identification through extensive literature reviews and discussing with glaucoma patients regarding obstacles faced by them during COVID lockdown. A multidimensional Questionnaire consisting of 1) Demographic and clinical data including age, gender, district of residence, diagnosis, and medication advised, which were extracted from electronic medical record 2) Questions pertaining to barriers for hospital visit, and barriers for medication adherence during the pandemic [Appendix 1] was developed. The questionnaires had both open and closed ended format for the ease of patient's understanding through telephonic interview.

Before formal commencement of the study, a pilot study was conducted with 20 patients to validate the questionnaire for testing feasibility as well as the acceptability of the protocol. Based on the pilot study results, sample size of 345 patients was estimated to be adequate. The internal consistency between each item in the questionnaire was statistically measured and had a Cronbach's alpha reliability coefficient of 0.623. Scaling system of response was not used in the questionnaire since most

of the patient could not comprehend well through telephonic interview, thus maintaining low acceptable Cronbach's alpha value. The face validity of the barrier statements was tested through expert review by three glaucoma specialists. Two different bilingual translators did forward and backward translation of the questionnaire between English and native language (Tamil). Two trained study coordinators administered the questionnaire through cellular phone for 10-15 minutes after obtaining verbal consent from the selected patients. Patients were excluded if they refused to be interviewed or unable to contact (the patient did not answer the call after a total of three attempts; 1 × 3 different days). The flowchart of the study was depicted in Fig. 1.

Statistical analysis was performed using STATA statistical software, Version 14.0 (StataCorp, College Station, Texas, USA). Age of the participants was expressed as mean ± standard deviation and categorical variables are presented with frequency (percentage). Univariate and multi-variable logistic regression was done for adherence to glaucoma medications. Odds ratio with 95% confidence interval was given and *P* values < 0.05 were considered as statistically significant

Results

Of all the patients contacted, 7 declined to participate in the telephonic interview. In total 363 patients completed the questionnaire through telephonic interview. Of the 363 patients interviewed, the mean age was 62.16 ± 12.39 years, 236 participants were (65%) ≥60 years of age and 182 (50.14%) were males. Table 1 represents the demographic characteristics of the patients. Socioeconomic status was assessed with reference to modified Kuppusamy scale 2020.^[21] Most of the patients (65.02%) in our study was in low socioeconomic status (upper lower and lower class) and 42.7% were unemployed, depending on the family members for the medical expenses. 185 (50.96%) patients had to travel >50 km for the hospital visit, thus making the follow-up visit even more difficult during the lockdown restriction. The most common type of glaucoma in the study group was primary open angle glaucoma in 339 eyes (51.83%) and 162 patients were on more than one drug regimen for glaucoma.

160 patients reported to have ocular symptoms, with visual deterioration as the common symptom experienced by 83 patients. Nervousness or stress due to the pandemic were reported in 123 patients, and graded to be affected to some extent by 115 patients and to a great extent by 8 patients. An elaborate questionnaire about psychosocial status of the patient during pandemic was beyond our study scope due to constrain of time in telephonic interview.

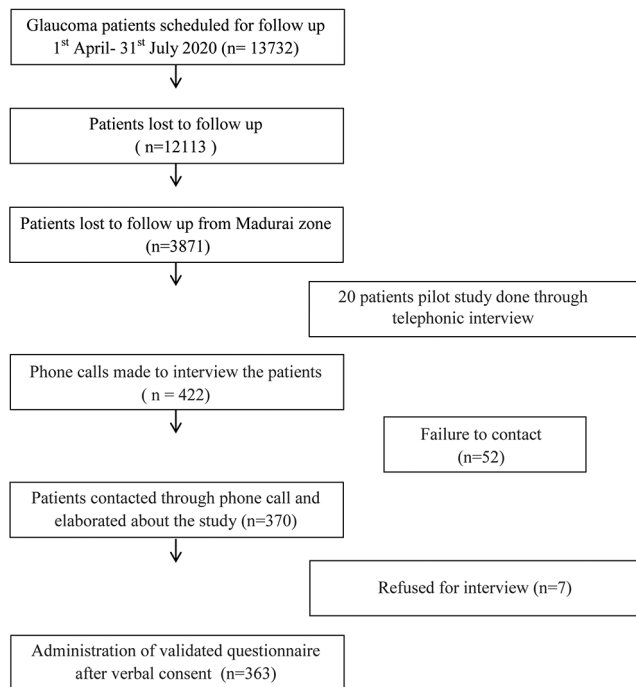
Barriers for follow-up visit during lockdown

Most patients (78.24%) cited multiple reasons for impediment for hospital visit and number of patients who reported each barrier was quantified as depicted in Table 2. The most common hindrance faced by the glaucoma patients during the pandemic for the follow-up visit were the lockdown restrictions and lack of public transport facility. Around 51% of the study patient had to travel >50 kms for the hospital visit, thus making the glaucoma follow-up more difficult during the pandemic situation. The other barriers for follow-up were lack of knowledge about the disease where patient said to have no symptoms or unaware of the importance of regular follow-up,

Table 1: Demographic and clinical parameters of the study participants

Parameters	n (%) (n=363)	Parameters	n (%) (n=363)
Mean (SD) age years		Area:	
Aged 18-39 y	62.16 (12.39)	Urban	212 (58.4)
Aged 40-59 y	17 (4.68)	Rural	151 (41.59)
Aged 60 y	110 (30.30)	Distance travelled to the hospital	
>60 y	236 (65.02)	<50 km	178 (49.04)
		>50 km	185 (50.96)
Male:Female	182: 181	Time since glaucoma diagnosed,	
Education:		<1 year	74 (20.39)
Illiterate	27 (7.44)	1-5 years	161 (44.35)
Primary/Middle school	98 (27)	5-10 years	86 (23.69)
High school	103 (28.37)	Above 10 years	42 (11.57)
Diploma/Graduate	135 (37.19)		
Socioeconomic status:		Glaucoma diagnosis:*	
Upper middle class	53 (14.6)	PACG	193 (29.51)
Lower middle class	74 (20.39)	POAG	339 (51.83)
Upper lower class	209 (57.58)	Secondary angle closure glaucoma	18 (2.75)
Lower class	27 (7.44)	Secondary open angle glaucoma	104 (15.90)
Employment status:		Number of anti-glaucoma medication advised:	
Employed/Retired	208 (57.3)	1	201 (55.37)
Unemployed	155 (42.7)	2	96 (26.45)
Districts:		3 and above	66 (18.18)
Madurai	120 (33.05)		
Others [†]	243 (66.94)		

*Total eyes-654; [†]Virudhunagar, Sivagangai, Ramanathapuram and Dindigul

**Figure 1: Flow diagram of study participants**

financial difficulties to bear the cost of travel and hospital visit, hospital restriction for nonemergency services during the initial phases of lockdown, lack of escort, other illness, and other obligations. Only 42 (11.57%) patients had visited other hospital during the four months period, particularly nearby primary or secondary centers of Aravind eye institute.

Barriers for adherence to medication

Around 89 patients (24.52%) had stopped using antiglaucoma eyedrops for a period ranging from 3 days to 6 months with the mean of 1.78 (1.34) months. Out of 274 patients using glaucoma medication, 119 (43.43%) reported missing their eye drop dose during last 1 month. Most of the previous studies, analyzed the adherence for past one or two week medication history in view of remembrance of the patient.^[14,18] Since many of our patients reported to have reduced the frequency of medication for more than a month, the adherence question was modified to analyze the same. 71 (19.56) patients reported to be non-complaint to medication even before the pandemic, emphasizing the persistence of non-adherence to medication in glaucoma patients as a perennial problem.

Multiple reasons were cited by patients for not using or for missed dose as shown in Fig. 2 and the most common was non availability of medicines (54.81%). Other common barriers reported were financial difficulties (30.29%), nonavailability of caretaker to buy medicines (10.10%), other illness (17.79%), unaware of the importance of regular medications (14.42%) or didn't feel much improvement with eye drops (20.19%). Few patients became non adherent due to illness caused by COVID (3.36%, 7 patients) or responsibility of caring the sick family member (1.44%) or forgetting the eye drop dose (1.44%).

Both the group of patients, who have stopped using medication or missed the dose of antiglaucoma medication were considered nonadherent to medication and a multiple logistic regression model was used to assess the association between the independent variable and adherence to medication as depicted in Table 3. Longer distance to hospital, using more than one antiglaucoma medication, lack of awareness about

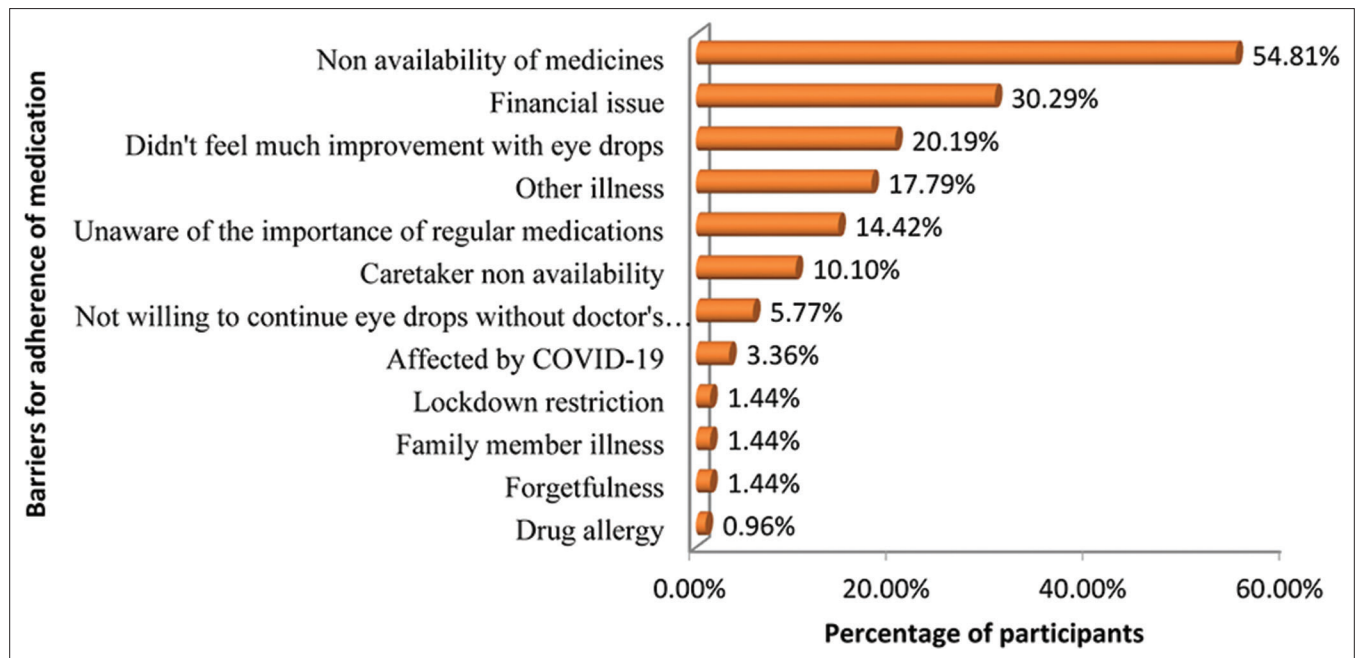


Figure 2: Bar graph for barriers for medication adherence during COVID 19 pandemic

glaucoma, poor drug compliance even before pandemic, and psychological affection due to pandemic lockdown were found to be statistically significant in association with poor medication adherence. Independent variables that were statistically significant in isolation such as lower socioeconomic status, education status, income and duration of glaucoma were not statistically significant explanatory variables in multiple variable models.

Discussion

The main hypothesis of the study was to identify challenges faced by glaucoma patients during lockdown due to COVID-19 pandemic. 88.21% patients had missed their follow-up visit from April 1, 2020 to July 31, 2020 in the tertiary care center due to lockdown restrictions, lack of transport facilities and financial difficulties. Regular follow-up is crucial in glaucoma management as an association between worsening of glaucoma severity and poor follow-up had been well documented in many studies.^[22,23] With the preexisting poor follow-up for glaucoma in a developing country like India,^[15] the pandemic has indubitably magnified the problem and imposed huge strain for continuity of glaucoma care.

Adherence to medication has been affected in many chronic diseases during the pandemic, pertaining to lack of availability or accessibility to medication.^[7] Poor adherence to glaucoma medication which was a persistent problem globally was amplified during the lockdown. 57.3% of the patients were not using or missed the dose of antiglaucoma medication in our study. The main reason for nonadherence to medication was non availability of the drugs nearby. This may be attributed to limitation in availability of glaucoma medication in rural or semi urban areas which was reported as the common barrier in another study in south India.^[24] Most patients in our study reported that the prescribed anti glaucoma medications were not available in nearby pharmacy and they usually get their medications during

the hospital visit and stock in excess for future use. But due to travel restrictions pertaining to the pandemic, the patients missed their hospital visit and the medication refill. Many patients had reduced the frequency of the doses or using single eyedrop when more than one anti glaucoma medication had been advised, due to difficulty in getting the medication. Thus, patients from longer distance and more than one antiglaucoma medication users were found to be more irregular in using the eyedrops due to difficulty in getting the medication.

Furthermore, economic crisis due to the pandemic as evident with declined employment rate in India by 26.1% during the lockdown further affects the underprivileged people more.^[25] Financial difficulties which was shown to impact the adherence to medication and follow-up in previous studies,^[15,24,26] has become even more glaring during this time. With majority of the participants in low socioeconomic strata with difficulty for daily wages during the pandemic, expense for hospital visit and medications was hard to meet up.

Lack of awareness and poor understanding of glaucoma poised a known barrier for adherence to glaucoma treatment.^[15,24] In our study, patients had stopped medication since no improvement in vision was noticed or was not aware to continue the medication even if follow-up visit was missed. Thus, patients who were non adherent to glaucoma eye drops even before the pandemic were found to be persistently non complaint due to lack of knowledge about glaucoma.

The psychosocial effect of the pandemic is immense among people with even more negative effects in patients with chronic disease. Self-isolation, restriction in movement and fear of acquiring infection has increased the stress and anxiety level, affecting the disease course and medication adherence of patients with chronic disease.^[27,28] Anxiety and stress due to the pandemic was found to have significant impact on non-adherence to medication by multivariant

Table 2: Participant's response to the Questionnaire

Parameters	n (%) (n=363)	Parameters	n (%)
Awareness of glaucoma:		Barriers for follow-up visit during COVID-19:	
Yes	312 (85.95)	Lockdown restriction	329 (90.63)
No	51 (14.04)	Transport problem	270 (74.38)
Using glaucoma eye drops:		No symptoms	33 (9.09)
Yes	274 (75.48)	Financial difficulties	15 (4.13)
No	89 (24.51)	Advised not to come due to hospital restriction	13 (3.85)
Missed eye drop doses in last 1 month:		Lack of escort	11 (3.03)
Yes	119 (43.43)	Other illness	5 (1.38)
No	155 (56.56)	Work responsibilities	4 (1.10)
Alternate hospital visits during last 4 months		Unaware of the importance of regular follow-up	3 (0.83)
Yes	42 (11.56)		
Presence of ocular symptoms:			
Vision deterioration	83 (22.86)		
Pain	32 (8.81)		
Discomfort	45 (12.39)		
Medication Non adherence before pandemic	71 (19.56)		
Nervous/stressed due to COVID-19 pandemic?			
Some extent	115 (31.68)		
Great extent	8 (2.20)		
Not at all	240 (66.12)		

Table 3: Estimated odds ratio of glaucoma medication adherence during COVID-19 associated with the demographic and clinical parameters of the participants

Parameters	Univariate model		Multi variable model	
	OR (95% CI)	P	OR (95% CI)	P
Mean (SD) age	1.016 (0.99-1.03)	0.061 (NS)	1.01 (0.989-1.03)	0.615 (NS)
Female [†]	0.925 (0.61-1.4)	0.716 (NS)	1.30 (0.68-2.48)	0.422 (NS)
Distance travelled to hospital				
<50 Km*	1.00		1.00	
>50 Km	1.43 (0.94-2.17)	0.090 (NS)	1.86 (1.05-3.31)	0.017 (S)
Employed [†]	1.36 (0.89-2.08)	0.144 (NS)	1.75 (0.88-3.46)	0.106 (NS)
Lower middle [†]	2.34 (1.136-4.85)	0.021 (S)	2.30 (0.76-6.0)	0.129 (NS)
Upper lower	2.82 (1.51-5.29)	0.001 (S)	2.82 (1.04-7.61)	0.041 (S)
Lower	4.25 (1.56-11.53)	0.005 (S)	29.21 (0.48-1759.57)	0.107 (NS)
Primary/Middle school [†]	0.79 (0.31-1.99)	0.622 (NS)	10.35 (0.24-438.53)	0.221 (NS)
High school	0.72 (0.28-1.8)	0.483 (NS)	16.21 (0.37-703.75)	0.148 (NS)
Intermediate or Diploma/Graduate	0.33 (0.13-0.82)	0.017 (S)	9.91 (0.22-429.66)	0.233 (NS)
Length of glaucoma	0.92 (0.88-0.96)	0.001 (S)	0.959 (0.91-1.01)	0.190 (NS)
No. of AGM used:				
1 eye drop medication used daily*	1.00	<0.001 (S)	1.00	<0.0001 (S)
2 and more drops daily	2.98 (1.92-4.63)		3.32 (1.83-5.97)	
Awareness of glaucoma [†]	0.0098 (0.006-0.16)	0.001 (S)	0.015 (0.0005-0.19)	0.002 (S)
Medication compliance before COVID-19, Yes [†]	0.012 (0.002-0.093)	<0.0001 (S)	0.016 (0.002-0.089)	<0.001 (S)
Nervous/stressed due to pandemic [†]				
Some extent	6.81 (3.87-11.97)	<0.0001 (S)	6.83 (3.37-13.84)	<0.001 (S)
Great extent	2.1 (0.49-9.01)	0.315 (NS)	7.37 (1.71-31.34)	0.007 (S)

*Reference category; [†]Male gender, Unemployed, Upper middle class, Illiterates, No awareness of glaucoma, No compliance in using medications before COVID-19; Not at all nervous due to COVID-19 are the groups taken as reference category; S - Significant ($P<0.05$); NS - Not significant

analysis in our study which is in accordance with prior studies where psychological factors had an impact on the medication adherence of glaucoma patients.^[18,29]

Impact of the study and recommendations for future avenues

With the unforeseeable future of the pandemic, we need to focus on integrated strategies that could involve both health

technologies and primary eye care centers for continuity of healthcare services. A new boon in telemedicine has replaced the conventional face to face consultation during lockdown to continue medical care for the needful patients.^[30,31] Teleglaucoma is an advancing field with many programs for screening, diagnosing and monitoring glaucoma, piloted with success in the past.^[32,33] But with difficulty in technological

approach in rural areas, primary vision centers plays a vital role in bridging the gap. Aravind eye care system cadres 82 vision centers in Tamil Nadu with 32 centers in Madurai zone alone. Rural vision centers should leverage on the use of cost-effective tools for monitoring of glaucoma patients through telemedicine and provision for medication refill. In order to promote continuous accessibility of glaucoma medication in remote areas the tertiary centers can promote mobile medical van and courier services in collaboration with primary vision centers.

Improving knowledge about glaucoma through proper counselling, regular awareness programs and focus group discussion has to be emphasized. A multi facet counselling involving the family members should be focused as many of our patients are unemployed and dependent on family members for financial support as well as an escort for the hospital visit. In addition, psychological counselling of the patient to alleviate the stress and anxiety due to the pandemic is the need of the hour. Since stress due to the pandemic has found to have significant effect on medication adherence, developing and implementing appropriate mental health interventions has to be planned.

During these uncertain circumstances, collaborative efforts are needed from the government as well as the Non-governmental organizations (NGOs) to provide financial aid for the chronically diseased patients for their ease in accessibility to the healthcare systems and continuity of medications. As most of the glaucoma patients are old age patients, mobile medical vans can be organized for eye examination and to provide medication with all safety precautions.

Limitations

Firstly, the study participants were recruited only from Madurai zone for the ease of further follow-up of the patients. As distance is one of the main cofounding factors for nonadherence, percentage of nonadherence to medication may increase for patients in far distance from the hospital. Secondly, through the telephonic interview, the anti-glaucoma medications used by the patients cannot be cross verified, hence can give false high positive rate of adherence. Further, lack of standardized assessment using psychosocial rating scales to analyze the psychological impact of COVID may be attributed to the narrative nature of phone-based interview.

Conclusion

The dreadful calamity of COVID-19 pandemic, crippled the health care services throughout the world. This has affected the follow-up visit of glaucoma patients as much as 88% in a tertiary care center in south India and 57% were non adherent to glaucoma medication during the pandemic lockdown in our study. The main barriers encountered during the pandemic for the medication adherence were difficulty in accessibility of medication and financial difficulties for our patients. This study shall pave way for planning strategies for continuum of glaucoma treatment during natural disaster and emergencies. The need for decentralization of glaucoma care to primary centers and paradigm shift to teleophthalmology should be the future to meet the need of the glaucoma patients.

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Conflicts of interest

There are no conflicts of interest.

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Questionnaire

Demographic Details:

Study ID : _____ MR Number: _____ UIN: _____

Date : _____ (DD-MM-YYYY)

Name : _____ Age: _____ in Years

Gender : Male Female

Address :

District : Madurai Virudhunagar Sivagangai Ramnad Dindigul

Diagnosis : Right Eye: _____ Left Eye: _____ BE: _____

Medication advised: _____

Call Status: No Responses/Not Reachable Not Willing Willing to participate in study

Telephonic Assessment Questionnaire

1. Are you aware that you have glaucoma?
 Yes No
2. How long you have been diagnosed with glaucoma? _____ Years/Months
3. Reason for not attending the scheduled appointment in glaucoma clinic, Aravind eye hospital, Madurai? (April 2020–July 2020)
 Lockdown restriction Transport problem
 Financial difficulty Systemic illness Caretaker non availability
 Not aware about the need for schedule follow-up
 Advised not to come due to hospital restriction
 Personal work others _____
4. Any other alternate hospital visit during the last four months? Yes No
a. If Yes, The nature of the hospital : Private clinic Other AEH centers
 Vision center
5. Are you using glaucoma eye drops? Yes No
6. If using, how many eye drops bottles are you using? _____/-per day
7. How frequently you are using each eye drops? Bottle 1 _____
Bottle 2 _____
Bottle 3 _____
8. If not using eye drops, how long not using glaucoma eye drops? _____ Days/Months
9. Did you miss taking glaucoma medication in last one month?
 Yes No
10. Reasons for not using eye drops?
 Non availability of medicines Financial difficulty
 Caretaker non availability Other illness Forgetfulness
 Unaware of the importance of regular medication
 Didn't feel much improvement with eye drops
 Not willing to continue eye drops without doctor's consultation
 Others, _____

11. Are you having any eye problem now? Yes No
If Yes, Vision deterioration Pain Discomfort Others, _____
12. Were you regular in using medications before COVID -19? Yes No
13. Are you feeling nervous or stressed due to COVID-19 pandemic?
 Some extent great extent Not at all
15. What is the highest level of education that you have completed?
 Illiterate Primary school certificate Middle school certificate
 High school certificate Intermediate or diploma
 Graduate Profession or Honors
16. Occupation:
 Unemployed Elementary Occupation
 Plant & Machine Operators and Assemblers
 Craft & Related Trade Workers
 Skilled Agricultural & Fishery Workers
 Skilled Workers and Shop & Market Sales Workers Clerks
 Technicians and Associate Professionals
 Professionals legislators, Senior Officials & Managers Retired
17. Monthly Income of the family:
 ≤ 10,001 10,002-29,972 29,973-49,961
 49,962-74,755 74,756-99,930 99,931-199,861 ≥ 199,862