Do motivational cards really benefit sibling screening of primary open-angle glaucoma probands?

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Purpose: To compare the impact of Sibling Motivational Card (SMC) and oral counseling in screening siblings of primary open-angle glaucoma (POAG) probands. Methods: Two hundred and thirty-four newly diagnosed POAG probands were randomized to receive either oral counseling or SMC to motivate their siblings for a glaucoma screening at a tertiary eye care hospital in South India from July 2015 and June 2017. A total of 116 probands were orally counseled with a standard template of dialogs about the importance of family screening to motivate their siblings for a screening. One hundred and eighteen probands were randomized to receive SMC, bearing the details of the proband, sibling, and a message stressing the importance of family screening, in addition to oral counseling. We assessed the response rate in each group. Additionally, we evaluated the prevalence of POAG in the siblings. Results: A total of 95 siblings of 234 POAG probands were screened. The mean age distribution was 53.33 ± 10.9 years (range 28-79 years). The male to female ratio was 3:4. The percentage of siblings screened was more in the oral counseling group (63.2%) than in the SMC group (36.8). About 43 (45%) siblings had some form of glaucoma, and 13.6% had POAG. An additional 22.1% were disk suspects, and 5.2% had ocular hypertension. Conclusion: SMC did not have an additional benefit over the standard oral counseling in promoting sibling screening. Our study stresses the importance of sibling screening in POAG probands. Targeting siblings of POAG probands with oral counseling may offer a relatively inexpensive way of detecting glaucoma.



Key words: Oral counseling, randomized control trial, Sibling Motivational Card, siblings screening

Glaucoma is the leading cause of irreversible blindness in the world.^[1] It is estimated that there are more than 64.3 million cases of glaucoma worldwide, and the numbers are expected to reach 111.8 million by 2040.^[2] Various population-based studies have estimated that the prevalence of glaucoma in India ranges from 1.62% to 3.51%.^[3] Detection of glaucoma at an earlier stage of the disease is likely to reduce the morbidity and health-care expenditure related to glaucoma management and improve the quality of life.^[4] Population-based screenings, however, have had limited effectiveness in glaucoma detection, primarily because it is a difficult disease to diagnose definitively, given the low sensitivity of intraocular pressure (IOP) measurement as a screening tool and high variability in the appearance of the optic nerve head.^[5] Relatively low prevalence of glaucoma in the general population also renders the screening less cost-effective, except for the specific subgroups at higher risk.^[5] Screening may be helpful in high-risk populations with a higher prevalence of glaucomas, such as the elderly, myopes, those of African-American ancestry, and those with a family history. The positive predictive value of available screening tests is greatly enhanced in populations at higher risk of glaucoma.^[5] Family history is a useful risk factor to screen upon

Received: 07-Jun-2022 Accepted: 08-Aug-2022 Revision: 26-Jul-2022 Published: 30-Nov-2022 as it does not need a formal eye evaluation. The importance of family history in primary open-angle glaucoma (POAG) has been very well established.^[6-9] The Rotterdam study found the prevalence of POAG in first-degree relatives to be 10.4% in the siblings and 1.1% in the offspring of patients with POAG.^[10] The Baltimore eye survey found that a total of 16.1% of the POAG cases reported a positive family history of glaucoma among the first-degree relatives.^[11]

Cross-sectional studies seem to suggest close to 50% of all primary glaucomas to be familial, and a positive family history confers a threefold increase in the risk of developing open-angle glaucoma.^[12] Examining the family members of those diagnosed with POAG could be an effective way to identify those at greater risk of glaucoma, facilitating earlier detection and treatment.^[13] Among the first-degree relatives, siblings have an increased risk compared to the rest as they share both the genetic and environmental components.^[14] Hence, effective screening programs should be established for this high-risk group.^[15]

Though many studies have been done to screen the first-degree relatives of POAG patients, so far, no novel tools have been used in these studies to encourage the screening.

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Most of the studies have utilized oral counseling as the predominant mode of sibling screening in POAG patients.^[5,13,16] The other modalities that have been employed for uptake of sibling screening of POAG probands are telephone calls^[17] and short message services (SMS).^[18] Additionally, the efficacy of the methods used for screening has not been studied in detail. In this study, we wanted to analyze whether issuing motivational cards will encourage the siblings of POAG patients for glaucoma screening compared to the regular verbal counseling in a randomized fashion. Additionally, we aimed to estimate the prevalence of POAG in siblings of the POAG probands screened.

Methods

This prospective randomized control trial was performed at a tertiary eye care hospital in South India. The study protocol was approved by the institutional review board, and written informed consent was obtained from all the study participants, both probands and siblings. The study complied with the tenets of the Declaration of Helsinki.

Participants

A total of 234 newly diagnosed probands with POAG and all their siblings were invited to participate in the study. The recruitment period was from July 2015 to June 2017. Participants were recruited from the glaucoma services of our tertiary eye care hospital in South India. Probands were not eligible if they were previously on treatment with us or elsewhere.

Randomization

POAG probands attending our glaucoma clinic during the study period were randomly assigned to one of the two groups by using a computer-generated binary random number. One group was only verbally counseled using a standard template of dialogs, stressing the importance of family screening and early diagnosis, and its members were advised to motivate their siblings for screening by an experienced counselor. The other group members were similarly counseled by the same counselor and, in addition, were handed over a Sibling Motivational Card (SMC) to bring their siblings for screening. Both the groups were counseled by a single well-experienced counselor to maintain the uniformity in counseling, and the duration of counseling in the two groups was also kept same to avoid any untoward bias. Each proband was allowed to contribute any number of siblings.

Sibling screening motivational card

The front part of the SMC includes the sibling's name, age, gender, name of the probands, diagnosis, and medical registration number. The back part of the card has a message explaining the importance of family screening in glaucoma in the local language Tamil, as nearly 100% of the patients attending our outpatient department are well versed with Tamil [Fig. 1].

Clinical assessment

The diagnosis of POAG in the probands was confirmed with clinical evaluation, including gonioscopy, field analysis, and optical coherence tomography (OCT), by one of the investigators (RV, SK). All the siblings from both groups, upon presentation, were directed to the glaucoma services at the base hospital. They underwent a standardized baseline interview to collect demographic data, including name, age, gender, address, occupation, family history of glaucoma, and previous treatment history. All the siblings underwent complete ophthalmic evaluation including vision, refraction, slit-lamp biomicroscopy of the anterior segment, IOP evaluation with Goldmann applanation tonometry, gonioscopy with two mirror gonio lens, and, if needed, indentation with four mirror gonio lens (Ocular Instr. Inc., Ohio, USA) and dilated fundus examination using a +90 Diopter lens (Volk Optical, Inc., Ohio, USA). All the clinical tests were completed by a single senior glaucoma consultant (SK). Humphrey field analysis (HFA) (740i-42212; Humphrey systems, Carl Zeiss Meditec, Inc., Dublin, CA, USA) and OCT (Cirrus HD-OCT 5000, Carl Zeiss Meditec, Inc.) were performed by trained technicians whenever it was

அரவிந்த் கண் மருத்துவமனை - பாண்டிச்சேரி கண்நீர் அழுத்த நோய் குடும்ப பர்சோதனை அட்டை தொலைபேசி என் : 0413-2819100, இரைப்பு : 135 தேர் :	(கண்டீர் அடிக்க இநாய்)
பரிசோதனைக்கு வரும் நயரின் பெயர் : வயது / இனம் : உறபு முறை : நோயாளியின் பெயர் : நோயின் வகை : நோயின் வகை : நோயின் வகை : தோங்கள் பரிசோதனைக்கு வரும் பொழுது அறை எண் 01-ல் உள்ள	கண்ணில் உள்ள நீர் அழுத்தம் சாதாரண அளவைவிட அதிகரிப்பது கண்நீர் அழுத்த நோய் எனப்படும். இதனால் கண்ணில் உள்ள பார்வை நரம்பு பாதிக்கப்பட்டு எவ்வித அறிகுறியுமின்றி படிப்படியாக பார்வை இழப்பு ஏற்படுகிறது. இந்நோய் பரம்பரையாக வரும் வாய்ப்பு அதிகம் உள்ளது. அதனால் குடும்பத்தில் உள்ள அனைவரும் கண் பரிசோதனை தவறாமல் செய்து கொள்ளவேண்டும் என மருத்துவரால் பரிந்துரைக்கப்படுகிறது.

Figure 1: (a-front, b-back): Image depicting the Sibling Motivational Cards in vernacular language used for screening siblings of POAG probands. POAG = primary open-angle glaucoma

deemed necessary by the glaucoma consultant. For diagnosing the siblings of POAG patients, POAG was defined as an IOP greater than 21 mmHg and definitive glaucomatous optic disk changes with or without visual field changes. Disk suspect was described as a patient with normal IOP having clinically suspicious optic disk (cup disk ratio [CDR] >0.7 in either eye or asymmetry in CDR of >0.2 between the eyes), which required detailed glaucoma evaluation. Ocular hypertension was defined as an IOP of more than 21 mmHg with normal optic disk and visual field.

Statistical analysis

The mean (standard deviation [SD]) or frequency (percentage) was used to describe summary information. The Chi-square test or Fisher's exact test was used to assess the association between categorical variables. *P* values less than 0.05 were considered statistically significant. All statistical analyses were done by Stata 11.1 (StataCorp LLC, College Station, TX, USA). A sample size of 138 siblings was needed with a 10% prevalence of POAG in siblings of probands with POAG and assumed with 5% precision error and 95% confidence interval.

Results

A total of 234 POAG probands were recruited. One hundred sixteen probands were randomized to the oral counseling group, and 118 were randomized to the motivational card group [Table 1]. A total of 95 siblings of 234 POAG probands were screened in the study. Out of 95 siblings who turned up for screening, 60 belonged to the oral group and 35 belonged to the motivational card group. A total of 320 SMCs were issued to 118 POAG probands, but only 35 siblings turned up for screening (response rate: 10.9%). The response rate in the oral group was 20.1% [Table 2].

The mean age distribution of siblings was 53.33 ± 10.9 years (range 28–79 years) for the total population, with the motivational card group being significantly older (57.09 ± 9.36 years) than the oral group (51.02 ± 11.21 years) (P < 0.009). The mean age distribution was higher in females (57.6 years) compared to males (42.4 years). The male to female ratio was 3:4 (40 males and 55 females). The difference in the gender distribution was statistically insignificant (P = 0.716, Chi-square test) [Table 3]. Among those screened, 43 siblings (45.2%) were diagnosed with some form of glaucoma. The most common diagnosis was disk suspect (22.1%) followed by POAG (13.6%) and ocular hypertension (5.2%) [Figs. 2 and 3; Table 4]

Discussion

Our study demonstrated that oral counseling is beneficial in motivating screening among the siblings of South Indian POAG probands. We did not find any additional benefit with SMC. The prevalence of POAG in siblings of POAG probands was found to be 13.6%. The percentage of siblings screened was more in the oral counseling group (63.2%) than the motivational group (36.8%).

Out of 118 POAG probands who were issued 320 SMCs, only 35 turned up for screening (response rate, 10.9%). The probable reasons could be the lack of knowledge in the siblings about glaucoma and family screening, not being interested in evaluation, not able to take out time off from their work, absence

Table 1: The number of siblings screened in oral counseling and Sibling Motivational Card groups

Group	POAG probands	Siblings screened (<i>a</i>)	% Siblings screened (<i>a/n</i>)
Oral counseling	116	60	63.2
Motivational card	118	35	36.8
Total	234	95 (<i>n</i>)	100%

POAG=primary open-angle glaucoma

Table 2: Siblings' response rate in oral counseling and Sibling Motivational Card groups

POAG probands	No. of siblings	No. of siblings who turned up	% of siblings who turned up (response rate)
118 (SMC group)	320	35	10.9
116 (oral group)	298	60	20.1

POAG=primary open-angle glaucoma, SMC=Sibling Motivational Card



Figure 2: Bar chart depicting the percentage distribution of different glaucoma diagnosis in the screened sibling population

of eye-related complaints, and residing elsewhere/in their native place. The age group of the siblings varied between 28 and 79 years. Though glaucoma is predominantly seen in those beyond 40 years, our study included all the siblings irrespective of their age. We had 13 (13.68%) siblings under the age of 40, of whom six (6.31%) had some form of glaucoma. The mean age distribution of the siblings was 53.33 ± 10.9 years (range 28–79 years) for the total population, with motivational card subjects being significantly older (57.09 ± 9.36 years) than the oral group (51.02 ± 11.21 years) (P < 0.009). This highlights that the younger generation was probably motivated for screening with oral counseling alone compared to the older generation. Also, elderly people might depend on others to escort them to the hospital.

We found POAG prevalence to be 13.6% in siblings of POAG probands. Our results are in agreement with the previously published literature.^[11,12,16,19,20] The Rotterdam study found the prevalence of glaucoma among first-degree relatives to be 10.4% in siblings and 1.1% in the offspring of patients.^[19] The Baltimore Eye Survey found that a total of 16.1% of cases reported a positive family history of glaucoma among first-degree relatives. The stronger association was with siblings (9.9%; odds ratio 3.69) than with parents (5.6%;



Figure 3: (a) Pie chart depicting the total percentage distribution of different diagnosis in the screened sibling population. (b) Pie chart depicting the gender distribution of siblings screened in oral and motivational card groups

Table 3: Demographic details of oral counseling group and Sibling Motivational Card group					
Details		Group		Р	
	Oral	Sibling Motivational Card			
Age					
Mean (SD)	51.02 (11.21)	57.09 (9.36)	53.33 (10.90)	0.009ª	
MinMax.	28-79	37-76	28-79		
Gender, <i>n</i> (%)					
Male	26 (27.3)	14 (14.7)	40 (42.1)	0.716 ^b	
Female	34 (35.7)	21 (22.1)	55 (57.8)		

SD=standard deviation. at-test, bChi-square test

Table 4: Distribution of various glaucoma diagnosis		
Glaucoma diagnosis (%)	n (%)	
Disk suspect	21 (22.1)	
POAG	13 (13.6)	
OHT	5 (5.2)	
PACG	2 (2.1)	
PACS	1 (1.0)	
PAC	2 (2.1)	
NTG	1 (1.0)	

NTG=normal tension glaucoma, OHT=ocular hypertension, PAC=primary angle closure, PACG=primary angle-closure glaucoma, PACS=primary angle-closure suspect, POAG=primary open-angle glaucoma

odds ratio 2.17) and the weakest association was with their children (1.2%; odds ratio 1.12).^[11] The Finish twin Cohort Study conducted in Finland showed the heritability estimate of chronic open-angle glaucoma in siblings was 10.2%.^[20] The Barbados Family Study found that 19.8% (67/338) of siblings had open-angle glaucoma (OAG) in a population mainly consisting of Afro-Caribbeans.^[12] Similarly, Rajendrababu *et al.*^[5] concluded that POAG prevalence among first-degree relatives of persons with glaucoma was 13.3% higher than in the general population, as reported in previous studies. Moreover, 60% of those diagnosed with glaucoma were siblings.^[5]

We have enough literature showing that the siblings of POAG patients are at increased risk of glaucoma, and the risk increases with age.^[14,15] Furthermore, glaucoma is often asymptomatic without any warning symptoms. Hence, it becomes essential to develop ways to motivate screening among people of this high-risk group. Various studies have been published on family screening in POAG probands. Rajendrababu *et al.*,^[5] in their family screening study, motivated

screening by mailing a letter to the first-degree relatives, which described the screening program and invited their participation. They also used a brochure highlighting the familial association of glaucoma and the need to detect the disease early and treat it to prevent vision impairment and unnecessary blindness. They found a response rate of 7% among siblings, which is low compared to our study.

Similarly, in another study by Kong et al.[16] conducted in Shanghai, all the first-degree relatives (parents, siblings, and offspring) of previously diagnosed POAG probands were invited by oral counseling method to screen subjects. The control probands formed a pool of volunteers recruited by a poster displayed in the hospital, many of whom were cataract patients or residents in the nearby community. Both the groups underwent complete comprehensive ophthalmic examination to determine their glaucoma status. The response rates of first-degree relatives in the case group and the control group were 82.3% and 81.2%, respectively, which are much higher than our sibling response rate. This might be partially because of the fact that the patients who were visiting the hospital for other reasons like cataract were considered. The Nottingham Family Glaucoma Screening Study by Sung *et al.*^[14] conducted the sibling screening of POAG probands in two phases 6-7 years apart. In the first screening phase of the study, 330 siblings (of 188 POAG probands) were invited to attend screening between 1994 and 1997 by oral counseling. In the second phase of the screening (i.e., 6–8 years after the initial study), siblings negative for glaucoma (including those originally defined as suspects) in the initial screening study were invited to attend a second screening examination by oral counseling. The response rate of siblings in the first phase was 82.7% and in the second phase was 66.5%. As compared to our sibling response rate, this is very high. Vegini et al.^[15] performed a study among the first-degree relatives of POAG patients who came with their first-degree relatives to the glaucoma department and were screened for glaucoma. The eye examination of first-degree relatives identified 16.8% of individuals with glaucoma. The previous studies with high response rates included both the newly diagnosed patients and all those who were previously under treatment. Also, these studies had all the first-degree relatives, and moreover, they were population-based surveys. But we included only the newly diagnosed POAG probands and counseled them to bring only their siblings for screening. Previously diagnosed POAG were not included in the study as patient's knowledge about the disease might influence the sibling response rate. This implies that creating awareness about glaucoma and patients' knowledge about the disease condition will highly influence the response rate.

Most of the earlier landmark studies have stressed oral counseling for motivating sibling screening of POAG probands. Though many studies have been done to screen the first-degree relatives of POAG patients, no specific tools have been used in these studies to encourage them for screening. Hence, we wanted to analyze whether issuing motivational cards will encourage siblings of POAG patients for glaucoma screening. To the best of our knowledge, this is the first randomized study for screening siblings of POAG probands by using two different methods in the South Indian population.

Moreover, randomizing the probands eliminated the bias. Furthermore, we identified 45.2% of the siblings with some form of treatable glaucoma, including POAG, who may not have been identified otherwise. The most common diagnosis was disk suspect (22.1%), followed by POAG (13.6%), ocular hypertension (5.2%), primary angle-closure glaucoma (2.1%), primary angle closure (2.1%), primary angle-closure suspect (1%), and normal tension glaucoma (1%). However, we did not find any added advantage of the SMC. There might be various reasons for this. Probands and siblings might not be living in the same house or city. With the more common nuclear family set up in recent years, handing over the SMC to the siblings might have been an issue. On the other hand, calling them over the phone might have been very convenient for the probands. In a recent study by Shroff et al.,^[21] on family screening of first degree relatives of probands with glaucoma, they found a response rate of 12.9% through communication letters and phone calls. They also assessed the barriers for family screening. Nearly half of probands said that their relatives could not participate because they did not live in the region, and one-fifth of them reported that their relatives had other commitments. This is in line with our study. They also highlighted that the average cost for screening per proband was INR 588 and first-degree relative was INR 2422. Our study involves screening through oral counseling as well as by use of motivational cards, which does not incur any cost. We believe that standard oral counseling is a cost-effective model for future large-scale sibling screening of glaucoma probands.

Our study had a few limitations. The sample size was lesser than estimated (95/138). No specific date was issued for screening siblings while counseling or giving cards. One of the reasons for a poor response might be not offering a deadline for screening. We could not screen all the siblings for various reasons (not in their native place, not willing, travel cost, etc.). We tried finding out the reasons for refusal among siblings by enquiring about some of the probands during their review visits. The most common reasons included not being interested in eye check-ups, not able to take time off from their work, having no eye-related complaints, residing in remote areas far off from the hospital, and lack of motivation to attend the hospital for eve screening. Our results do not lie in line with the logical expected outcomes, but then we believe our results are pragmatic reflecting the possible real-life scenario. Moreover, our results Highlighting the factors beyond our control, including the sibling's age, employment, affordability, knowledge about the disease, distance from the base hospital, nature of the job, and so on, which might have influenced the results.

Furthermore, though we randomized the probands, we could not control the number of siblings per proband and we feel it is practically difficult to randomize probands based on the number of siblings. This might have influenced our results. Hence, we need to develop proband-independent ways to encourage screening, which should be still pragmatic, like sending messages encouraging the siblings for screening directly. We need further research to analyze the best possible way to screen this population at risk.

Conclusion

In summary, we found POAG prevalence to be 13.6% in siblings of POAG probands in a South Indian population who had attended a comprehensive screening examination. SMC did not have added advantage over oral counseling in motivating the siblings of POAG probands for a screening. Targeting siblings of POAG probands may offer a relatively inexpensive way of detecting glaucoma and the suspects at risk of glaucoma. Glaucoma specialists and clinicians should be proactive in developing proband-independent, innovative methods using modern technologies targeting this high-risk group. Future research is warranted to address the barriers and challenges faced in glaucoma screening in order to curb the glaucoma blindness.

Compliance with ethical standards

The article has not been submitted elsewhere for consideration of publication. The article complies with the ethical standards outlined by the Declaration of Helsinki.

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Conflicts of interest

There are no conflicts of interest.

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