Knowledge and Practice Related to Compliance with Mass Drug Administration during the Egyptian National Filariasis Elimination Program

Khaled M. Abd Elaziz, Maged El-Setouhy, Mark H. Bradley, Reda M. R. Ramzy, and Gary J. Weil*

Department of Community, Environmental, and Occupational Medicine, Faculty of Medicine, and Research and Training Center on Vector of Diseases Ain Shams University, Cairo, Egypt; Global Community Partnerships, GlaxoSmithKline, Brentford, United Kingdom; Infectious Diseases Division, Department of Internal Medicine, Washington University School of Medicine, Saint Louis, Missouri

Abstract. Lymphatic filariasis (LF) has been targeted for global elimination by 2020. The primary tool for the program is mass drug administration (MDA) with antifilarial medications to reduce the source of microfilariae required for mosquito transmission of the parasite. This strategy requires high MDA compliance rates. Egypt initiated a national filariasis elimination program in 2000 that targeted approximately 2.7 million persons in 181 disease-endemic localities. This study assessed factors associated with MDA compliance in year three of the Egyptian LF elimination program. 2,859 subjects were interviewed in six villages. The surveyed compliance rate for MDA in these villages was 85.3% (95% confidence interval = 83.9–86.5%). Compliance with MDA was positively associated with LF knowledge scores, male sex, and older age. Adverse events reported by 18.4% of participants were mild and more common in females. This study has provided new information on factors associated with MDA compliance during Egypt's successful LF elimination program.

INTRODUCTION

Lymphatic filariasis (LF), also known as elephantiasis, is endemic in 73 countries in the tropics and subtropics.¹ An estimated 40 million persons worldwide have significant clinical manifestations of the disease, predominantly lymphedema, elephantiasis, and hydrocele. The World Health Organization has targeted LF for global elimination by 2020.¹

Microfilariae are filarial larvae that circulate in the blood of infected persons, and these are ingested by mosquitoes when they feed on infected humans. Ingested parasites develop in mosquitoes over a period of two weeks to become larvae that are infective for humans. The global elimination strategy was designed to reduce the supply of microfilariae that can be taken up by mosquitoes by mass administration of drugs that clear microfilariae from the blood of endemic populations. If high compliance rates can be achieved for mass drug administration (MDA) over a period of years, this should reduce infection rates to low levels and interrupt transmission. The World Health Organization recommends MDA with a single dose of diethylcarbamazine (DEC) combined with albendazole annually for 4–6 years to eliminate LF in countries such as Egypt, where there is no co-endemic onchocerciasis or loiasis.²

Egypt was one of the first countries to initiate a nationwide program for LF elimination based on World Health Organization recommendations. In the year 2000, Ministry of Health (MOH) officials made a strategic decision to provide MDA with DEC and albendazole to the entire at risk population from the start of the program. The alternative would have been to scale up MDA over a period of years. The program targeted approximately 2.7 million persons in 181 endemic villages and towns in eight governorates.³ Pre-MDA infection rates were as high as 19% in endemic communities.⁴ The study reported here was conducted in 2002 after three rounds of MDA had been distributed with high reported coverage rates (85–90%). Social mobilization activities (distribution of pamphlets and posters and short advertising programs on television and the radio) delivered messages about the disease to the target communities with the goal of enhancing community awareness and participation in the MDA program.⁵

A study carried out in Haiti showed that knowledge about filariasis and its mode of transmission was positively associated with MDA compliance.⁶ Another paper reported that age, sex, and educational level influenced attitudes regarding MDA for filariasis in India.⁷ Egypt's LF elimination program achieved unusually high MDA compliance rates. However, little has been published on factors that affected compliance with MDA during this program. Such information might help other countries increase MDA compliance by refining health education messages and improving drug distribution strategies.

Therefore, the primary objective of this study was to investigate factors related to MDA compliance at the midpoint of Egypt's national LF elimination program (after three rounds of MDA). The study also independently assessed reported MDA compliance shortly after the country's third round of MDA.

MATERIALS AND METHODS

Study participants. The study protocol was reviewed and approved by an institutional review board at Ain Shams University. Surveys were conducted approximately three months after the third round of MDA in six semi-urban villages with populations in the range of 10,000-20,000. Three villages were in Giza governorate and three were in the governorates of Menofiya, Kafr El Shiekh, and El Sharkia in the Nile Delta. The Giza and Delta villages were demographically similar, and their Wuchereria bancrofti microfilaremia prevalence rates ranged from 3.5% to 11.5% before initiation of the MDA program in 2000. Villages were mapped and houses were numbered before the start of the study. The surveys were performed in approximately 100 randomly selected houses per village. Interviewers recorded demographic and MDA compliance information on preprinted forms after obtaining informed consent from study subjects. Approximately 500 persons > 16 years of age were assessed in each village.

^{*}Address correspondence to Gary J. Weil, Infectious Diseases Division, Department of Internal Medicine, Washington University School of Medicine, Campus Box 8051, 660 South Euclid Avenue, St. Louis, MO 63110. E-mail: gweil@dom.wustl.edu

The compliance rate was calculated for all study participants based on their history of ingesting antifilarial medications during the third round of MDA. Thus, this study looked at overall compliance among adults without correcting for those who were not eligible for MDA (e.g., pregnant women).

Questionnaire. The questionnaire had 40 questions in 5 sections. The first section collected demographic information. The second section evaluated the person's knowledge of the transmission, control, and prevention of LF. The third section assessed knowledge of transmission, control, and prevention of filariasis and elephantiasis, and this included a question to determine whether the person understood the relationship between LF and elephantiasis. Answers in this section were used to generate a LF knowledge score, which was expressed as a percentage based on a maximum of 50 points. The fourth section assessed the person's participation in the previous MDA round. Questions in this section assessed intake of the last dose of MDA, occurrence of adverse events, treatment and severity of adverse events, and whether the person had heard any publicity about MDA before the last round. The fifth section included questions on whether the person had ever been given a diagnosis of filariasis or had been treated for clinical filariasis (lymphedema or hydrocele).

The field work was conducted by 12 people, including 5 physicians, 3 senior medical students, and 4 experienced field staff. Interviewers had special training sessions before the survey to minimize interviewer bias. The training included mock interviews using the questionnaire.

Data analysis. Double data entry and data cleaning were performed by using SPSS data entry builder version 3.0 (SPSS, Chicago, IL). All data analysis was conducted with the SPSS Base Module Version 11.0.1. Knowledge about LF was recoded into a knowledge score that had a total of 50 points. The Mann-Whitney test was used to assess differences in quantitative variables and a chi-square test was used to compare proportions.

RESULTS

Interviews were conducted with 2,859 persons, including 1,527 in Giza villages and 1,332 in the Delta villages. The study population included 1,555 female (54.4%) and 1,304 male participants (45.6%). The mean \pm SD age of the studied persons was 34.5 \pm 16.0 years (median = 30 years and age range = 16–92 years).

Knowledge about LF. Survey results on this topic are summarized in Table 1. Most (90.5%) persons in the study had heard about LF, but only 64.7% had heard of elephantiasis. Forty-four percent of persons understood that the two terms are related to a single disease. Persons reported a variety of sources for their knowledge about LF. The most commonly reported source of information was television advertisements that were broadcast before each MDA round. Persons also reported that they learned about LF from medical personnel distributing MDA, relatives, and friends, and from written materials, such as newspapers and posters.

The mean \pm SD LF knowledge score for the studied sample was 29.8 \pm 20.7%. Twenty-three percent of persons scored 0%, 15% scored between 1% and 25%, 48% had a scores between 26% and 50%, and 0.5% of persons had scores > 75%. The LF scores were higher in males (31.7 versus 28.3),

Table 1
Knowledge of surveyed study participants about lymphatic filariasis
(LF), Egypt*

Knowledge about LF	Participants with knowledge		
	No.	%	
Mode of transmission			
Mosquitoes	1,689	59.1	
Method of control			
MDA	1,539	53.8	
Bed nets	339	11.9	
Insecticides	627	21.9	
No opinion	663	23.2	
Treatment for filariasis			
MDA	1,578	55.2	
No opinion	998	34.9	

*MDA = mass drug administration.

in persons < 30 years of age (33.4 versus 26.6), and in persons with paying jobs (33.1 versus 26.8) (P < 0.01 for all of these comparisons). The LF scores for persons living in Giza (29.1) and the Nile Delta villages (30.6) were similar (P = 0.06).

Survey participants who could relate the two terms for filariasis had significantly higher mean knowledge scores than those who did not understand the relationship between the two terms (36.3% versus 24.8%; P < 0.0001). Only 59.1% of study participants knew that mosquitoes transmit filariasis.

Television advertisements seemed to have played an important role in improving the study population's knowledge about the disease; persons who reported having watched television announcements or stories about LF had significantly higher mean LF knowledge scores than those who had not viewed announcements or stories (P < 0.0001).

Reported compliance and adverse events after the third round of MDA. Survey participants reported high compliance with MDA (85.3%, 95% confidence interval = 83.9-86.5%) (Table 2). Compliance rates were similar in the Giza and Delta regions. The mean \pm SD age for those who reported ingestion of antifilarial medications in round 3 was 34.9 ± 16.2 years and was significantly higher than those who had not complied with MDA (31.9 ± 14.2 years). Persons who reported that they had

TABLE 2 Reported compliance for the third round of mass drug administration for lymphatic filariasis (LE). Equat

for lymphatic filariasis (LF				
	Compliance			Odds ratio (95%
Characteristic	No.	%	Р	confidence interval)
Sex			0.026	1.11 (1.01–1.21)
M, n = 1,304	1,133	86.9		
F, n = 1,555	1,305	83.9		
Age, years			0.001	1.43 (1.16–1.76)
< 30, n = 1,337	1,108	82.9		
\geq 30, n = 1,522	1,330	87.4		
Location of villages			0.53	1.0 (0.92–1.15)
Giza	1,308	85.7		
Delta	1,130	84.8		
Know mode of transmission			0.001	1.42 (1.16–1.75)
Yes, n = 1,720	1,498	87.1		
No, n = 1,139	940	82.5		
Television LF information			0.288	1.12 (0.9–1.3)
Yes, n = 1,791	1,537	85.8		
No, n = 1,068	901	84.4		
Relate LF and elephantiasis			0.008	1.33 (1.07-1.65)
Yes, n = 1,257	1,097	87.3		
No, n = 1,602	1,341	83.7		

Mass drug administration compliance by occupation, Egypt			
Occupation	No.	%	Compliance, No. (%)*
Housewife	1,254	43.9	1,041 (83.0)
Manual worker†	419	14.6	361 (86.2)
Student	393	13.7	349 (88.8)
Farmer	266	9.3	232 (87.2)
Merchant or office worker	191	6.7	164 (85.9)
Other‡	99	3.5	79 (79.8)
No work	237	8.3	212 (89.5)

TABLE 3 Mass drug administration compliance by occupation Egypt

*Differences in compliance rates are significant by chi-square test (P = 0.05). †Carpenter, plumber, builder, technical worker.

*Professional or shop owner.

complied with MDA in round 3 had a higher mean LF knowledge score than noncompliers, and compliance was also higher in those who knew that elephantiasis and filariasis referred to the same disease. However, MDA compliance was not significantly associated with a history of viewing television programs or advertisements related to LF or the elimination program. Compliance rates differed by occupation, but differences were small; students, farmers, and the unemployed had slightly higher compliance rates than professionals and shop owners (Table 3). Reasons provided by study participants for noncompliance with MDA are shown in Table 4. The most common reasons for noncompliance were absence during MDA and pregnancy.

A logistic regression analysis was performed to determine which variables had the highest impact on compliance with MDA among the studied population. The variables that were entered into the stepwise logistic regression model were sex, age, overall LF knowledge score, and knowledge about the mode of transmission of the disease. Results are shown in Table 5. Age, awareness of the mode of transmission, and lack of knowledge relating LF and elephantiasis were independently related to compliance; younger persons and those who were unaware of the mode of transmission were less compliant with MDA. Sex was not independently linked to compliance.

Some study participants reported that they had experienced adverse events (AEs) after the third round of MDA (n = 450 or 18.5% of 2,438 participants who reported taking MDA) (Table 6). However, these AEs were mostly mild and transient; dizziness and fatigue were most common. Adverse events after MDA were more common in females than in males, but age was not linked to AEs.

DISCUSSION

This study was conducted to assess knowledge about LF in disease-endemic Egyptian villages during the National Filaria-

TABLE 4 Reported reasons for non-compliance with mass drug administration,

Causes of non-compliance	No.	%
Not at home	119	28.3
Pregnancy	98	23.3
Fear of adverse events	53	12.6
Team did not deliver drugs	46	10.9
Breast feeding	31	7.3
Dislike medicine	19	4.5
Liver disease	8	1.9
No excuse	47	11.2
Total	421	100.0

TABLE 5 Logistic regression model for factors affecting compliance with mass drug administration. Egypt*

Variable	Wald	Р	Odds ratio (95% confidence interval)
Relate LF and elephantiasis	3.4	0.06	1.23 (0.98–1.54)
Know mode of transmission	10.1	0.001	1.43 (1.14–1.79)
Age group†	16.0	0.000	1.54 (1.24–1.90)

*Calibration of the model: Hosmer and Lemeshow test $\chi^2 = 3.37$, P = 0.642; model discrimination: area under the curve = 0.578, 95% confidence interval = 0.549–0.607.

[†]The model considered age centiles (10-year intervals); the referent age group was the lowest age group (< 20 years of age). This group was actually 16–20 years of age because we only surveyed persons \geq 16 years of age.

sis Elimination Program. It also gathered information on reported compliance and AEs after the third round of MDA in this campaign.

Most (90.1%) study participants had some knowledge about filariasis. This percentage is similar to that reported by Mathieu and others for an endemic area in Haiti.⁶ Mathieu and others also reported that 36.4% of their study participants knew that mosquitoes transmit the disease. This value was higher in the present study (59.1%). Males in our study had better scores than females for knowledge about LF, and they also had better compliance rates with MDA. This finding is consistent with results from a study in India that found that males were better informed about the disease and its mode of transmission.⁷

Regarding compliance with MDA, our study participants reported 85.3% compliance after the third round of MDA. This value was slightly lower than the official coverage rates reported by the Egyptian government after the third round of MDA 93.3% (range 90–93% for all implementation units). This finding may be explained in part by our inclusion of persons who were not eligible for MDA in our compliance calculation. Surveyed compliance excluding pregnant women was 88.3%. However, the surveyed coverage rates and the government rates are excellent and comparable to results reported by Ramzy and others for four villages in Egypt during the MDA program.³ These compliance rates are higher than those reported from many national LF elimination

TABLE 6 Adverse events reported by survey participants approximately three months after the third round of mass drug administration, Egypt

			,
362	80.4		
53	11.8		
13	2.9		
10	1.8		
12	0.8		
328	72.9		
89	19.8		
33	7.3		
No.	%†		
157	13.9	0.001	1.78 (1.4-2.2)
293	22.4		
206	18.6	0.8	
244	18.4		
	53 13 10 12 328 89 33 No. 157 293 206	53 11.8 13 2.9 10 1.8 12 0.8 328 72.9 89 19.8 33 7.3 No. %† 157 13.9 293 22.4 206 18.6	53 11.8 13 2.9 10 1.8 12 0.8 328 72.9 89 19.8 33 7.3 No. %† 157 13.9 0.001 293 22.4 206 18.6 0.8

*Percentages of persons with any adverse event that reported different symptoms.

†Percentages of all persons interviewed who reported adverse events after taking MDA (by sex and age). Note that noncompliant persons who did not receive mass drug administration were not included in this analysis. programs. For example, overall MDA coverage reported from Haiti after the third round of MDA was $78.5\%^8$ in adults, and 61% in persons > 14 years of age. Moreover, in India after six rounds of MDA, the coverage was only 54– 75% of the eligible population,⁹ and in Vanuatu the MDA coverage after two years was 72%.¹⁰ Reported MDA coverage rates were around 45% in Ghana and Kenya.¹¹ Males reported higher MDA compliance than females in our study, and this finding is consistent with results reported from Haiti, where compliance was 77.7% in males and 54% in females.⁴

It was interesting to see that knowledge about the mode of spread of LF was associated with better compliance with MDA in the current study. This finding was statistically significant by univariate and multivariate analysis, and the finding is also consistent with results reported from Haiti.^{4,6} In other parts of the world, educational messages related to LF are often transmitted in person,¹² but television seems to have been important for delivering information about LF and MDA in Egypt. This finding supports the decision of the Egyptian MOH to invest heavily in electronic media for publicizing the LF elimination program.⁵

It was also interesting that although younger persons and shop owners had higher LF knowledge than the general surveyed population, they also had lower MDA compliance rates. This group may have been more likely to have been absent at the time of drug distribution than other groups. Special efforts may be needed to target subpopulations who deny that they are at risk for LF. Fear of side effects or complications of MDA has been a serious problem for programs in some parts of the world.¹³ However, only 12.6% of the noncompliers in our study listed fear of AEs as a reason for not taking MDA. Absence at the time of MDA and pregnancy were the main factors associated with noncompliance in the present study.

This study has provided interesting information on disease/ project-specific knowledge in an LF-endemic population during Egypt's national LF elimination program. Systematic post-MDA monitoring will be required to verify whether LF has actually been elimination from the country.¹⁴ It is difficult for a study like ours to capture the essence of what made Egypt's LF elimination program successful. However, we believe that a number of factors contributed to this success. First, Egypt has a strong primary health care network with MOH units in most towns and larger villages. In addition, the MOH had had significant experience with large-scale programs such as polio vaccination and schistosomiasis control in LF-endemic areas.¹⁵ These factors are likely to have increased the public's confidence in the health system and willingness to participate in the MDA program. Vigorous social mobilization and health education activities were developed for the LF elimination program, and these activities improved awareness of the importance of the disease before MDA in disease-endemic areas.

The method used for MDA distribution in Egypt was also important. Teams of health workers from local primary health centers distributed the medications on a house-tohouse basis over a two-week period each year, and teams directly observed ingestion of the pills in most cases. We believe that this distribution method is preferable to distribution of MDA from fixed locations. The MOH and the program also benefitted from partnerships with filariasis experts from universities in Egypt and other countries. Finally, it is important to recognize significant financial and technical support that the MOH received from partner organizations, such as the World Health Organization, GlaxoSmithKline, and the Arab Fund for Social and Economic Development. Public health experience and infrastructure, preparation, planning, partnerships, and commitment (financial and political) all helped to make this program successful. Although recipes vary in details from country to country, most successful LF elimination programs include these ingredients.

Received August 10, 2012. Accepted for publication May 8, 2013.

Published online June 10, 2013.

Acknowledgments: We thank all study participants for their cooperation and physicians, field staff, and senior medical students for conducting interviews.

Financial support: This study was partially supported by National Institutes of Health grants AI-35855 and AI-65715 and by a grant from GlaxoSmithKline.

Authors' addresses: Khaled M. Abd Elaziz and Maged El-Setouhy, Faculty of Medicine, Department of Community, Environmental, and Occupational Medicine, Ain Shams University, Cairo, Egypt, E-mails: khaledabdu@yahoo.com and maged.elsetouhy@gmail.com. Mark H. Bradley, Global Community Partnerships, GlaxoSmithKline, Brentford, UK, E-mail: mark.h.bradley@gsk.com. Reda M. R. Ramzy, Egyptian Ministry of Health, National Nutrition Institute, Cairo, Egypt, E-mail: reda.mr.ramzy@gmail.com. Gary J. Weil, Infectious Diseases Division, Department of Internal Medicine, Washington University School of Medicine, St. Louis, MO, E-mail: gweil@dom.wustl.edu.

REFERENCES

- World Health Organization, 2010. Progress Report 2000–2009 and Strategic Plan 2010–2020 of the Global Programme to Eliminate Lymphatic Filariasis: Halfway Towards Eliminating Lymphatic Filariasis. Geneva: World Health Organization, WHO/HTM/NTD/PCT/2010.6.
- 2. Ottesen EA, 2006. Lymphatic filariasis: treatment, control, and elimination. *Adv Parasitol* 61: 395–441.
- Ramzy RM, El Setouhy M, Helmy H, Ahmed ES, Abd Elaziz KM, Farid HA, Shannon WD, Weil GJ, 2006. Effect of yearly mass drug administration with diethycarbamazine and albendazole on bancroftian filariasis in Egypt: a comprehensive assessment. *Lancet* 367: 992–999.
- World Health Organization, 2003. Global Progam to Eliminate Lymphatic Filariasis. Annual Report on Lymphatic Filariasis 2003. Geneva: World Health Organization.
- Ramzy RM, Goldman AS, Kamal HA, 2005. Defining the cost of the Egyptian lymphatic filariasis elimination programme. *Filaria J 4*:7.
- Mathieu E, Lammie PJ, Radday J, Beach MJ, Streit T, Wendt J, Addiss DG, 2004. Factors associated with participation in a campaign of mass treatment against lymphatic filariasis, in Leogane, Haiti. Ann Trop Med Parasitol 98: 703–714.
- Babu BV, Hazra RK, Chhotray GP, Satyanarayana K, 2004. Knowledge and beliefs about elephantiasis and hydrocele of lymphatic filariasis and some socio-demographic determinants in an endemic community of eastern India. *Public Health* 118: 121–127.
- Mathieu E, Direny AN, de Rochars MB, Streit TG, Addiss DG, Lammie PJ, 2006. Participation in three consecutive mass drug administrations in Leogane, Haiti. *Trop Med Int Health 11:* 862–868.
- Ramaiah KD, Das PK, Vanamail P, Pani SP, 2003. The impact of six rounds of single-dose mass adminstration of diethylcarbamazine or ivermectin on the transmission of *Wuchereria bancrofti* by *Culex quinquefasciatus* and its implications for lymphatic filariasis elimination programmes. *Trop Med Int Health 8:* 1082–1092.
- Fraser M, Taleo G, Taleo F, Yaviong J, Amos M, Babu M, Kalkoa M, 2005. Evaluation of the program to eliminate lymphatic filariasis in Vanuatu following two years of mass drug

administration implementation: results and methodologic approach. Am J Trop Med Hyg 73: 753–758.

- 11. TDR, 2000. Community-Directed Treatment of Lymphatic Filariasis in Africa. Report of a Multicenter Study in Ghana and Kenya. Geneva: World Health Organization.
- Cantey PT, Rout J, Rao G, Williamson J, Fox LM, 2010. 2010: increasing compliance with mass drug administration programs for lymphatic filariasis in India through education and lymphedema management programs. *PLoS Negl Trop Dis 4*: e728.
- 13. Babu BV, Kar SK, 2004. Coverage, compliance and some operational issues of mass drug administration during the programme

to eliminate lymphatic filariasis in Orissa, India. *Trop Med Int Health 9:* 701–709.

- 14. World Health Organization, 2011. Monitoring and Epidemiological Assessment of Mass Drug Administration in the Global Programme to Eliminate Lymphatic Filariasis: A Manual for National Elimination Programmes. Geneva: World Health Orgnaization, WHO/HTM/NTD/PCT/2011.4.
- World Bank, 2008. Arab Republic of Egypt National Schistomiasis Control Project. Available at: http://siteresources.worldbank.org/ EXTWBASSHEANUTPOP/Resources/egypt_schistosomiasis_ ppar.pdf. Accessed February 2013.