Review Article

Epidemiology of lymphatic filariasis with special reference to urogenital-manifestations

S. P. Pani, V. Kumaraswami[1], L. K. Das

Vector Control Research Centre, (Indian Council Medical Research), Pondicherry, India; [1]Tuberculosis Research Centre, (Indian Council Medical Research), Chennai, India

ABSTRACT

Lymphatic filariasis (LF) is currently endemic in as many as 80 countries round the globe, particularly in the tropics and sub-tropics. *Wuchereria bancrofti* as a causative organism accounts for over 90% of the global burden. India contributes about 40% of the total global burden and accounts for about 50% of the people at the risk of infection. In India, states like Andhra Pradesh, Bihar, Gujarat, Kerala, Maharastra, Orissa, Tamil Nadu, Utter Pradesh and West Bengal contribute to about 95% of total burden. *W. bancrofti* is the predominant species accounting for about 98% of the national burden, widely distributed in 17 states and six union territories. Diethylcarbamazine (DEC) is an effective drug acting on the parasite (without report of resistance in past five decades) and mass annual single dose community drug administration with selective vector control could result in effective elimination of infection by interruption of transmission. The WHO has called for targeting filariasis elimination by 2020. India is the largest LF endemic country and has targeted the elimination of LF by 2015.

Key words: Epidemiology; Lymphatic filariasis; Urogenital filariasis

Lymphatic filariasis (LF) is currently endemic in as many as 80 countries round the globe, particularly in the tropics and sub-tropics. It is a vector borne parasitic disease caused by three lymphatic dwelling nematode parasites namely, *Wuchereria bancrofti*, *Brugia malayi* and *B. timori*.[1] Filariasis is a disease of the poor and is a cause and effect of poverty. Majority of the people at risk of filariasis live in rural areas. Lymphatic filariasis has been identified as one of the only six diseases, which could be targeted for elimination/eradication based on considerations that human beings are the only reservoir of infection. Diethylcarbamazine (DEC) is an effective drug acting on the parasite (without report of resistance in past five decades) and mass annual single dose community drug administration with selective vector control could result in effective elimination of infection by interruption of transmission. This has led to the articulation of the World Health Assembly Resolution (1997) for global elimination of lymphatic filariasis.[2] The WHO has now called for targeting 'filariasis elimination' by 2020.[3] India is the largest LF endemic country and has targeted elimination by 2015.[4] Transmission control and disability/morbidity management/control are the two pillars of the global elimination strategy.[5,6] For transmission control, mass annual single dose administration of DEC and or DEC + Albendazole to entire communities at risk of infection has been recommended.[1,7,8] Recognizing that episodic acute adeno-lymphangitis (ADL) attacks are associated with the progression of lymphoedema through stages and these are caused by secondary bacterial infections, foot hygiene has been recommended as a morbidity management strategy for LF elimination.[9]–[11] However, morbidity management strategy needs to be evolved for LF patients who suffer from genito-urinary (GU) manifestations, the burden of which is larger compared to lymphoedema.[12–18] Prior to development of a blue print for case detection, referral and organizing the logistics and funds for management, it is important to review the epidemiology, distribution and burden of hydrocele and other GU manifestations.

For correspondence: SP Pani,
Deputy Director (Senior Grade), Vector Control Research Centre, Indian Council Medical Research, Indira Nagar, Medical Complex, Pondicherry – 605006,
E-mail: sp_pani@vsnl.com

EPIDEMIOLOGY

Global and regional distribution

Of the three parasites causing LF, *Wuchereria bancrofti* accounts for over 90% of the global burden. *Brugia malayi* is limited in its distribution to Asia and *Brugia timori* to a few islands in Indonesia.[16] It has been estimated that 1100 million people are exposed to the risk of infection living in areas endemic for this disease and there are about 120 million cases with either disease or infection (microfilaria carriers). Almost half (49.2%) of the 120 million estimated cases are in the South East Asian region and another 34.1% of cases are in the African region [Table 1].[12] The 120 million cases of LF include 83.63 million cases of microfilaria carriers, 16.02 million cases of lymphoedema and 26.79 million cases of hydrocele; which clearly shows that the burden of genital manifestations of filariasis in terms of hydrocele is higher compared to lymphoedema (Table 1).[12]

Filariasis problem in India

India contributes about 40% of the total global burden and accounts for about 50% of the people at the risk of infection. Of the people exposed to the risk of infection, individuals with microfilaraemia, suffering from lymphoedema and hydrocele cases in the globe; India alone accounts for 39.0, 37.9, 46.4 and 48.1%, of respectively.[12] The relative burden for the two parasites *W. bancrofti* and *B. malayi* (global and Indian estimates) are compared in (Table 2). A recent standardized estimate has shown that out of the 25 States/Union territories in India, for which surveys have been carried out, 22 are endemic and nine states (Andhra Pradesh, Bihar, Gujarat, Kerala, Maharastra, Orissa, Tamil Nadu, Utter Pradesh and West Bengal) contribute to about 95% of total burden. Of the 466 districts in India, 289 have been surveyed for filariasis until 1995 and 257 of these are found to be endemic. A total of 553 million people are at risk of infection and there are approximately 21 million people with symptomatic filariasis and 27 million microfilaria carriers. *W. bancrofti* is the predominant species accounting for about 98% of the national burden, widely distributed in 17 states and six union territories. *B. malayi* is restricted in

Table 1: Global estimate of the number of cases and prevalence of filariasis (infection and chronic disease) due to *W. bancrofti* and *B. malayi* combined by endemic region (estimates of the number of cases are given in millions, while prevalence is in percentages; figures are for both genders combined)

Region†	Population	Infections‡	Lymphoedema	Hydrocele	Total number of cases<&	Total out of global cases*
SSA	512	27.87	4.64	10.20	40.02 (7.81)	33.60
OAI	793	16.40	3.00	1.9	20.64 (2.66)	17.33
IND	849	31.26	7.44	12.88	48.11 (5.67)	40.39
CHN	1134	7.54	0.84	1.63	9.61 (0.85)	8.07
LAC	441	0.32	0.03	0.057	0.395 (0.09)	0.33
MEC	391	0.24	0.06	0.06	0.34 (0.09)	0.29
WORLD	4119	83.95	16.01	26.79	119.12 (2.89)@…	100

†Regions as defined in the global burden of disease study (world bank, 1993). SSA: Sub–Saharan Africa; OAI: Other Asia and islands; IND: India; CHN: China; LAC: Latin America and Caribbean; MEC: Middle Eastern crescent.

‡microfilaraemia cases.

<&Equals to the sum of number of patients with microfilaraemia alone plus the number of patients with overt disease (lymphoedema and hydrocele) less the number with both overt disease and microfilaraemia (estimated to be 8.9% of lymphoedema cases and 22% of hydrocele cases). Lower numbers denote the prevalence in each region.

@&represents the global prevalence for endemic population only.

#as per Michael et al. 1996.

*In percentages.

Table 2: Relative magnitude of problem due to *W. bancrofti* and *B. malayi*, comparison between global and Indian estimates.

Parameters	Global@		India@		India as % of global	
	Wb	Bm	Wb	Bm	Wb	Bm
Microfilaria Carriers	73.3	10.4	29.5	1.8	40.2	17.3
Lymphoedema Cases	13.2	2.8	6.9	0.9	52.3	32.1
Hydrocele	26.8	NA *	12.9	NA *	48.1	NA *
Total cases#	106.2	12.9	48.1	2.6	42.8	20.2

#The total cases exclude a proportion of individuals who may have over lapping infection/lymphoedema/hydrocele.

*Not Applicable, since *B. malayi* does not result in hydrocele.

@ Cases in millions

distribution, with decreasing trend. An overview of the traditional endemic foci shows a concentration of infection mainly around river basins and eastern and western coastal parts of India (Figure 1).[19]

Age and gender distribution and relation with infection status

Understanding the age and gender distribution of the disease is important to identify the target groups for intervention. The prevalence of infection and disease are significantly higher in males compared to females.[14,18,20,21] Young adults in age group of 15–44 recorded the highest prevalence of infection.[13] This group also formed the predominant age class in the population. Micheal et al.(1996) estimated that globally, this age class contributes to 58.5% of all microfilaria (mF) carriers, 47.2% of lymphoedema cases and 58.3% of hydrocele cases and constituted 46.9% of the total population.[12] Children and young adults below the age of 20 years also record high prevalence infection, detected by newer techniques for antigenaemia.[22,23] The prevalence in these individuals ranged between 6.74 in South India (VCRC unpublished data) and 7.70% in Ghana.[22] This suggests that they are also infected, but do not exhibit mF in the night in peripheral blood for some or other reason. Therefore, coverage of mass treatment in these age classes will be crucial.

Prevalence of chronic disease increases monotonically from young adult age classes (about 15 years) onwards to reach a peak in older age classes due to a cumulative effect, as chronically diseased persons remain life long diseased.[12,14,21] The incidence of acute ADL also shows a similar age pattern as chronic disease prevalence, since episodes of ADL predominantly occur in people with severe chronic disease.[24] Males record very high prevalence of disease particularly due to occurrence of hydrocele. However, if hydrocele is not considered, the patterns are similar for both genders.[14] In stable endemic areas, the prevalence of chronic disease and hydrocele show an age dependent rise. A distinct monotonic increase in age prevalence is seen for hydrocele. In most Asian and African stable endemic sites, the prevalence of hydrocele can be as high as 50% in older age classes above 45 years of age. Meta-analyses in 1996 have also shown an age specific rise in hydrocele prevalence. However, as the total number of males in the age class of 15–44 is highest among all males in the endemic countries, this most productive age class accounts for 15.62 out of a total of 26.79 million hydrocele cases in the world.[12]

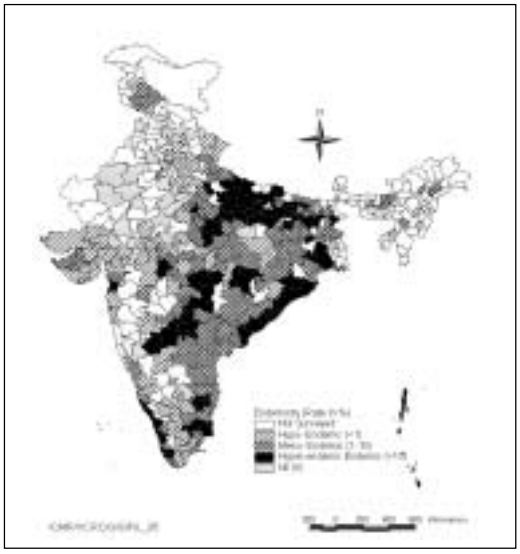

Figure 1: Filariasis distribution in India

Epidemiological uses of hydrocele detection

It is important to understand that hydrocele being the predominant manifestation in Bancroftian filariasis, detection of scrotal swellings among a fixed number of males in study sites by trained health workers has been found to be a valid method of rapid assessment procedure (RAP).[25] The prevalence of scrotal swelling as detected by trained health workers had a positive significant correlation with that detected by physicians. Therefore, data obtained for scrotal swelling prevalence by physical examination of males by health workers can also be used for rapid epidemiological mapping for filarial disease prevalence.[25] Recently hydrocelectomies conducted (as proportion of all surgical operations carried out) in some areas has been used successfully as an indirect marker of prevalence of disease in these localities and this could be pursued, as a method for rapid assessment, rapid mapping and also for assessing the current burden on available surgical facilities in different parts of the world.[26] The detection of hydrocele is useful for disease burden estimation and mathematical models for prediction of intervention outcome.[27]

Constraints in interpretation of epidemiological data

There are certain constraints in interpreting the data on clinical epidemiology studies of LF. For example, the surveys have followed different designs and definitions of disease states, which could crucially influence the outcome of the studies.[14]

The reported differences in the clinical picture of filariasis in different parts of India, was found to be more artefactual than real as most study designs did not consider the effect of age and gender structure of samples. More importantly, the surveys are often carried out by persons other than physicians and clinical examination of genitals is not insisted upon. In such a situation, the diagnosis of genital manifestations including hydrocele is often missed. Further, manifestations such as chyluria are also not recognized in point prevalence studies, as the phenomenon is intermittent and could be confused by the patient for many other conditions. Similarly, the detection of microscopic intermittent haematuria, although well documented in known microfilaria

carriers, community surveys may not reveal the condition due to its intermittency. Therefore, patients with other urogenital manifestations are identified most often when they approach for medical care to hospitals. These, therefore, are usually recorded as case reports and in the absence of a denominator regarding population covered it is difficult to appreciate the epidemiological significance of these. There is no doubt that epidemiological data need to be gathered in different parts of the world on the prevalence and incidence of other urogenital manifestations of filariasis. As a first step, it may be important to gather hospital data of past 5–10 years on these manifestations in the known Bancroftian filariasis endemic areas.

Filarial etiology of endemic hydroceles

There have been some studies to address the question whether all hydroceles seen in endemic areas are of filarial origin. A study in Pondicherry has shown by taking multiple criteria (clinical, histo-pathological, parasite demonstration in fluid and tissue, presence of filarial specific antibody/antigen, etc.) that 69% of hydroceles could be assigned to be of filarial origin in Pondicherry.[28] However, since hydrocele is a pathological condition persisting for lifetime and since the specific evidence of filariasis infection may not persist that long, it is difficult to exclude filariasis as an aetiological factor in all cases in endemic areas. Since the prevalence of other hydroceles in nonendemic areas is considerably low, unless otherwise proven all hydrocele in *W. bancrofti* endemic areas are to be considered as of filarial origin. This question however, requires reexamination, from the viewpoint of improved diagnostic tests made available currently (ICT card test and OG4C3 ELISA for filarial specific antigens and ultra sound examination for detection of adult parasite in the scrotum. Although scrotal ultrasound can be helpful in early diagnosis of hydrocele secondary to LF, either by identifying living adult worms or lymphangiectasia and or fluid, ultrasound will probably not be available at many endemic sites. An epidemiological study on cumulative exposure and disease development showed that hydrocele is a passive phenomenon after infection, not quantitatively related to exposure, unlike lymphoedema.

Size of hydrocele and relation with acute disease-results of a TDR study

In a multicentre study conducted by WHO/TDR during 1992–1995, clinical epidemiology of LF was addressed using a uniform protocol and definition of disease.[17] The sites included three from India (Pondicherry, Madras-currently Chennai and Vellore), two from Africa (Ghana and Tanzania) and one from the Philippines. The study not only addressed the issue of prevalence of different manifestations of LF but also relation of disease with the incidence of acute episodic ADL in the same population. These studies revealed that the overall prevalence of chronic disease ranged between 2.38% in Tanzania and 19.96% in Pondicherry. The prevalence of lymphoedema was lower than that of hydrocele in all study areas (lymphoedema was not recorded in Philippines). Hydrocele was graded into those less and those greater than tennis ball size and it was observed that in the three Indian sites, the prevalence of small hydrocele was higher (two thirds of total prevalence) compared to that of large hydrocele. In Ghana, the prevalence of these two grades was more or less equal; however, in Tanzania and in the Philippines the prevalence of larger hydrocele was higher. The coprevalence of both hydrocele and lymphoedema in males ranged between 0.32% in Ghana and 3.77% in Vellore. The coprevalence was relatively more common in India, than in Africa. The mean age of the patients with smaller hydrocele was lower (ranging between 31.2 $\pm$ 13.7 and 48.8 $\pm$ 17.8 years) compared to those with larger hydroceles (ranging between 40.7 $\pm$ 19.0 and 46.6 $\pm$ 12.4), suggesting the progression of smaller to larger hydrocele in course of time.

It is well known that ADL attacks form a part of the natural history of scrotal disease and that repeated acute attacks could lead to progression to the most severe forms, including lymph scrotum.[18] These attacks are could be linked to the presence of superficial bacterial and fungal infections, as is the case also with lymphoedema of the legs; or due to parasite induced inflammation. Episodic attacks ADL (acute filarial disease) continue to occur in established cases of chronic disease and in fact are responsible for the progression of chronic disease. The annual incidence of ADL per 1000 cases was generally higher in patients with lymphoedema compared to those with hydrocele. Overall, in hydrocele cases the ADL incidence ranged between 73.0 and 565.6 attacks per year per 1000 cases. These ADL attacks are responsible for severe physical disability and resultant loss of work.

SOCIO-ECONOMIC BURDEN

The social impacts of the disease in terms of physical disfigurement, loss of self-esteem, lowered employment opportunity, interference in sexual activity and family discord. Poor marriage prospects, stigma within the community, poor job opportunities are common. The degree of stigma is associated with the severity and visibility of the disease There is a considerable psychosocial stress on the individual and families including sexual disabilities of men afflicted with hydrocele or genital abnormalities and of women with lymphoedema of breasts or genital and finally the poor quality of life of individuals with the disease is obvious.

In 1993, the global burden of filariasis was estimated to be 8 50 000 DALYs lost, which is seen as a serious underestimate due lack inclusion of acute disease

morbidity (World Bank, 1993). The disease is causing direct and indirect economic loss to individuals and families including loss in productivity, functional impairment. Recently, it has also been estimated that economic loss to India is to the tune of US $ 840 million–$ 1.5 billion per annum.

DISABILITY / MORBIDITY PREVENTION / MANAGEMENT / CONTROL

Since most clinically asymptomatic infected individuals have lymphatic abnormalities, they may be at risk of developing disease. Diethylcarbamazine or ivermectin or coadministration of both or DEC/ivermectin with albendazole administration in these cases is expected to clear the infection and make them free from infection, so that it is expected that the pathology will not progress to overt disease. Prevention of repeated episodic attacks of ADL will be important not only to prevent sufferings of the patients (thus reduce burden of disease) but also for the prevention of progression of existing chronic disease. Regular foot hygiene prevents incidence of episodic ADL attacks. The current basis of medical management of lymphoedema lies in limb care, exercise, physiotherapy including manual massage and possibly use of drugs. Coadministration of Daflon with DEC or DEC alone can result in significant reduction of filarial lymphoedema. Surgical management of lymphoedema is indicated in certain specific cases and prevention of acute attacks after surgery is important for sustaining the benefit of surgery. Surgery is the method of choice for hydrocele management.[17] However, currently it is done by passive case detection and patient seeking treatment. The inclusion of this as a public health measure will require not only developing and using rapid assessment techniques, methods for line listing, setting up of facilities at different levels for case detection and surgery and referral system.

There is no consensus on the management modalities of different urogenital manifestations and there is an urgent need for developing consensus by review and expert group discussion. India has not only the problem but also a large body of experienced clinicians and scientists, who have a responsibility of producing the lead document on the management of genito-urinary manifestations of filariasis.

REFERENCES

1. Das PK, Pani SP, Krishnamoorthy K. "Prospects of Elimination of Lymphatic Filariasis in India." ICMR Bulletin 2002; 32 (5 & 6): 41-54.
2. World Health Assembly. A 50.29. Elimination of lymphatic filariasis as a public health problem. Resolution 50.29 of the World Health Assembly, May 1997.
3. World Health Organization: Resolution of the Executive Board of the WHO: Elimination of Lymphatic Filariasis as a Public Health Problem. Fiftieth World Health Assembly, Geneva 13 May 1997; WHA 50.29.
4. Ministry of Health and Family Welfare, Government of India: National Health Policy 2002
5. Dreyer G, Addiss D, Bettinger J, Dreyer P, Noroes J, Rio F: Introduction. Lymphoedema Staff Manual. Treatment and Prevention of problems Associated with Lymphatic Filariasis (WHO, Geneva) 2000;V-Vii.
6. Appavo NC, Pani SP, Das PK. The Science of arts of Lymphatic filariasis elimination in India: Hopes for the next millenium. Progress in lymphology XVII 2000;173-92.
7. Ramaiah KD, Vanamail P, Yuvaraj J, Pani SP, Das PK. The effect of six rounds of single dose mass treatment with Diethylcarbamazine or ivermectin on Wuchereria bancrofti and its implications for lymphatic filariasis elimination. Tropical Medicine and International Health 2002;7:767-74.
8. Das PK, Pani SP. Towards elimination of lymphatic filariasis in India: Problems, challenges, opportunities and new initiatives. Journal of International Medical Sciences Academy (Special Issue: emerging and re-emerging parasitic infestations in India) 2000; 13:18.
9. Pani SP, Yuvaraj J, Vanamail P, Dhanda V, Michael E, Greenfell BT, Bundy DAP. Episodic adenolymphangitis and lymphodema in patients with bancroftian filariasis. Trans Roy Soc Trop Med and Hyg 1995;89:72.
10. Vijayalakshmi N, Samabasiva Rao R, Anand Paul Kumar MP, Yuvaraj J, Pani SP. Role of aerobic bacteria in the aetio-pathogenesis of acute adenolymphangitis (ADL) in filarial lymphoedema. Progress in lymphology 2000;XVII:163.
11. Pani SP, Lall R. Clinical features, pathogenesis and management of Lymphatic filariasis. ICMR Bull 1998;28:41.
12. Michael E, Bundy DAP; Grenfell BT. Re-assessing the global prevalence and distribution of lymphatic filariasis. Parasitology 1996;112:409.
13. Sasa M. Human Filariasis. A global survey of epidemiology and control, University of Tokyo Press 1976;336.
14. Pani SP, Balakrishnan N, Srividya A, Bundy DAP, Grenfell BT. Clinical epidemiology of bancroftian filariasis: effect of age and gender. Trans Roy Soc Trop Med Hyg 1991;5:260.
15. Vector Control Research Centre. 25 years of research. Silver Jubilee Publication. 2000;95.
16. World Health Organization. Lymphatic filariasis: the disease and its control. Fifth report of the WHO expert committee on filariasis. WHO Technical Report Series. 1992;821:1.
17. WHO Report of Informal Consultation on Surgical approaches to the uro-genital manifestations of lymphatic filariasis.WHO, Geneva.2002;15-6.
18. Pani SP, Dhanda V. Natural-history and dynamics of progression of clinical manifestation of filariasis. In: Tropical Disease: Molecular Biology and Control Strategies 1994;1.
19. Sabesan S, Palaniyandi M, Das PK. Mapping of lymphatic filariasis. Annals Trop Med Parasit 2000;94:591.
20. Michael E, Grenfell BT, Bundy DAP. The association between microfilaraemia and disease in lymphatic filariasis. Proceedings of the Royal Society of London, series B 1994;256:33-40.
21. Pani SP, Srividya A. Clinical manifestations of bancroftian filariasis with special reference to lymphoedema grading. Indian Journal of Medical Research 1992;102:114-8.
22. Addiss DG. Clinical, parasitological and immunologic observations of patients with hydrocele and elephantiasis in an area endemic with lymphatic filariasis. J Infectious Dis 1995;171:755-8.
23. Ramaiah KD, Vanamail P, Pani SP, Das PK. The prevalences of Wuchereria bancrofti antigenaemia in communities given six rounds of treatment with diethylcarbamazine, ivermectin or placebo tablets, Ann. of Tro. Med. & Parasitology 2003; 97(7):

737-41.
24. Ramaiah KD, Ramu, Vijaya Kumar KN, Guyatt H. Epidemiology of acute filarial episodes caused by *Wuchereria bancrofti* infection in two rural villages in Tamil-Nadu, South-India. Trans Roy Soc Trop Med Hyg 1996;90:639.
25. Srividya A, Lall R, Ramaiah KD, Ramu K, Hoti SL, Pani SP, Das PK. Development of rapid assessment procedures for the delimitation of lymphatic filariasis-endemic areas. Tropical Medicine and International Health 2000;5:64.
26. Srividya A, Palaniyandi M, Michael E, Pani SP, Das PK. A geostatistcial analysis of the geographical distribution of lymphatic filariasis prevalence in Southern India. Am J Trop Med Hyg 2002; Proceedings of the 17th International Congress of Lymphology, Chennai." Lymphology XVII:173-92.
27. Chan MS, Srividya A, Norman RA, Pani SP, Ramaiah KD, Vanamail P. et al. DAP. EPIFIL: A Dyanamic models of infection and diseases in lymphatic filariasis. Am J Trop Med Hyg 1998;59:606.
28. Shenoy RK, Sandhya K, Suma TK, Kumarasami VA. Preliminary study of filariasis related acute adenolymphangitis with special reference to precipitation factor and treatment modalities. Southeast Asian J Trop Med Public Health 1995;26:301.
29. World Health Organization. Lymphatic filariasis. Reasons for hope. Division of control of tropical diseases. WHO/CTD/FIL/97.4 World Health Organization 1997;1.
30. Das PK, Pani SP. "Filariasis" Epidemiology and control in Helminthology in India; Ed M. L. Sood. 2001.

How to cite this article: Pani SP, Kumaraswami V, Das LK. Epidemiology of lymphatic filariasis (LF) with special reference to urogenital-manifestations. Indian J Urol 2005;21:44-9.