INTRODUCTION AND REVIEW OF LITERATURE

Lymphatic filariasis (LF), a mosquito vector-borne disease is a major public health problem in many parts of the tropics. The term “lymphatic filariasis” denotes infection by *Wuchereria bancrofti* and *Brugia malayi*. India contributes about 40% of the total global burden (filariasis) 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 (Michael *et al.*, 1996). The World Health Organization (WHO) estimates that 1.1 billion people live in high risk areas, 120 million of these people are already infected with LF, and 76 million people have suffered from damaged lymphatic and renal systems. (Ottesen *et al.*, 1997) (Global program to eliminate lymphatic filariasis: progress report on mass drug administration in 2008, WHO weekly Epidemiology Report 2009). The World Health Organization estimated in 1994 that 751 million people live in areas endemic for lymphatic filariasis. Of those, 72.8 million were infected with *W. bancrofti* (Gratz and Jany, 1994).

LF is a major health problem affecting about 250 million persons in tropical countries. The disease is endemic in 80 countries, and more than two billion people worldwide are estimated to be at risk. Approximately 128 million people in tropical and subtropical areas of the world are infected (Parija, 2005). The largest number of cases of filariasis occurs in India, where over 300 million people live in endemic zones. It is estimated that at least 6 million attacks of acute filarial disease occur every year in India and that over 15 million persons have chronic filarial disease (Agrawal and Sashindran,
The mosquito-borne parasitic disease LF is endemic in around 81 tropical countries, has a global burden of around 120 million cases, and is classified by the World Health Organization as the second most common cause of long term disability after mental illness (Ottesen, 2006).

Three species of filarial parasites cause LF. *W. bancrofti*, the cause of Bancroftian filariasis, accounts for 90% of the cases worldwide. Brugian filariasis is caused by *B. malayi*, which is found in eastern Asia, and *Brugia timori*, which is confined to Timor and adjacent islands. All three species cause similar lymphatic disease but only Bancroftian filariasis causes hydrocele and all are controlled and treated by the same methods (Melrose, 2002). LF has a wide clinical spectrum ranging from debilitating acute bacterial dermatolymphgangioadenitis (ADLA) attacks, covert lymphatic and renal disease, and various degrees of lymphedema, to the terrible disfiguring, and often socially ostracizing, chronic manifestations of hydrocele and elephantiasis (Ottesen et al., 2008). Infection often occurs in childhood but the obvious clinical effects of the disease such as filarial lymphedema or hydrocele may not occur until they reach adolescence (Witt and Ottesen, 2001). Shenoy et al., (2007 and 2008) have shown covert abnormalities in the lymphatics with lymphoscintigraphy and worm nests by Doppler ultrasonography in *B. malayi* LF-infected adolescents as young as three years. Importantly, it has also been shown that these early lymphatic changes can be reversed by rug administration (Shenoy et al., 2009).

Lammie et al., (2002) and Pfarr et al., (2009) have explained that the mechanisms involved in the development of filarial lymphedema are not fully understood but they are known to be a complex interaction between the parasite and the host’s immune system.
The effects of LF on the lymphatic system often become apparent during adolescence when the lower limb swells due to lymphedema and males develop hydrocele (Gordon et al., 2011). Lymphatic filariasis, the second leading cause of permanent and long-term disability, affects 120 million people globally. Hydrocele, an accumulation of fluid in the scrotum that causes it to swell, is one of the chronic manifestations of LF among men and there are about 27 million men with hydrocele worldwide. Babu et al., (2009) described the impact of hydrocele on marriageability, and some women expressed that a hydrocele patient is “last choice”.

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, Maharashtra, Orissa, Tamil Nadu, Uttar 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 distribution, with decreasing trend.

An overview of the traditional endemic foci shows a concentration of infection mainly around river basins and eastern and western costal parts of India (Sabesan et al., 2000 and Pani et al., 2005). *W. bancrofti* is widely distributed in tropical and subtropical countries and is responsible for the condition known as filariasis, with the most obvious longstanding outcome being elephantiasis of an affected limb. Adult worms are found in
the lymphatic channels, which eventually find their way into the blood stream. Spread is via inoculation by mosquitoes, either nocturnal or diurnal. Ingestion of microfilaria by the mosquito during a blood meal allows transfer to another host, where larvae invade the lymphatic channels and develop into adult worms. Clinical manifestations are acute or chronic, with the cardinal manifestation that of acute lymphangitis. An eventual lymphatic obstruction results from the chronic manifestations of lymphangitis caused by the adult worms. This condition may also affect the scrotal sac by presumed obstruction to the lymphatic channels of the scrotal contents but more often results in epididymitis and a hydrocele (Adejolu and Sidhu, 2011).

Several different mosquito species within the genera *Culex*, *Anopheles*, *Aedes* and *Mansonina* can serve as primary vectors of LF parasites. Biological transmission of filarial worms is termed cyclodevelopmental, i.e., the parasite undergoes development within the vector to become infective to the vertebrate host, but does not multiply. In competent vectors, microfilariae (mf), produced by adult female worms and found circulating in the peripheral blood, are ingested with a blood meal and will quickly (within 2 hr) penetrate the midgut epithelium to access the hemocoel (Christensen *et al.*, 1984). Brancroftian filariasis is prevalent in both urban and rural areas. It is caused by the nematode worm *W. bancrofti* transmitted by female mosquito *Culex quinquefasciatus*. The major prevalence is among the poorer sections of society (Ramaiah *et al.*, 2000), rural filariasis has not received mosquito control operations (Rajagopalan *et al.*, 1981). The existing National Filaria Control Programs (NFCP) caters for only 11% of the population who live in the endemic foci (Sharma *et al.*, 1995) and its control measures cannot be adopted in rural areas because of operational problems (Ramaiah *et al.*, 1989).
\textit{C. quinquefasciatus} is widely distributed in tropical and subtropical areas and closely associated with human habitation because of its anthropophilic, endophilic blood feeding habits and breeding areas (Forattini \textit{et al.}, 1993 a, b, c and d). \textit{C. quinquefasciatus} was reported to be a highly efficient insect host for the larval development of nocturnally periodic \textit{W. bancrofti} (Sucharit and Harinasuta, 1975 and Jitpakdi \textit{et al.}, 1998). Lymphatic filariasis is characterized by a wide spectrum of clinical manifestations; asymptomatic microfilaraemia stage is characterized by the presence of microfilariae in blood during night but without any overt clinical manifestations of filariasis. It is possible that some of these have hidden lymphatic pathology in the form of dilatation at high risk of developing disease. Acute manifestations are characterised by recurrent attacks of fever associated with inflammation of the lymphnodes and lymphvessels - acute adenolymphangitis (ADL). Various factors related to parasite like release of toxins, immune response infected human host, trauma in the affected areas and secondary bacterial and/or fungal infections play a role in causing the ADL attacks. The inflamed lymphatics of the male genitalia lead to funiculitis or epididymoorchitis. Chronic manifestations are hydrocele, lymphoedema and elephantiasis. While hydrocele is the commonest genital manifestation in the male population, chronic epididymitis, funiculitis and lymphomatous thickening of scrotal skin can be the other genital manifestations.

Lymphoedema commonly affects the lower limbs, some times the hands and rarely the genitals and breast in females. There may be repeated attacks of ADL. Lymphoedema progresses from pitting oedema (reversible on elevation) and then non-pitting oedema followed by increase in oedema fluid volume, resulting in fibrous tissue
formation, followed by skin thickening, ulceration, nodule formation and disfiguration (elephantiasis). Chyluria is prevalent in some endemic areas. The major occult filarial manifestations include tropical pulmonary eosinophilia (resulting from allergic reaction to parasite and characterized by nocturnal paroxysmal cough and hypereosinophilia), glomerulopathies, endomyocardial fibrosis, monoarthritis, tenosynovitis, acute abdomen, central serous retinopathy (CSR), iridocyclitis, urticaria, haematuria etc. in adults (www.jbtdrc.org). The result of analysis of blood samples of filarial patients for filarial IgG antibodies and antigen have shown that the absence of microfilaraemia number of clinical conditions in filarial endemic area showed presence of either antigen or antibody or both confirming filaria aetiology in adults as well as in children (Harinath et al., 1996). Genital lymphedema secondary to filariasis is a common problem in most of the filarial endemic regions of the world. Repeated filarial attacks lead to obstruction of lymph flow resulting in various types of genital manifestations in both males and females (Manokaran, 2005).

Humoral immune parameters like total immunoglobulins and specific antibody levels in serum were studied in filarial chyluria patients attending the filariasis clinic of Government General Hospital, Madras. Mean serum IgG was significantly reduced in this group compared to normal controls, while IgA and IgM levels remained comparable to controls. Anti-filarial antibody titre as measured by enzyme-linked immunosorbent assay also was significantly reduced. However, the total and specific IgE antibody titre was similar to that of controls. Specific IgE contents of the patients sera could be related to their microfilaraemic status (Raja et al., 1984). Malhotra et al., (1982) observed the presence of IgM antibody in 91 out of 100 microfilaraemia cases Lunde and Ottensen
(1980) have shown the presence of specific anti egg antigen IgM in all the 13 patients of early schistosomiasis thereby indicating that IgM is associated with active infection. Absence of specific anticulture antigen IgM in 9 microfilaraemia cases may be due to the transition of these cases into chronic stage where IgM antibody is mostly absent. However they did not show any early clinical manifestation when examined. Five out of the 13 endemic normals who showed the presence of IgM antibody when further examined for microfilariae by concentration test were found to be negative. There of these endemic normals were further examined by Diethylcarbamazine (2 mg/kg body wt.) provocative test and were found to be negative for antibodies. Of 462 individuals from Pipri and Sukalibai villages, screened by night wet blood smear examination, 188 were found to be positive for microfilariae. When the filter-paper blood samples of these individuals were analysed by ELISA using *W. bancrofti* mf ES antigen and antihuman IgG + IgM + IgA-penicillinase conjugate, 184 of the 188 microfilariae-positive cases and 38 of the 274 microfilariae-negative cases showed a positive reaction for filarial antibody (Harinath et al., 1984). Chy luria is one of the many clinical manifestations of filariasis. It is the commonest of the chylous complications of lymphatic obstruction. Several studies have analysed the cellular and humoral immune parameters of lymphatic filariasis patients (Desowitz et al., 1976).

The immunodiagnosis of bancrofitian filariasis is a major challenge to the immunoparasitologist *W. bancrofti* microfilarial excretory-secretory antigens were found to be specific and highly sensitive requiring as little as 0.35 ng antigen protein per well in penicillinase enzyme linked immunosorbent assay for detection of filarial antibody (Harinath, 1984). The humoral immune response in humans to filarial parasites is
generally dominated by the IgG4 isotype, when measured by ELISA against somatic adult worm extract; antibodies reactive to somatic extracts of infective larvae are more equally represented by IgG1 and IgG4 (Kurniawan et al., 1998).

Immunohistologic examination of local tissue inflammatory responses revealed an abnormal CD3+ perivascular infiltrate in 73% of the individuals with clinical disease and in 55% of the asymptomatic microfilaricmic individuals (Freedman et al., 1995). This CD3+ infiltrate was composed of predominantly CD8 T cells in the limbs of patients with clinical disease and predominantly CD4 T cells in the limbs of the asymptomatic microfilaricmic individuals. Individuals with clinical disease have also been found to have elevated levels of soluble CD8 molecules and of CD8+ HLA-DR+ T cells in their circulation (Lal et al., 1989 and 1990), so this T-Cell subset may be important in the pathogenesis of the disease. In another study, freedman and colleagues found that in sections of skin punch biopsies from filarial patients; vascular cell adhesion molecule-1 (VCAM-1) staining was present on the vascular endothelial surface in individuals with clinical disease, but not in asymptomatic microfilaricmic individuals (Freedman et al., 1996). It was hypothesized that VCAM-1 may preferentially increase transmigration of CD8 T cells which, in turn, could be important sources of local cytokine production. More recently, freedman and colleagues have found that individuals with lymphatic filariasis, regardless of disease status, have distinct and limited T-cell populations concentrated in affected tissue, when compared with tissue of normal subjects, with no difference in cytokine expression (Freedman et al., 1999). Human IgG antibody responses to *W. bancrofti* third stage infective larvae (L₃) surface and antigens were
studied and found that children and young adults (aged 10-20 years) tended to have antibodies to more L$_3$ somatic antigens than older adults. (Hanan et al., 2000).

The modulation of immune responses by active infection is clearly associated with the absence of overt pathology in infected persons. The pathogenesis of lymphatic filariasis is one of the least understood aspects of the infection, due to its multifaceted nature. The presence of adult worms results in the dilation of lymphatic vessels, and is likely to be the primary lesion that predisposes to disease (Eileen and Yazdanbakhsh, 2001). The mechanisms of antigen-specific immune unresponsiveness was seen in microfilaremic patients with bancroftian filariasis; T and B cells precursor frequency analysis was performed using PBMC from individuals with either asymptomatic microfilaremia (mf, n=7) or chronic lymphatic obstruction (CP, n=20). Highly purified CD3$^+$ cells were partially reconstituted with adherent cells and their proliferative response to parasite antigens determined in cultures of T cells by limiting dilution analysis.

A filter immunoplaque assay also assessed the frequency of both total and parasite-specific Ig producing B cells. While the lymphocyte proliferation to mitogens and to a nonparasite antigen (Streptolysin-O, [SLO]) were similar in all groups of patients, the frequency of parasite-specific CD3$^+$ T cells was significantly lower (geometric mean [GM], 1/3, 757) in mf patients when compared to that in CP patients (GM1/1,513; P<0.001). Similarly, the proportion of lymphocytes producing parasite-specific IgE or IgG was significantly lower in mf patients (IgE mean, 0.2% IgG mean, 0.33%) compared with CP patients (IgE mean, 3.2% IgG mean 1.76%; P<0.05 for both comparisons). These observations imply that low numbers of parasite-specific T and B
lymphocytes may be partially responsible for the severely diminished capacity of lymphocytes from patients with mf to produce parasite-specific antibody and to proliferate to parasite antigen in vitro. Such differences in parasite-specific lymphocyte responses suggest that tolerance by clonal energy may be a critical mechanism for maintaining the microfilaremic state (King et al., 1992). Circulating filarial antigen was examined by monoclonal antibody Og4C3-enzyme-linked immunosorbent assay (ELISA) from 114 mean with hydrocele, living in an endemic area. Nocturnal blood and hydrocele fluid were collected and examined for microfilaria. ELISA was performed on serum and hydrocele fluid for detection of antigen. Amongst 114 cases, 5 (4.4%) showed microfilaria in blood but none in fluid. ELISA was positive in 13 (11.40%) serum and 5 (4.4%) fluid samples. All five fluid antigen positive cases were positive for antibodies and showed microfilaria in blood (Shah and Mulla, 2007). Lymphatic filariasis was diagnosed by microscopic examination of thick blood films (TBF) collected between 8.30 pm to 12 midnight and evaluated the TropBio Og4C3 serum ELISA as a tool for detection of W. bancrofti microfilaria carriers using Dried Blood Spots (DBS) (Suman et al., 2007).

The major vectors for W. bancrofti are culicine mosquitoes in most urban and semiurban areas, anophelines in the more rural areas. Larvae in the blood of human hosts are ingested when the insect vectors feed. Within the vector, the microfilariae migrate to specific site and develop from first-stage larvae into infective third-stage larvae. The vector transmits the infective larvae into a human host when feeding. Mosquitoes deposit the larvae on the host skin adjacent to the puncture site and the third stage larval [L3] parasites migrate through the venous system and lungs to eventually take up residence in
the lymphatics Africa and Latin America (de Vries, 2005). The manifold increase in filariasis during last four decades reflects failure of filariasis control programs (Sabesan et al., 2000). Currently there may be up to 31 million microfilaraemics, 23 million cases of symptomatic filariasis, and about 473 million individuals potentially at risk of infection in the country. LF is a major impediment to socioeconomic development (estimated loss $1 billion per year) and is responsible for immense psychosocial suffering among the affected (ICMR, 2002).

Considerable progress has been made in diagnosis and treatment of filariasis in the last decade and new strategy for filariasis elimination aims at transmission control through mass drug administration (MDA) and at disease control through individual patient management. Annual single-dose or co-administration of two drugs (ivermectin + diethylcarbamazine (DEC) or albendazole) reduces blood microfilaria by 99% for a full year while a single dose of one drug (ivermectin or DEC) administered annually can result in 90% reduction. Field studies confirm that such reduction of microfilarial loads and prevalence can interrupt transmission (Ottesen et al., 1997). The 50th World Health Organisation (WHO) to identify the global elimination of lymphatic filariasis as a public health problem (WHO, 2004; Preface. Elimination of lymphatic filariasis, 2002). Mass drug administration of eliminate lymphatic filariasis is already in place in 32 of the 83 endemic countries (Ramaih and Das, 2004).

In India, annual mass drug administration with single dose of DEC was taken up as a pilot project covering 41 million population in 1996-97 and extended to 77 million population by 2002 (Govt. of India. Cited 2005 May 14) (http://www.namp.gov.in/)
The single dose mass therapy with DEC has been found to be as effective as 12 day therapy as a public intervention (Agrawal and Sashindran, 2006). Diethyl Carbamazine citrate (DEC) 6 mg/kg body wt./day in 3 divided doses for 21 day in each month for 3-12 months or more followed by for clinical relief and cure. Recurrence of manifestations was observed only in 0.2–0.5% of clinical filarial cases followed up in hospital study (Harinath and Reddy, 1997). The mass drug administration (MDA) is one of the strategies of eliminate LF in India. Eleven districts are endemic for the disease in Madhya Pradesh state of India, which conduct MDA activities annually. A mid-term evaluation was conducted with the objectives to review the progress of the single dose of DEC administration and to understand the functioning of the programme to recommended mid-term amendments. The mass drug implementation study noted that MDA is restricted to tablet distribution only and the major issues of implementation in compliance, health education, side effect and morbidity management, and the logistics were not being given due attention.

The implementation should be strengthened immediately in the MDA programme in India to achieve the goal of LF elimination by 2015 (Lahariya and Mishra, 2008). Side effects of DEC were reported to be minimum, transient and drug-specific in a MDA program in 2006 for elimination of lymphatic filariasis in endemic areas of Gujarat (Pradeep Kumar et al., 2008). The data collected during drug coverage surveys indicate that prevalence data collected by questionnaires tend to underestimate the morbidity prevalence compared with data collected by clinical examination. Due to the limited resources currently available for lymphatic filariasis in general and for morbidity programs in particular, it will be difficult for program managers to spend large amounts
of resources on population-based clinical surveys. For this reason, it was suggested to use existing clinical data from mapping or sentinel site activities to estimate LF morbidity prevalence (Mathieu et al., 2008).

Prevalence of LF was found to vary between the communities in Southeastern Nigeria in 2010; the socioeconomic status and the local environmental conditions of the communities could be responsible for these variations. Understanding differences in disease rates between men and women might be helpful in understanding the pathogenesis of the disease (Evans et al., 1993). Among 48.55% residents of ‘Officers Colony’ of Andhra Pradesh Paper Mill checked, mf rate was zero. However, lymphedema was found in seven elderly persons (disease rate 3.23%), which vary with our past findings in 2007 (Mukhopadhyay et al., 2007a, b). Diseased persons only consumed DEC tablets. Man-mosquito contact in ‘Officers Colony’ was found to be very low (MHD of *C. quinquefasciatus* was only 1.5) due to the reason that doors and windows of houses were fitted with wire mesh to prevent entry of insects, underground drainage and 64.52% residents were using mosquito repellents at night; that was one of the reasons of zero mf rate in Andhra Pradesh Paper Mill ‘Officers Colony’ (Mukhopadhyay, 2010).

Lymphatic filariasis occurs in individuals of all ages and both sexes but prevails in those of low socioeconomic status (Ottesen et al., 1997). As the chronic manifestations of lymphatic filariasis appear most frequently later in life, clinical and pathological investigations have focused on the adult population. The study of Sherchand et al., (2003) indicates that the prevalence of chronic forms of lymphatic filariasis is age-
dependent in both sexes, but generally higher in males that in females. Of the 81 consecutive lymphedema cases assessed, 40% in grade-I, 55% in grade-II, 77.3% in grade-III and 94.7% in grade-IV lymphedema cases had functional limitations either in joint movements or power of muscles or both. The effective loss of locomotor function (combined loss of joint movement and power of muscles in %) increased with stage of lymphedema (grade-I-4.3+7.4, grade-II-7.0+8.4, grade-III-15.4+14.8 and grade IV-33.3+22.8). The degree of loss varied significantly between the grades (P<0.0001) (Das et al., 2008). Lower limb lymphedema is an important and frequently observed clinical manifestation of lymphatic filariasis both in males and females (Michael et al., 1996 and WHO, 2000). There is an increase in the frequency of episodic attacks of acute adenolymphangitis (ADL) with progression of lymphedema from early reversible stage to irreversible and complicated stages (Pani et al., 1995; Shenoy et al., 1998) leading to physical suffering, permanent disability, loss of productivity and economic loss (Ramu et al., 1996; Ramaiah et al., 1997 and Ramaiah et al., 2000). Myopathies in the forms of myositis, myofibrositis are common features in oedematous legs (Norseman et al., 1992; Sundaray et al., 1992). Involvements of joints like arthritis and arthropathies are known to be of filarial aetiology (WHO, 1992). Accumulation of fluid, involvement of joints and muscles contribute to the permanent loss of locomotor function in these cases (Das et al., 2008).

Repeated filarial attacks lead to obstruction of lymph flow resulting in rupture of dilated lymphatic into urinary system. Prolonged chyluria results in loss of weight and subcutaneous fat, hypoprotenemia, lymphopenia and anemia. Initially medical treatment should be tried in every case, which consists of dietary modification, antifilarial drugs,
bed rest and high amount of fluid intake (Ramaiah et al., 2003). Microfilaria of *W. bancrofti* were detected in the pleural fluid on cytological examination and treatment with diethylcarbamazine cleared the pleural effusion in patients of Baroda (Marathe et al., 2003). Control or elimination of LF using annual MDA is one of the cheapest and most beneficial disease control strategy in the annals of public health history (Ramaiah and Das, 2004). LF is a leading cause of chronic disability worldwide; an estimated 120 million persons are infected with the filarial parasites that cause the disease and an estimated 40 million persons suffer from chronic clinical manifestations, primarily lymphedema and hydrocele (Addiss, 2005). LF causes physical disability, psychological despair, social isolation and loss of economic productivity to the tune of about 1.5 billion dollars annually in India alone. The global elimination of LF programme has been launched in many countries. The entire population at risk in the endemic areas is to be treated with annual single dose of filaricidal drug combination of albendazole and DEC for 4-5 years to cover the life span of the adult filarial worms (Das, 2005).

The most significant and noteworthy involvement of the lymphatic system is seen in the Glandular Fever Syndrome and in Lymphatic filariasis (Melrose and Goldsmid, 2005). *W. bancrofti* was found to be widely prevalent in Puri district with certain pockets of *B. malayi* while *W. bancrofti* was the only species in Ganjam district of Orissa. The microfilaraemia (mf) rate was found to be 9.5 and 11.1 per cent; and circulating filarial antigenaemia (CFA) was 16.8 and 17.8 per cent in Puri and Ganjam respectively. The geometric mean intensity (GMI) of mf per ml of blood among positive individuals was 387 in puri and 454 in Ganjam. The overall disease rate in Puri was 7.9 and 8.9 per cent in Ganjam. The prevalence of chronic manifestations was found to be significantly
higher (P<0.001) than the acute manifestations in both the districts. The prevalence of geo-helminthiases was 31.8 per cent in Puri and 42.1 per cent in Ganjam; and the heavy infection was found to be significantly higher (P<0.001) in Ganjam compared to Puri district (Chhotray et al., 2005). During November 2004, Singh et al., (2006) a lymphatic filariasis survey was carried out in seven randomly selected villages from four PHCs of Patna district examined 1878 night blood smears (NBS); 117 were found positive for *W. bancrofti* infection (mf rate 6.2%). Microfilaria carriers were detected from all surveyed villages. In all areas prevalence of microfilaria generally increased with age to maximum 15-34 years and then decline within most age-groups. More males (6.4%) were affected than the females (5.8%). All microfilaria (mf) carriers were residents of Patna district. Over all diseases rate was 9.1%. Out of 171 diseased individuals, 121 persons were having hydrocele (6.4%). Disease rate was higher in males (12.0%) than females (4.1%). The mean mf density was 11.7. There was no significant difference of mean mf density in males and females. Vector density ranged from 205 to 780 per ten man hours. Lymphatic filariasis infection is first acquired mostly during childhood. It is also known that the early pathology of this disease demonstrated even in children, namely the dilation of lymph vessels, tends to be permanent even with treatment (Shenoy, 2006). A 21 year old man, resident in a filariasis endemic region, presented with multiple matted lymph nodes with cystic areas forming a large mass in his left axilla (Basu et al., 2006).

A survey on 26 villages showed the mf rate to vary from 6.4% to 17.8%. The disease rate ranged from 1.9% to 10% and total infection rate from 8.2% to 26.4%. The median microfilaraemia density among positives was 10% and 90% of persons had density below 60% and 10% above this level. The mf rate among those who never used
bednets while sleeping was found to be 11.8%, 15.7% higher than 10.2% among those who ever used bednets (8.7% in regular users and 10.7% among irregular users) to protect from mosquitoes bites (p<0.05). The lymphatic disease was found to be 3.8%, 3.7% in males and 4.1% in females. Of the males, 16.3% had acute disease, 51.8% hydroceles of varying grades and 32% edema of different grades including elephantiasis. Of the females with lymphatic diseases, 25.6% acute disease, 62.8% edema including elephantiasis and 11.6% had mastitis (Anil Kumar et al., 2006). Goel et al., (2006) reported 14% of cases were positive for filarial antigen and antibody in hydrocoele patient serum, while 15% of cases were positive for filarial antigen and antibody in the serum of non-hydrocoele patients among 100 hospitalized patients in Govt. Medical College, Surat, Gujarat, India.

Protective immunity to filarial parasites has been demonstrated in both human and animal models (Zang et al., 2000). However, the mechanism of protective immune response in the humans is largely unknown. This information is especially important for developing an effective vaccine against lymphatic filariasis due to W. bancrofti because there are very limited animal models available (Anand et al., 2007). Doctors, both qualified and unqualified practitioners were not uniformly following DEC during schedule. Tendency of unnecessary usage of florocid injections and steroids was observed in both the groups of doctors (Patnaik et al., 2007). The Global Programme to Eliminate Lymphatic Filariasis (GPELF) has two major goals: to interrupt transmission of the parasite and to provide care for those who suffer the devastating clinical manifestations of the disease (morbidity control). This latter goal addresses three filariasis-related conditions: acute inflammatory episodes; lymphedema; and hydrocoele.
Research during the last decade has confirmed the importance of bacteria as a cause of acute inflammatory episodes in filariasis-endemic areas, known as acute dermatolymphangioadenitis (ADLA). Of the clinical manifestations targeted by the GPELF, hydrocele has been the focus of the least attention (Addiss and Brady, 2007). The delivery-strategy of health information and Diethylcarbamazine (DEC) drug to the urban community using the AWWs could achieve relatively higher coverage and consumption than reported in other urban areas (Nandha *et al.*, 2007). On a survey of 7168 respondents, 1216 were from East Godavari district, 1108 from West Godavari, and 1596 from Visakhapatnam district, 1316 from Krishna district, and 1932 from Chittoor district. Out of 7168 respondents, 4636 (64.67%) of which 3006 (41.93%) respondents were from urban and 1630 (22.73%) from rural areas knew that filaria is a disease. Causative agent of LF, helminthes is known to only 1136 (15.84%) persons, of which 904 (12.61%) were from urban and 232 (3.23%) were from rural areas (Mukhopadhyay *et al.*, 2008). The importance of cytology in diagnosis of filariasis in lesions clinically anticipated to be of neoplastic and to review the cytomorphology of Bancroftian filaria and its association with neoplasm. This is a retrospective study was carried out in cytology department of Tribhuvan University Teaching Hospital. 14 cases of cytological specimen out of 4291 (0.3%) showed microfilaria; 12 cases were from FNAC from different sites and 2 cases were from pleural fluid. 2 cases showed ova in addition to microfilaria and one of them in addition showed fragment of adult worm. Microfilaria in 4 cases of FNAC and one case of pleural fluid were associated with malignant cells (Jha *et al.*, 2008).
A survey on 56 lymphoedema patients showed that there was no difference (P>0.05) between the proportion of patients attending government (37.5%) and private (44.3%) medical care facilities there was also no difference in the proportion of patients first consultations in private or government health care facilities. About 57.1% patients approaching governmental institutions opted for primary/secondary health care system. No particular sequential pattern of seeking health care was observed and the 56 study subjects followed 40 treatment-seeking routes by switching from one care provider to the other. The causes of not coming to the clinic for further check-up were ‘no acute attacks’ (30.4%), ‘reduction in oedema volume’ (21.7%), ‘advised treatment being taken at home’ (26.1%) and ‘loss of daily wages’ (21.7%) (Abidha et al., 2008). The DEC mass drug administration programme to eliminate lymphatic filariasis in Kerala was launched initially in Alappuzha and Kozhikode district in 1997 on a pilot basis and extended to all the 11 endemic districts from 2005 onwards. The reasons for noncompliance indicated that the community is not fully convinced about the programme (Showkath Ali et al., 2008). During March 2008, LF survey was carried out in 14 randomly selected villages (six primary health centres) and 4 Mohallas of Lucknow city. Out of 3,654 night blood smears (NBS) collected and examined, 209 were found positive for *W. bancrofti* (Microfilaria rate: 5.7%). Microfilaria (mf) carriers were detected from all surveyed villages and Mohallas. The age of these positive persons ranged from 6-70 in all areas, prevalence of microfilaraemia generally increased with age up to 21-30 years. Males (6.7%) were more affected than females (3.9%). All mf carriers were residents of Lucknow district. Overall disease rate was 4.7%. In all, 175 individuals had disease manifestations of LF. Out of 108 males, 81 had hydrocele (75%). Disease rate was
similar in males (4.7%) and females (4.8%). The mean mf density was 9.5 per 20 cmm blood, but no significant difference between males (9.4) and females (9.9). Vector density ranged from 150 to 810 per ten-man-hours. Infectivity and infection rates were 0.14% (Sukhvir Singh et al., 2009).

A community-based cross-sectional study conducted by faculty, trained medico-social workers and health educators of the Department of Community Medicine, Kasturba Medical College, Manipal, Karnataka within a week following MDA programme during September 2007 in Udupi district of Karnataka state showed that there is a need to strengthen the MDA programme planning and implementation in terms of creating awareness through appropriate media in the community (Ashwini Kumar et al., 2009). Prasanthi et al., (2009) reported the case of 33 years old man with severe dyspnoea and chest pain, referred from a private nursing home with a provisional diagnosis of unresolving pericarditis. Pericardial tap revealed massive pericardial effusion with actively motile microfilariae. No microfilariae (mf) were seen in the peripheral blood. Haemorrhagic effusion resolved completely with DEC. Though relatively uncommon, tropical diseases must always be considered in the etiological diagnosis of pericardial effusion. Careful screening of FNAC smears help in detecting microfilaria even in asymptomatic patients and thus play a significant role in recognition of the disease and institution of specific treatment (Mitra et al., 2009).

Communication exercises targeted at the areas with relatively low compliance and designed to improve perceptions of the benefits and usefulness of MDA against filariasis could be the key to a successful control programme (Aswathy et al., 2009). The study 78 clinically confirmed cases calculated a microfilarial rate of 6.9% and 1.65% in males and
females respectively. The microfilarial density among confirmed cases ranged from 3.1 to 10.6 per 20 cmm. Majority of the cases were males who worked in open filed and there was a lack of proper management of these cases at village level (Mishra and Bhadoriya, 2009). Kolte et al., (2010) did not find any case of microfilaria with secondary deposits.

The presence of microfilaria in association with the metastatic deposits is an incidental finding and that the patient was harboring sub-clinical filariasis when the tumor metastasized. No microfilariae were detected in the peripheral smears. This case illustrates the coexistence of microfilariae with secondary deposits of adenocarcinoma, which is a rare finding. This also highlights the importance of screening smears for parasites even in the absence of clinical symptoms, particularly in highly endemic areas. However, out of 3,428 night blood smears collected and examined 42, were found positive for *W. bancrofti*. Microfilaria (mf) carriers were detected from 5 surveyed villages and 5 urban localities of Singtam and Rangpoo with mf rate ranging from 0.5% to 4.2%. The mean mf density was 5.4 per 20 cmm blood. All mf carriers were residents of east district, Sikkim except two persons who were from Bihar. The detection of microfilaria in young children who had never moved from the area indicates probable indigenous transmission. Out of 15 surveyed areas LF disease was found in 11 areas with prevalence ranging from 0.4% to 7.0%. (Disease rate was 1.6%) (1.7% for Males & 1.4% for females). One local individual was found with lymphedema and also mf positive. Vector density ranged from 70 to 435 per ten-man-hours, sufficient from transmission of LF.712 female *C. quinquefasciatus* were dissected to detect the filarial infection and none was found positive (Singh et al., 2010).
The annual microfilaria (mf) survey for the year 2007 reports mf rate of 0.63% out of which 177 districts have rates<1% and 73 districts >1% (Srivastava and Dhillon, 2008 and Ranganath, 2010). In a cross-sectional study of rural Puducherry, of the 1282 individuals surveyed, 661 (51.6%) were females and 939 (73%) were literates. As per the guidelines, 1231 (96%) were eligible to receive DEC. This survey revealed that 938 (76.2%) of the 1231 eligible persons received DEC during the MDA (coverage rate) and 88.7% of them consumed it (compliance rate). The ‘Effective coverage rate’ which is a product of coverage rate and compliance rate, was 67.6% (95% CI: 65-70.2) (Mahalakshmy et al., 2010). Ray et al., (2011) interviewed a total of 166 (one from each household) respondents in a district of West Bengal, India. Majority were females (72.29%) and mostly (66.87%) in the age group of 18-45 years. In the 166 families out of 807 persons, 778 (96.41%) were eligible for anti-filarial drugs. Children under two years, pregnant women and severely ill persons were exclude. Out of 166 families, 109 families received drugs, and drug distributor did not visit the other families. In these 109 families, 46 persons did not receive drugs for various reasons. Drugs were received by 435 (55.91%) persons in those 109 families (total eligible 481). Drug distributor gave inappropriate doses to 7.9% persons due to fear of side effects or misclassification. In these families also, 9.56% persons refused the drug or drug distributor did not give the drug as they were suffering from various diseases.

Dharukaswami et al., (2012) reported that majority of beneficiaries of MDA programmes were at the age group of 15-60 years (72.3%) and male (53%). The overall coverage of MDA in Bidar district was 62.3%. Compliance among those who had received the tables was 60.4%. Coverage and compliance was more in rural areas compared to urban. The most common reason quoted for not consuming drugs was fear
of adverse effects (72.2%). The incidence of adverse events was 0.2%. Even though
75% of them were aware of the disease elephantiasis, only 45.4% had knowledge
regarding MDA programme. The knowledge of drug distributors towards MDA and
filariasis was found to be adequate. The prevalence of hydrocelectomy among the
hospitals and ZHC cases ranged from 59 (0.16%) to 121 (29.4%) and from 59 (0.16%) to
325 (12.9%), respectively; the frequency of hydrocelectomy cases showed an initial raise
with patient age, reaching a peak at the older age groups and then dropping thereafter
(Dogara et al., 2012). Age, education of family, type of house structure and awareness
about the filarial disease directly influenced the disease prevalence in a village of
Karimnagar District, Andhra Pradesh, India (Murty Upadhyayula et al., 2012).

Reasons to select Pedana for filarial study

Pedana municipality in Krishna district of Andhra Pradesh is having history of
vector borne diseases like Filariasis, Malaria, Dengue, Japanese encephalitis and
Chikungunya (Plate 1). Of all the vector borne diseases, filariasis is found to be a wide
spreaded epidemic disease in Pedana as nearly 15% of the Pedana population is at the
risk of filariasis. In Pedana municipality, some localities especially weavers colonies
including Harijanawada (S.C colony) (7th ward), Jaganadha Rao colony and
Thotammoola wavers colony (8th ward), Kaapula veedhi (11th ward), NTR Park (13th
ward), Agastheswarapuram I & II (14th ward), Indira Colony and Arava gudem (18th
ward), Dakshina telugu palem (19th ward), Kotha peta and High School (20th ward),
Rama Lakshmi weavers colony (21st ward) and Matam center and Sada siva lingeswara
weavers society (22nd ward) are endemic for the transmission of filariasis since long ago.
Filariasis is perennial in these localities. Heavy density of Culex larvae were recorded in
drains and ditches of Pedana (Plate 2, Fig.1, Fig.2 and Fig.3). People are facing lot of
socio-economic problems by filarial disease manifestation. Hence, a new vista has been opened to study the Immuno-diagnosis of Lymphatic Filariasis in Weavers Community of Pedana.

The present investigations are designed to study the following:

1. Survey on the prevalence of lymphatic filariasis in Weaver’s Community of Pedana (23 wards) with regard to age and sex.
2. To evaluate the incidence of filariasis in endemic areas by means of field survey to detect the mf density, mf rate, disease rate and endemicity in the community
3. Collection of blood samples from filarial positive patients during the study period
4. Analysis of blood samples for haemoglobin, RBC, WBC, platelets, lymphocytes, monocytes, granulocytes and eosinophils.
5. Analysis of serum AST, ALT, ALP, protein, albumin, globulin and albumin globulin ratio in the filarial positive patients.
6. Estimation of total serum IgA, IgG and IgM levels from filarial positive patients before and after treatment of filariasis.
7. Counting of lymphocytes, CD3, CD4, CD8 and CD4/CD8 ratio from the blood of filarial positive patients before and after treatment of disease.
8. To evaluate the effect of DEC (long term) along with hygiene measures and antibiotic therapy in the management of clinical filarial cases.