**Original article:**

# Total protein and fibrinogen variations before and after diethyl carbamazine(dec) treatment in filariasis

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**Abstract:**

Lymphatic filariasis is a disableing and disfiguring dieases effecting mankind since antiquity.This infection is prevalent in both urban and rural areas. In the present study effect of diethyl carbamazine before and after treatment for fialariasis has been observerd. We enrolled 48 patients with Micro Filaraemia(MF),50 patients Clinical Filaraemia(CF) and control 52 and counducted study in GGH Kakinada, Andhrapradesh ,India, as Kakinada and its surrounding areas are highly endemic for filareasis . We found there is no significant variations in total protein and fibrinogen levels of patients before and after the treatment of DEC , Hence it can be approved that this drug does not causes damage to the synthatic functions of the liver cells (hepatocytes).There are no reports on the status of serum proteins in filariasis. Hence the present study is under taken to estimate the levels of serum protein and plasma fibrinogen influence in the disease process, and the variations in these parameters before and after DEC treatment.

**Keywords:** Filiriasis, carbamazine

## Introduction:

Lymphoedema is a common clinical problem in India. This is endemic in many parts of our country. As lymphoedema is the commonst clinical manif-estation of filariasis, there exits a vast number of patients afflicted by this crippling disease. Repeated attacks of fever, lymphangitis and lymphadenitis are accompanied by progressive oedema of the limbs. This is associated with fibrosis and thickening of the skin resulting in the hideous looking limbs often called Elephantiasis[1, 2, 3].

Globally about 120 million people are affected with the disease of which one third live in India alone. This disease is caused by any one of the parasites

Wuchereria bancrofti, Brugia malayi, or Brugia timori. It is a disease of the poor and is prevalent in urban, peri urban and rural areas. The transmission is from man to man by mosquitoes of the genus Culex. In human beings the adult parasite live in the lymphatic system, producing millions of microfilaria which propagate the infection. The infection is usually acquired in childhood. Infection by B.timori does not occur in India[4].

The disease casused by Wuchreria bancrofti is often called bancroftian failariasis. Brugia malayi caues Malayan filariasis. The similar infection caused by Brugia malayi and brugia timori are grouped together as brugia filariasis. Bancroftian filariasis occurs around the world in the latitude between 41˚N and 30˚S, especially in Srilanka, India, Bangladesh, Burma, Thailand, Malaysia, China, The Philippines, Indonesia and less in the middle East, North and Central Africa, the Caribbean, central and south America, the Pacific islands. Malayan filarisis occurs in Burma, Thailand, Vietnam Korea Japan, Borneo, New Guinea. Brugia timori causes disease only in Indonesia.

In India, infection of filariasis have been recorded as early as 6$^{th}$ century B.C., by the famous Hindu Physician "Susruta" in his treatise "Susrutha Samhitha". Madhavakar(700 A.D) Described the signs and symptoms of the disease in his treatise "Madhava Nidhana" which holds good even today. As early as 500 BC, the laws of Manu stated that a priest should not marry a woman with a family history of tuberculosis, epilepsy, leprosy or elephantiasis. The famous sun temple Konark near Puri in Orissa (1300 AD) depicts a couple with hydrocele and elephantiasis. Thus this disease has been with us through the centuries

Filariasis is the first disease proved to be transmitted by insects [5,2] . Althogh lymphatic Filariasis has been identified as eradicable or potentially eradicable among the six infectious diseases by the international Task force for disease eradication, it is still a major health problem in many parts of the world including India[6].

According to the estimates made in 1995, globally, there are 1,100 million people are living in areas endemic for lymphatic filariasis and exposed to the risk of infection: and there are 120 million cases of filariasis, either having potent microfilaraemia or chronic filarial disease. LF is endemic in atleast 80 countries. Recent estimates have shown that out of the 25 states/union territories in India (before bifurcation of states of Bihar, Madya Pradesh and Uttar Pradesh), for which surveys were carried out, 22 were found endemic for filariasis, and nine states (Andhra pradesh, Bihar, Gujarat, Kerala, Maharastra, Orissa, Tamilnadu, Uttar Pradesh and West Bengal) contributed to about 95% of total burden of filariasis. A total of 289 districts in India were surveyed for filariasis until 1995; out of which 257 were found to be endemic. In India a total of 553 million people are at risk of infection and there are approximately 30 million people are estimated to be harboring Wuchereria bancrofti microfilariae. 21 million people with symptomatic filariasis and about 20 million suffer with chronic manifestations such as hydrocele (13 million) and lymphoedema (7 million). W. bancrofti is the predominant species accounting for about 98% of the national burden , widely distributed in 17 states and 6 union territories. B.malayi is restricted in distribution, with decreased trend. An overview of the traditional endemic foci shows concention of infection mainly around river basins, and eastern and western coastal parts of India[7,3].



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Filariasis is a chronic and debilitating disease caused by nematode parasite of the order "filaridea" commonly called filariasis. Different types of filarial infections including lymphatic filariasis are caused by Wuchereria bancrofti and Brugia malayi.Poor sector of the community are the predominant effe-cted group. Although never directly fatal but chronic infestation can lead to disability, disfigurement causing untold pain and misery.

In East Godavari District especially Kakinada and surrounding areas are highly endemic for filariasis. The aim of the present study is to compare the protein changes due to filarial infestation with the endemic normal group. There was no proper review in this aspect of the study. So the present study may give some facts about the protein influence in the prognostic aspect of the disease.

**Materials and Methods:**

For this study 48 patients of MF, 50 Patients of CF and 52 age & sex matched endemic controls(52 were selected.Blood samples were collected. All the patients were informed for consent. Plasma samples were collected and used for the estimation of total protein,albumin and fibrinogen.

1.ESTIMATION OF TOTAL PROTEINS BY BIURET METHOD, END POINT(on ERBA CHEM-7 Semi Auto Analyser)[8].

2.ESTIMATION OF ALBUMIN BY BCG DYE METHOD ,END POINT(on ERBA CHEM-7 Semi Auto Analyser)[8].

3.ESTIMATION OF PLASMA FIBRINOGEN BY PRECIPTATION METHOD (KING AND WOOTTON,1956) (on Coagulometer)

**Observation and Results:**

1. In the present study a total number of 150 individuals are included and they are placed into three different groups as summarized in Table-1. Among them 98 were filarial infected groups constituting of 48 microfila-raemics (32%) and 50 clinical filarial patients (33.3%). The patients were mianly from the o.p .of Regional Filarial Control Unit-Kakinada of East Godavari district in Andhrapradesh.

**TABLE 1 : DISTRIBUTION OF STUDY CASES IN TO DIFFERENT GROUPS OF FILARIASIS**

| Study Group | Number | Percent (%) |
|---|---|---|
| Microfillarial carrier (MF) | 48 | 32.0 |
| Clinical filarial patients(CL) | 50 | 33.3 |
| Endemic Normals(EN) | 52 | 34.7 |
| TOTAL | 150 | 100 |



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**2.** Age and sex wise distribution of all the study cases are shown in Table-2 & 3. Maxium number of individuals representing 58.3% of the total 48 cases of micro filaraemic cases were in the age group of 11-30 years. where as maximum number of individuals representing 50% of the total 50 cases of clinical filarial cases were in the age group of 31-50 years (Table-2).

**TABLE-2 DISTRIBUTION OF STUDY CASES ACCORDING TO AGE**

| AGE GROUP | TOTAL EXAMINED No.(%) | MICROFILARIAL CARRIERS No.(%) | CLINICAL FILARIAL CARRIERS No.(%) | ENDEMIC NORMALS No.(%) |
|---|---|---|---|---|
| 10 Yrs | 01(0.6) | 01 (2.1) | --- | --- |
| 11-30 Yrs | 49(32.7) | 28(58.3) | 06(12) | 15(28.8) |
| 31-50Yrs | 63(42) | 11(22.9) | 25(50) | 23(44.2) |
| ≥50 Yrs | 37(24.7) | 08(16.7) | 19(38) | 14(27) |
| **TOTAL** | **150(100)** | **48(100)** | **50(100)** | **52(100)** |

While male and female ratio was almost 1:2 in all the filarial cases, there were more females (32) than males (20)in the endemic normal group.(Table-3)

**TABLE-3 DISTRIBUTION OF STUDY CASES ACCORDING TO SEX**

| Study Group | MALE( %) | FEMALE(%) | TOTAL (%) |
|---|---|---|---|
| Microfilaraeemics (MF) | 16(33.3%) | 32(66.7%) | 48(100%) |
| Clinical filariasis(CL) | 12(24%) | 38(76%) | 50(100%) |
| Endamic Normals(EN) | 20(338.5%) | 32(61.5%) | 52(100%) |
| TOTAL | 48(32%) | 102(68%) | 150(100%) |



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**3.** Serum Albumin levels were significantly low, where as Globulins were increased in Clinical filarial cases. Plasma Fibrinogen levels in Clinical filariais were higher when compared to endemic normals(Table-4).

**TABLE-4 SERUM PARAMETERS IN ENDEMIC NORMAL AND CLINICAL FILARIASIS**

| S.No | Parameters | Endemicnormal N=52 mean±SD | Clinical Filariasis Cases N=50 mean±SD | 'Z' Value | 'P' Value |
|---|---|---|---|---|---|
| 1. | Total Protein g/dl | 6.9±0.6 | 7.0±0.7 | 0.77 | NS |
| 2. | Albumin g/dl | 4.0±0.2 | 3.7±0.4 | 4.76 | <0.001 |
| 3. | Globulin g/dl | 3.0±0.2 | 3.3±0.6 | 7.84 | <0.001 |
| 4. | Fibrinogen mg/dl | 270±40.3 | 354±167 | 3.46 | <0.001 |

**4.** Serum total protein levels were normal, but serum albumin levels in microfilaraemic cases were significantly low, Globulin levels were not elevated in microfilaraemic cases .Plasma Fibrinogen levels in microfilaraemic cases were low when compared to endemic normals(Table-5).

**TABLE-5 SERUM PARAMETERS IN ENDEMIC NORMAL AND MICROFILARAEMIC CASES**

**5.** Parameters of endemic normal and total filarial cases were compared and summarized.s Serum protein levels were normal in total filarial cases. Plasma fibrinogen levels were higher in total filarial cases(Table-6).

| S.No | Parameters | Endemicnormal N=52,mean±SD | Micro Filaraemic Cases N=48, mean±SD | 'Z' Value | 'P' Value |
|---|---|---|---|---|---|
| 1. | Total Protein g/dl | 6.9±0.6 | 6.9±0.65 | 0 | NS |
| 2. | Albumin g/dl | 4.0±0.2 | 3.7±0.7 | 2.86 | <0.002 |
| 3. | Globulin g/dl | 3.0±0.2 | 3.2±0.6 | 2.199 | NS |
| 4. | Fibrinogen mg/dl | 270±40.3 | 187±11.3 | 4.8 | NS |



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**TABLE-6 SERUM PARAMETERS IN ENDEMIC NORMAL AND TOTAL FILARIAL CASES**

| S.No | Parameter | Endemicnormal N=52 Mean ± SD | Total Filarial cases N=98 Mean ±SD | 'Z' value | 'P' Value |
|---|---|---|---|---|---|
| 1 | Total Protein g/dl | 6.9 ± 0.6 | 7.0 ± 0.7 | 0.971 | NS |
| 2 | Albumin g/dl | 4.0 ± 0.2 | 3.7 ± 0.6 | 4.5 | <0.001 |
| 3 | Globulin g/dl | 3.0 ± 0.2 | 3.3 ± 0.6 | 10.5 | <0.001 |
| 4 | Fibrinogen mg/dl | 270 ± 40.3 | 303 ± 27.9 | 1.149 | NS |

**6.** There were no significant changes in total protein,Albumin,Globulin & Fibrinogen levels before and after treatment with DEC(Table-7)

**TABLE-7 STATISTICAL DATA OF THE FILARIAL CASES BEFORE AND AFTER TREATMENT WITH DEC**

| S.No | Parameter | BEFORE TREATMENT n=8 mean ± SD | AFTER TREATMENT n=8 mean ± SD | 'T'value | 'P' Value |
|---|---|---|---|---|---|
| 1 | Total Protein g/dl | 7.6±0.70 | 7.3±0.30 | 1.114 | NS |
| 2 | Albumin g/dl | 4.0±2.0 | 4.2±0.25. | 0.77 | NS |
| 3 | Globulin g/dl | 3.6±0.50 | 3.2±0.35 | 1.854 | NS |
| 4 | Fibrinogen mg/dl | 205±77.0 | 170±50.0 | 1.08 | NS |



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**Discussion:**

The normal function of lymphatics is to return proteins, lipidis and water from the interstitium to the intravascular space. In a diseased state, the lymphatic transport capacity is reduced . This casuses the normal volume of interstitial fluid formation to exceed the rate of lymphatic return, resulting in the stagnation of high molecular weight proteins in the interstitium. It usally occurs after flow has been reduced by 80% or more. The result, was compared to other forms of edema that have much lower concentrations of protein, is high protein edema, or lymphedema with protein concentrations of 1.0 – 5.5 gm/ml .

There are no reports on the status of serum proteins in filariasis. Hence the present study is undertaken to estimate the levels of serum protein and plasma fibrinogen influence in the disease process,and the variations in these parameters before and after Diethyl carbamazine citrate(DEC) treatment.

A total of 150 individuals belongs to different groups namely clinical filarasis , microfilaraemic and endemic normals were included in the present study. The main function of lymph was transportation of serum albumin and fibrinogen from the liver and immunoglobulins , lymphocytes from lymph nodes to the plasma . Lymph also transports lipoprotein as chylomicrons from the small intestine. Lymph redistributes the extra celluar fluid and prevents its stagnation. These may be due to multiple reasons such as the patients poor living conditions in which poor diet may be one factor or the excretion of chyle In urine.

Serum total protein levels were normal in all the filarial cases. But the albumin to globulin ratio was alterd. Serum albumin levels in clinical filariasis ($p<0.001$), & in micro filaraemic cases($p<0.002$) were significantly low campared to endemic normals suggesting albumin loss may be due to microscopic or occationally macroscopic haematuria and proteinuria. Same findings also reported by Freedman et.al.,(1994) and Dryer at.al.,(1992)[6]. Globulins in clinical filariasis ($p<0.001$) was increased where as in microfilaraemic cases the elevation in the level was not statistically significant compared to endemic normals , suggested that filarial antibodies and circulating antigens were present in chronic cases like clinical filarial cases, where as in the new microfilaraemic cases were not able to develop the antibodies within short period of infection, so globulins were not elevated. Fibrinogen levels in clinical filarasis ($p<0.001$) and in microfilaraemic cases ($p<0.001$) were high compared to endemic normals.

In the present study the influence of Diethylcarbamazine citrate was tested in a small group of patients.. Chemotherapy with DEC is one of the main stratagies used in the control of lymphatic filariasis aiming at reduction in morbidity and filarial infection. Treatment with DEC resulted in clearing microfilariae for all the study samples.

The sample group is mainly from microfilaraemic patients, all were under the DEC treatment as per NATIONAL FILARIAL CONTROL PROGR-AMME GUIDELINES .

There was no significant change in serum total proteins after DEC treatment in the present study. As the sample group was small it may not be useful to come to a reasonable conclusion in this group. However further studies are required with large number of samples to evaluate the influence of DEC in protein metabolism.



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**Conclusion:**

There was no statistically significant changes in the total protein and fibrinogen levels in microfilaraemic and clinical filaraemic cases after the treatment with Diethyl carbamazapine citrate (DEC) .As the study group was small, it require further study to know the influence of DEC on protein metabolism.

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