

3. Clinical Epidemiology and Chemotherapy

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3.1. Operational feasibility and impact of co-administration of albendazole and DEC in controlling LF (S.P. Pani, K. Krishnamoorthy, B. Nanda, S. Sabesan, in collaboration with NICD, New Delhi, DPH, Kerala & Tamilnadu; National Co-ordinator for ICMR Task Force Project: P.K.Das; EM 9907 CEC; Duration: 6 years, Sep 2000 - Oct 2006)

This study was initiated in November 2000. The rationale, objectives and the design of the study have been described in the earlier annual reports of the centre. During the year 2004 the fourth round of annual mass drug administration (MDA) was carried out in two districts (DEC: Thanjavur; & DEC+Albendazole: Thanjavur) of Tamil Nadu, covering a target population of about 4.1 million. The coverage of drug distribution/consumption, adverse reactions and report of deworming were assessed by interviewing over 2000 individuals from each district (Table 3.1a). Over 85% of the population in both districts had received DEC tablets. However, in the district under co-administration, only 1.4% reported having received both DEC and Albendazole. The drug consumption was 56% and 40% in the DEC and the co-administration districts respectively (significantly lower compared to the previous round of MDA -- Fig. 3.1). The reporting by the media of deaths due to MDA in Tiruchi district was the main reason for non-consumption of the drug (Table 3.2). In the DEC and co-administration districts, adverse reaction was reported by 18% and 19% of the population respectively (Table

3.1a). However, this was mainly due to increase in non-specific reactions (Table 3.3). Deworming was reported by about 1% of the population in both the districts (Table 3.1a). In Kerala, due to adverse public opinion, the State Government cancelled the fourth round of drug distribution in the year 2004.

The impact of three rounds of MDA was assessed in all the four intervention districts (two each in Tamil Nadu and Kerala). Screening of about 20,000 persons for microfilaraemia (mf) and 3600 for circulating filarial antigen (CFA) by ICT card test (Tables 3.1a & 3.1b) showed a significant reduction in mf prevalence after three rounds of MDA in both districts in Tamil Nadu. However, the relative change between the arms was not significant (Table 3.4; Fig. 3.2). Analysis of co-variance by considering baseline mf prevalence and consumption as variables showed no significant difference in mf prevalence between the arms after three rounds of MDA. The post mf prevalence adjusted to the base mf prevalence of 4.22% and consumption of 67.9% showed 3.0% and 1.6% respectively in DEC alone and DEC+alb areas (Table 3.4 & Fig. 3.2). This showed that the reduction in the co-administration arm was higher by 33% compared to the DEC arm. This, although not statistically significant by a standard test, suggests the possible advantage of co-administration. The change in mf prevalence after three rounds of MDA in both districts of Kerala was marginal (Table 3.1a). Similarly, the prevalence of CFA in both districts of Tamil Nadu and the DEC district in Kerala was

reduced significantly after three rounds of MDA (Figs. 3.3a & 3.3b) compared to baseline. The difference in relative change in CFA prevalence between the DEC and the co-administration district in Tamil Nadu was significantly different. Persistence of antigenaemia prevalence in the age class 1-5 years in both the arms indicates that transmission was not totally interrupted. The reduction in overall prevalence was 37% in DEC+alb arm, while it was 5% in DEC arm. However, the overall reduction was significant only in the district with DEC+Albendazole. This suggests that DEC+alb has an edge over DEC alone in reducing the filarial worm burden. Geo-

helminth parasite continued to show reduction in prevalence in both DEC and DEC+alb districts in Kerala and DEC+alb district in Tamil Nadu (Tables 3.1a & 3.1b). Cost analysis for the two study districts for the first two rounds for drug distribution in Tamil Nadu showed that the cost/person distributed was Rs.1.41 and the cost/person consumed was Rs.2.02 for the DEC+alb district in the second round.

This progress and the results of the project were reviewed extensively (i) by the National Task Force on LF Elimination and the ICMR Filariasis Task Force (along with national & international

Table 3.1a. Summary of the results on different parameters monitored for evaluation of MDA in Tamil Nadu

Arm	DEC - (TVM)				DEC+ALBEN - (Tanjore)			
Year & Round	2001 1st	2002 2nd	2003 3rd	2004 4th	2001 1st	2002 2nd	2003 3rd	2004 4th
Sample	2587	2550	2542	2243	2214	2183	2241	2196
Distribution (%)	65.06	88.35	82.79	86.6	59.62	86.53	82.88	DEC-89.3; Alb- 1.4%
Consumption (%)	53.58	78.16	63.14	56.8	41.19	60.24	55.01	40.3
Side reaction (%)	4.40	11.05	10.02	17.8	7.65	11.86	6.98	18.9
De worming (%)	0.48	0.89	2.00	0.71	3.30	1.06	2.00	1.19
Impact evaluation								
Filariasis								
Infection	Base line	Post 1 st	Post 2 nd	Post 3 rd (2004)	Base line	Post 1 st	Post 2 nd	Post 3 rd (2004)
Mf survey - sample	3404	4566	4189	4497	5799	5264	5109	5777
Mf rate (%)	3.97	3.59	2.47	2.07	2.59	2.7	1.37	1.19
Mf intensity	1.22	0.62	0.26	0.3	0.29	0.32	0.13	0.09
Antigenaemia survey -sample	1187	-*	-	1200	1189	-	-	1200
Antigenaemia rate (%)	15.80	-	-	12.3	19.60	-	-	17.8
Disease survey - sample	1071	-	-	-	1200	-	-	-
Lymphoedema	0.3	-	-	-	0.66	-	-	-
Hydrocele	8.6	-	-	-	8.41	-	-	-
Geo-helminths Sample size	400	400	400	400	400	400	400	400
Prevalence								
Any worm	16.25	15.25	16.60	8.0	49.25	26.75	22.86	14.0
Round worm	1.75	1.25	0.50	0.5	1.25	0.00	0.00	0.0
Hook worm	9.25	8.00	12.00	5.5	44.86	25.75	21.71	13.5
Whip worm	6.00	7.25	3.50	3.5	9.77	2.75	2.86	0.5

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-* Not done as per protocol

Table 3.1b. Summary of the results on different parameters monitored for evaluation of MDA in Kerala

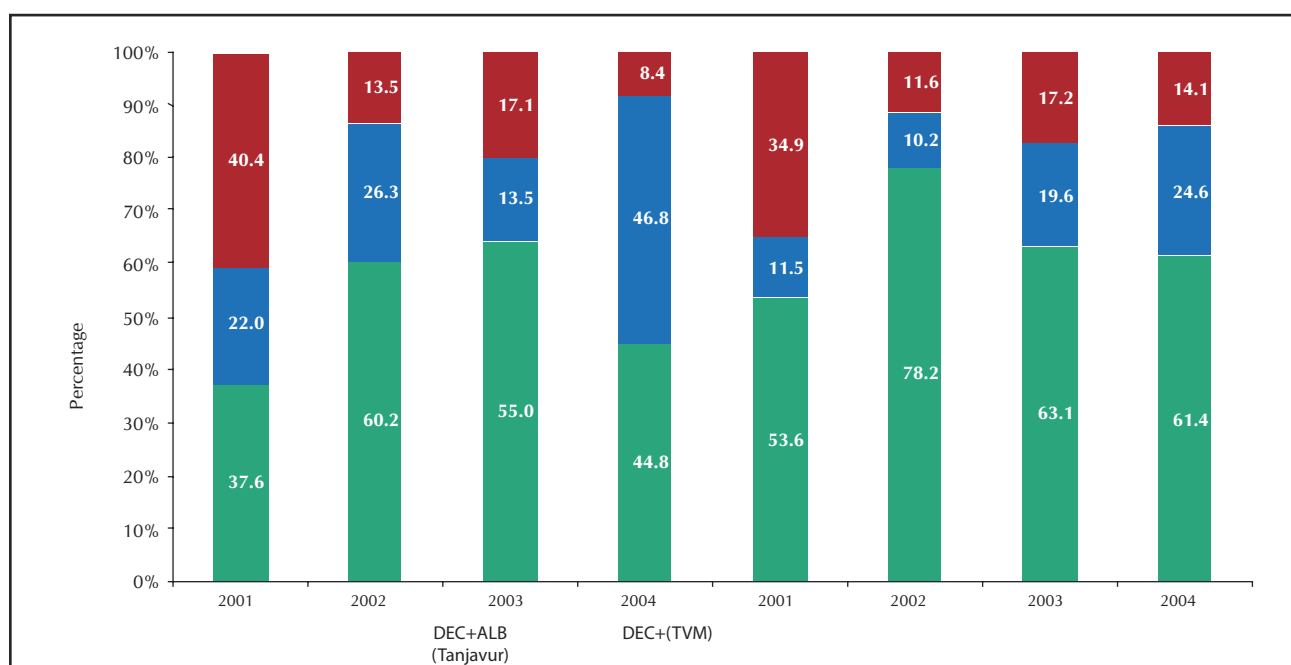
Impact evaluation	DEC - (Kozhicode)				DEC+ALBEN - (Alapuzha)			
	Base line (2001)	Post 1 st (2002)	Post 2 nd (2003)	Post 3 rd (2004)	Base line (2001)	Post 1 st (2002)	Post 2 nd (2003)	Post 3 rd (2004)
Filariasis								
(a) Infection								
Mf survey - sample	4609	4850	4870	8213	2309	2997	3490	3342
Mf rate (%)	0.90	0.72	0.87	1.21	1.00	1.00	0.63	0.51
Mf intensity	8.70	5.57	11.74	8.7	4.50	1.53	1.70	1.76
Antigenaemia survey Sample	1175	-*	-	1192	1174	-	-	ND
Antigeneamia rate (%)	6.20	-	-	2.6	0.00	-	-	-
(b) Disease - sample								
Lymphoedema	4609	-	-	-	2335	-	-	-
Hydrocele	0.82	-	-	-	2.56	-	-	-
Geo-helminths								
Sample size	400	419	324	508	400	499	461	399
Prevalence								
Any worm	35.00	7.64	15.70	16.5	19.40	10.80	4.6	8.2
Round worm	26.0	4.53	10.20	14.8	10.7	5.8	3.50	6.0
Hook worm	0.7	0.0	0.01	0.0	3.6	0.0	0.0	0.0
Whip worm	32.0	4.77	9.26	8.9	12.3	7.6	1.5	3.5

* Not undertaken as per protocol

experts) at ICMR Headquarters, New Delhi on 28th Feb 2004; (ii) by an expert group at TRC, Chennai on 24th and 25th February, and 13th August, 2004; and (iii) at a review meeting on

LF Elimination at National Vector Borne Disease Control Programme (NVBDCP), New Delhi on 18th November, 2004. The progress and results of the study were jointly reviewed by scientists

Fig. 3.1. Pattern of drug distribution and consumption in the two districts of Tamil Nadu



of VCRC and DPH, Tamil Nadu at DPH office, Chennai on 15th December 2004 and it was decided that MDA with DEC in Thanjavur district and co-administration of DEC with Albendazole in Thanjavur district will be continued in 2005.

3.2. Development of rapid & cost-effective method for delimiting endemic areas of bancroftian filariasis (L.K.Das, P.Vanamail, G.Vijayalakshmi; WHO/TDR ID A00602; EM 2009 CEC; Duration: 3 years, Apr 2002-Mar 2005)

Table 3.2. Reasons for non-consumption of drug reported during 2004 (4th round) compared to the previous year in the two districts of Tamil Nadu

	DEC (Thiruvanamalai)		DEC+ALB (Thanjavur)	
	2003-3rd round	2004-4th round	2003-3rd round	2004-4th round
Number surveyed	2896	2221	2241	2192
Not received	438	253	418	234
Received but not consumed	561	679	729	1070
Reasons for not swallowing (% out of received and not consumed)				
Out of station	12.30	4.42	13.31	4.21
Forgotten	38.68	14.14	27.52	5.33
Fear about the medicine	0.36	5.15	3.06	9.25
No instruction received	0.53	0.44	5.04	1.96
Fear of side reaction	27.45	27.98	34.35	16.07
Not interested	1.07	3.09	11.87	1.78
Old age/sickness	0.36	6.04	0.36	13.36
Under treatment for other complaints	10.70	0.44	12.59	0.65
Pregnant/lactating	4.99	1.62	3.06	1.03
Unaware of the programme	1.25	0.00	0.18	0.00
Not having the disease	0.89	0.15	0.00	0.09
Sickness (fever)	0.00	0.00	0.00	4.02
Refusal	0.00	0.00	0.00	0.00
Alcoholic	0.18	0.00	0.36	0.00
Lost the tablet	1.25	0.44	1.08	1.40
Others (TV News on "death")	0.00	36.23	0.00	40.84

Fig. 3.2. Pattern of drug distribution and consumption in the two districts of Tamil Nadu

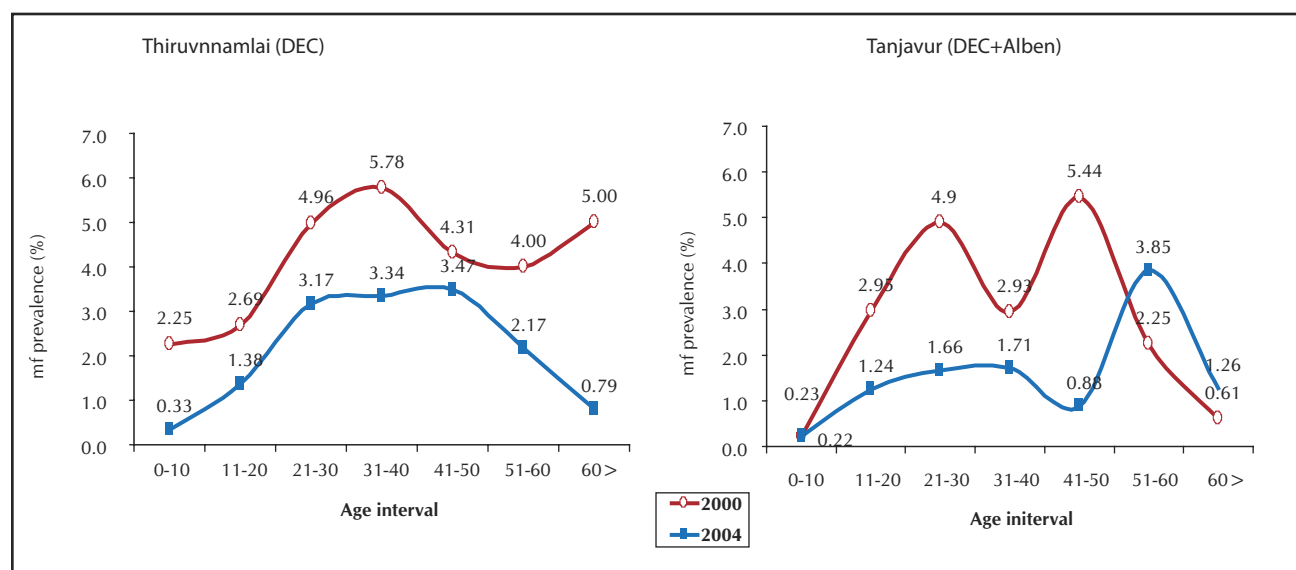


Table 3.3. Adverse reactions reported during 2004 (4th round) compared to the previous year in the two districts of Tamil Nadu

	2001		2002		2003		2004	
District	TVM	Tanjore	TVM	Tanjore	TVM	Tanjore	TVM	Tanjore
Drug			DEC	DEC+ALBEN	DEC	DEC+ALBEN	DEC	DEC+ALBEN
Number consumed	724	498	1008	498	896	498	667	492
Filaria specific	% out of consumed							
1. Fever	0.97	3.21	1.29	1.41	0.11	0.6	1.05	2.24
2. Headache	0.28	1	0.5	1.41	1	2.41	0.3	1.02
3. Myalgia	0	0	0	0	0	0	0.3	0.41
4 Swelling of limb	0	0	0	0	0	0	0	0
5. Swelling of nodes	0	0	0	0	0	0	0	0
6. Scrotal reaction	0	0	0.1	0.2	0	0	0	0
7. Presence of nodule	0	0	0	0	0	0	0	0
Subtotal	1.24	4.22	1.88	3.01	1.12	3.01	1.65	3.66
Geo-specific	0	0	0	0	0	0	0	0
1. Nausea	0	0.2	0.1	2.41	0.11	0.2	0.6	1.22
2. Vomiting	0.14	0.6	0.2	1.41	0.22	0.4	0.3	2.03
3. Abd. Pain	0	0	0	0	0	0	0.3	0.2
4. Diarrhea	0	0.6	0.2	0.8	0.22	0.8	0.75	1.02
Subtotal	0.14	1.41	0.5	4.62	0.56	1.41	1.95	4.47
Others	0	0	0	0	0	0	0	0
1. Dizziness	2.9	1.41	5.95	4.82	7.03	4.22	13.94	10.37
2. Fatigue	0.14	0.4	0	5.22	0.22	0.2	0.3	0.41
3. Rash	0	0	0	1	0	0.4	0	0
4. Loss of sleep	0	0	0	0	0	0	0	0
5. Chest pain	0	0	0	0	0	0	0	0
6. Eye irritation	0	0	0	0	0	0	0	0
Subtotal	3.04	1.81	5.95	11.04	7.25	4.82	14.24	10.77
Grand Total	4.42	7.43	8.33	18.67	8.93	9.24	17.84	18.9

Table 3.4: Comparison of Mf prevalence in sentinel sites of the two districts of Tamil Nadu

Drug & District	Sample		Mf rate (%)	c2 (AGE STRATIFIED)	p value	Mean mfc	t-value	p value
DEC (Thiruvannamalai)	2001	2201	3.86			0.94		
	2002	2201	3.50	0.62	0.43	0.64	1.26	0.21
	2003	2329	2.83	4.29	0.038	0.30	2.47	0.01
	2004	2380	2.23	10.46	0.001	0.27	2.57	0.01
DEC+albendazole (Thanjavur)	2001	2894	3.04			0.38		
	2002	3029	2.97	0.11	0.74	0.31	0.60	0.54
	2003	3016	1.69	11.26	<0.05	0.18	2.07	0.04
	2004	3030	1.39	18.12	<0.05	0.11	3.18	0.00

Fig. 3.3a. Change in age specific prevalence of filarial antigen prevalence (ICT test) between baseline and post 3rd round MDA in the two districts of Tamil Nadu

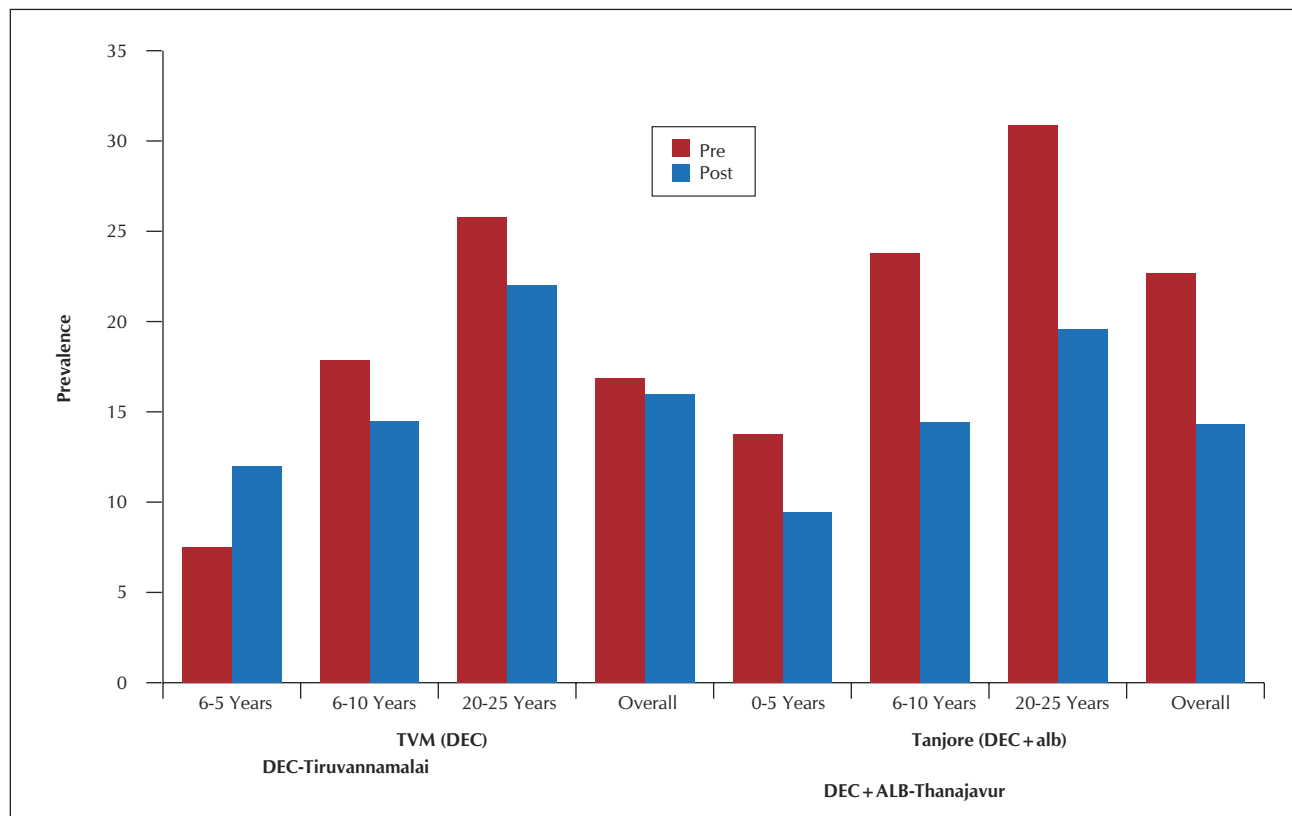
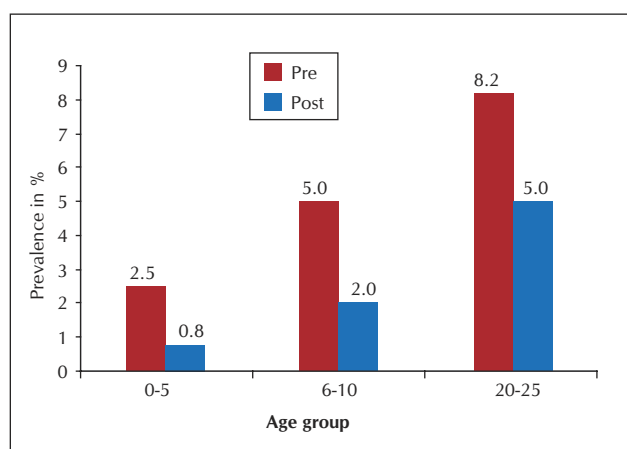


Fig 3.3b. Change in age specific prevalence of filarial antigen prevalence (ICT test) between baseline and post 3rd round MDA in DEC -- Kozhikode district of Kerala



The conventional night blood surveys for detection of Mf and immuno-chromatographic card tests are costly, cumbersome, inadequate and insensitive. Antigenaemia detection can overcome many of these shortcomings. The objective of the study was to determine the optimal pool size of filter

paper blood samples to detect circulating filarial antigenaemia (CFA) to identify communities positive for filarial infection.

- Filter paper blood samples were assayed for CFA using Og4C3 ELISA test kit with pools of 5, 10, 15, 20 and 25 filter papers for different levels of Mf prevalence, since pool size could be a function of Mf prevalence.
- There are some inherent problems with the Og4C3 ELISA test, as it did not detect all mf carriers as positive and it requires standardization for every batch.
- Preliminary results suggest that a minimum pool size of 20 filter papers is required for detecting a single positive sample, when Mf prevalence is below 10%.

3.3. Loco-motor disability in filarial lymphoedema patients (L.K.Das, G.S.Reddy, Supriya Vinod, P.Vanamail; IM 0103 CEC; Duration: 6 months, Sep 2003 – Feb 2004)

The objective of the study was to develop a method for assessing the degree of physical disability in filarial lymphoedema patients. Since the procedures recommended by Government of India are not specific for filariasis as they are for leprosy, poliomyelitis, etc., it was suitably modified. A scoring system was developed for additional values peculiar to filarial lymphoedema cases. The assessment of disability was done with movement of the joints and power of muscles, and scores for disfigurement, accumulation of fluid and non-traumatic pain.

During the period of reporting, inter-observer variation for movement of the joints (Table 3.5) and power of muscles (Table 3.6) was studied and there was no significant inter-observer variation in the assessment results.

The method developed can be used for assessing physical disability in filarial lymphoedema cases. This will enable not only the type of rehabilitation required, but also help in deciding issues such as eligibility for compensation, etc.

Table 3.5. Inter-observer variations in assessing the joint movement component (mean+/- SD, % loss)

Lymphoedema grade	Number of cases	% loss \pm SD by the 4 observers				P value#
		1	2	3	4	
I	7	0	0	0	0	
II	16	1.82 \pm 7.29	1.83 \pm 7.31	2.01 \pm 7.51	1.01 \pm 4.05	0.05
III	14	6.09 \pm 12.86	4.67 \pm 8.61	7.11 \pm 11.20	4.84 \pm 8.01	0.92
IV	9	12.81 \pm 17.49	10.06 \pm 10.79	6.90 \pm 13.84	5.25 \pm 6.02	0.28

Freedman Non-parametric test

Table 3.6. Inter-observer variations in assessing the muscle power component (mean+/- SD, % loss)

Lymphoedema grade	Number of cases	% loss \pm SD by the 4 observers				P value#
		1	2	3	4	
I	7	1.028 \pm 2.721	0	0	0	0.39
II	16	7.16 \pm 13.46	7.12 \pm 13.74	4.09 \pm 15.27	2.02 \pm 8.10	0.06
III	14	18.86 \pm 23.18	13.05 \pm 16.41	15.32 \pm 22.93	10.41 \pm 16.42	0.20
IV	9	26.14 \pm 22.22	19.15 \pm 18.16	13.80 \pm 27.69	10.50 \pm 12.05	0.39

Freedman non-parametric test