



Original Article

Geographical variation in the clinical presentation of endomyocardial fibrosis in India?



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ABSTRACT

Objectives: To compare the clinical presentation, clinical profile and survival of two groups of endomyocardial fibrosis patients.

Methods: The study was a prospective cohort study, or a prospective case series, comparing all consecutive echocardiographically proven patients with endomyocardial fibrosis seen in Medical College Trivandrum with the patients seen in Medical College Hospital, Alappuzha (Alleppey) (or TD Medical College). In all patients the clinical details like age, sex, type of endomyocardial fibrosis, the presence of anaemia, eosinophilia, neutrophilia and type of rhythm (Sinus or atrial fibrillation) etc were compared by both simple X2 and by Kaplan Meier survival curves.

Results: The mean age and the sex distribution was same in both places Briefly the incidence of biventricular endomyocardial fibrosis was more from Trivandrum than Alleppey, 64.9% vs 14.3% ($p < 0.0001$), the incidence of atrial fibrillation was more in Trivandrum 44.2% vs 16.3%. ($p < 0.001$) The overall survival of Trivandrum patients was poorer ($p < 0.0001$). The six year survival was 61% in the Trivandrum population whereas it was 91.5% in the Alleppey population.

Conclusions: These differences may have been due to the better nutrition of the Alleppey patients due to a higher exposure to fish compared to the Trivandrum population. Better nutrition would protect against Magnesium deficiency and prevent the absorption of Cerium in the patients from Alleppey, compared to those from Trivandrum.

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1. Introduction

Previous workers have postulated a geochemical basis for endomyocardial fibrosis¹. Endomyocardial fibrosis of tropical origin is a disease where the endocardium of either the right or the left ventricle, or both gets progressively thickened and the ventricles get obliterated. The fibrosis of the endocardium also extends into the subendocardial myocardium and hence the name tropical endomyocardial fibrosis². Various aetiologies³ have been postulated for endomyocardial fibrosis including rheumatic fever, toxic damage due to eosinophils (degranulated eosinophils), or due to cyanides in tubers, as the histological picture is similar to that

seen in hypereosinophilic syndrome, Löffler's endocarditis and in eosinophilic leukaemia^{3,4}.

Other researchers have demonstrated an increased interstitial cellularity and lymphocytic infiltration in tropical endomyocardial autopsy specimens in the heart, the myocardium⁵. This led to the belief that any toxin spread by the blood stream could cause endomyocardial fibrosis. A search for a pathogen included looking at filariasis, tuber consumption, implicating cyanides, eosinophil mediated damage, and finally damage due to heavy metals like Thorium^{1,6}. Thorium was found to be increased in endomyocardial fibrosis autopsy specimens compared to its content in normal hearts. Subsequently further studies showed that increased levels of Cerium was more prevalent in the myocardium of endomyocardial fibrosis hearts^{6,7}. On experimental studies it was found that cerium and thorium did not enter the tissues of normal animals, or normal tubers grown in tissue culture^{8,9}. When magnesium deficiency was created an excess of cerium and thorium entered the hearts of the experimental animals, and tubers grown in tissue

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culture media. It was also found that magnesium deficient soils grew magnesium deficient tubers. Laterite soil is the type of soil found in the high rain fall regions of Kerala, here excessive rainfall washes away all the magnesium in the soil. (unlike the forests where the retained leaves preserve the magnesium in the soil.) Laterite soil is deficient in magnesium. Researchers have compared the serum magnesium levels in school children to find out whether children from the lower socioeconomic groups had lower serum magnesium levels. This was found to be so¹⁰. The workers from Trivandrum found that the world over endomyocardial fibrosis occurs more between 15° north latitude and 15° south latitude. Kerala lies between 8 and 12° north latitude¹¹.

In Kerala most of the endomyocardial fibrosis patients have been found to be situated in certain areas, these areas, or Taluks have been found to be rich in monazite soils that are rich in Cerium and thorium¹¹. Ramankutty et al studied the distribution of 340 patients with endomyocardial fibrosis that had presented to the Sri Chitra Tirunal Institute of Medical Sciences and Technology, Trivandrum. They classified taluks, or areas as regions of high endemic endomyocardial fibrosis(4/100,000)population,Medium endemic areas(2-4/100,000 population) and those with less than 2/100,000 population as low endemic areas. They found that endomyocardial fibrosis had a strong spacial distribution,high endemic areas were all coastal in location. Trivandrum is a coastal area.17.0% of patients in the above series were from Trivandrum.

18% were from Quilon district and 20% were from Alleppey.

Valiathan and Eapen have found higher cerium levels in the blood of patients with endomyocardial fibrosis¹².

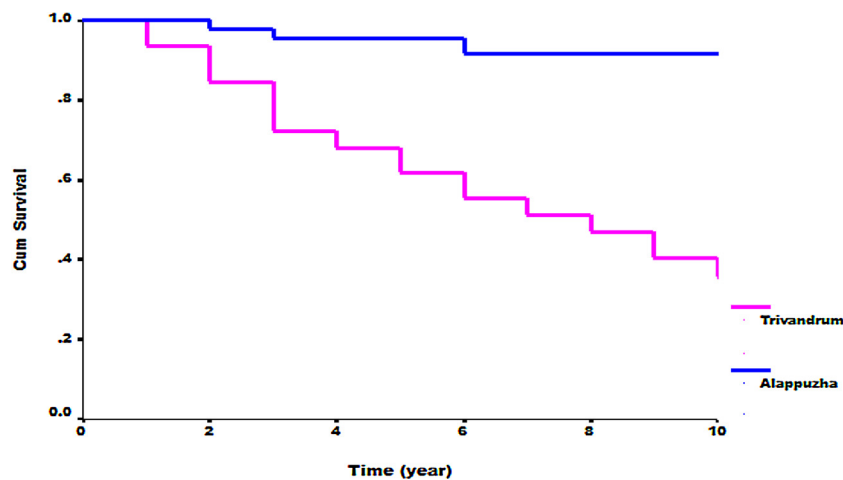
On analysis the endomyocardial fibrosis hearts were also deficient in magnesium. So it is logical to think that if a population eats a diet more deficient in magnesium,with higher levels of toxic minerals like cerium or thorium, they would have more severe endomyocardial fibrosis. This would probably mean involvement of more than one ventricle. Logically involvement of two ventricles should be considered to be a more severe disease/involvement when compared to involvement of only one ventricle. (This is only a hypothesis,it is not proven.)

Endomyocardial fibrosis was reported from the early 1970s from Kerala¹³. Two regions were commonly in the news, Trivandrum and Alleppey^{13,14}. Trivandrum is a coastal town with more government offices and no industry, and a relatively more backward lower socioeconomic class. Nearly every one had small pockets of land. They would cultivate tapioca, a tuber, or yam or sweet potatoes that they would eat with fish or a chutney, when they could not afford rice. Long ago pulses were not easily available and were not eaten as much as they are eaten now. So the average Kerala population would not eat much protein. They would not starve but ate low protein diets, the protein deficiency was aggravated by frequent illnesses like diarrhoea or lower respiratory infections. This would further aggravate any possible magnesium deficiency. Workers from Kerala found that there are two age peaks for the incidence of endomyocardial fibrosis. One peak was in the younger age group in males below the age of 15 years and another peak was in females of the reproductive age group. This was found by independent workers even before the geochemical basis was postulated. It was believed that physiological demands and frequent infections would aggravate any magnesium deficiency.

Trivandrum has more laterite soil and a more city based life. Alleppey is a coastal town with both access to the sea as well as to a large back water sea salt containing lake making access to fish easy. The two geographies are different. Alleppey is often water logged, and it is claimed that nothing like rice or simple crops like tapioca, or bananas can grow there. So of necessity the major food of most of the common man contains an amount of fish.

So it would be interesting to compare whether the pattern of endomyocardial fibrosis is different in the two parts of Kerala. That was the main aim of this study.

Trivandrum and Alleppey (Alappuzha) are two localities in Kerala from where endomyocardial fibrosis has been reported in the 1970s to 1980s¹³. Workers have earlier reported the survival in Endomyocardial fibrosis from another large tertiary care centre in Trivandrum¹⁴.We sought to discover whether the clinical features of endomyocardial fibrosis were different in Trivandrum and Alleppey.



P_value: 0.0001

Fig. 1. showing the survival of both Alleppey patients and Trivandrum patients with endomyocardial fibrosis.

2. Patients and methods

Compared to the patients already reported in The Medical Treatment of Endomyocardial Fibrosis¹⁵ we had 6 more patients with endomyocardial fibrosis detected after the previous paper. But these patients form part of another report so they are not included in this study. The same original 154 patients (of which 3 more died) were compared to the newer 49 patients with endomyocardial fibrosis collected from Alleppey Medical College during the period 2012 to 2014. All patients were assessed by echocardiography and the diagnosis was made based on Shapers's criteria or Mocumbi criteria^{16,17}. Patients who had the typical features of endomyocardial fibrosis namely – obliteration of the right ventricular apex, or left ventricular apex, or both, with tethering of the posterior mitral leaflet to the left ventricle, or plastering of a tricuspid leaflet to the interventricular septum, the presence of atrial dilatation, and intracavitary thrombi and pericardial effusion were classified and included in the study. Shaper's classification (the autopsy classification was extrapolated to echocardiography (like R1 was less than 50% involvement of the right ventricle, with apical obliteration.) was used initially and in the later patients Mocumbi's classification was used to diagnose endomyocardial fibrosis^{16,17}. But this data was not used in the analysis. The patients were just classified as dominant right ventricular endomyocardial fibrosis, dominant left ventricular endomyocardial fibrosis, or if significant obliteration of both ventricles was seen it was classified as biventricular endomyocardial fibrosis [See Figs. 1–3]. In all the patients the age at onset of presentation, the type of endomyocardial fibrosis (dominant right ventricular (RV) or dominant left ventricular (LV) or biventricular (BV) endomyocardial fibrosis were collected. In all patients the age at first diagnosis, the age at the first symptom, the duration of the disease before presentation, the presence of non-communicable diseases like systemic hypertension, diabetes mellitus, the NYHA (New York Heart Association) functional class at presentation, the presenting rhythm (Sinus rhythm, PAT with block (paroxysmal atrial tachycardia with block) or atrial fibrillation (AF) was noted. The underlying blood urea, S creatinine, the haemoglobin, the total count, the eosinophil counts, the drugs used were compared. Whether they developed any complication like ascites or heart

failure or stroke was noted in both groups. Their survival status was also recorded as months alive, or dead.

The drugs given were also noted.

The continuous variables were analysed by the Student T test and the discrete variables by the Chi square test. Survival was correlated with various variables by both univariate and multivariate analysis of variables by Kaplan Meier survival and two survivals were compared by the log rank test. Multivariate analysis was done by Cox Proportional Hazards multiple regression by Dr PSG.

Statistical significance was noted at the $p < 0.05$ level.

The location of Trivandrum and Alleppey are shown in the map. (Fig. 4). The waterways are shown in Fig. 5.

3. Results

The mean age at first presentation to the hospital of the Alleppey patients was 51.3± 11.9 years (N=49). The mean age of Trivandrum patients was – 51.9± 14.3 years. (NS) In Alleppey there were 31 females and 18 males. (63% vs 37% respectively). In Trivandrum also there were 98/154 females (63.6%) and 56 males (36.36%) (Chi square NS.)

When the rhythm was analysed there were significant differences. Trivandrum patients had significantly more atrial fibrillation than those from Alleppey. This might have been because of the significantly higher incidence of biventricular endomyocardial fibrosis in Trivandrum compared to Alleppey, and that biventricular endomyocardial fibrosis represents a later stage in the disease, more patients developing atrial fibrillation. (Tables 1 and 2) 8/49 (16.3%) of patients from Alleppey and 68/154 (44.2%) of patients from Trivandrum had atrial fibrillation. ($p < 0.001$) The incidence of biventricular endomyocardial fibrosis in Trivandrum was 35.1% (54/154) compared to 7/49 (14.3%) in Alleppey. ($p < 0.001$).

The Trivandrum patients seemed sicker. 6/49 (12.24%) from Alleppey were in NYHA classes 3 and 4 compared to 64/154 (41.55%) from Trivandrum. ($p < 0.001$) Eighty six out of one hundred and fifty four (86/154–55.84%) of patients were in sinus rhythm in Trivandrum compared to (68/154–44.15%) patients who were in atrial fibrillation. ($p < 0.001$.) More patients in Trivandrum

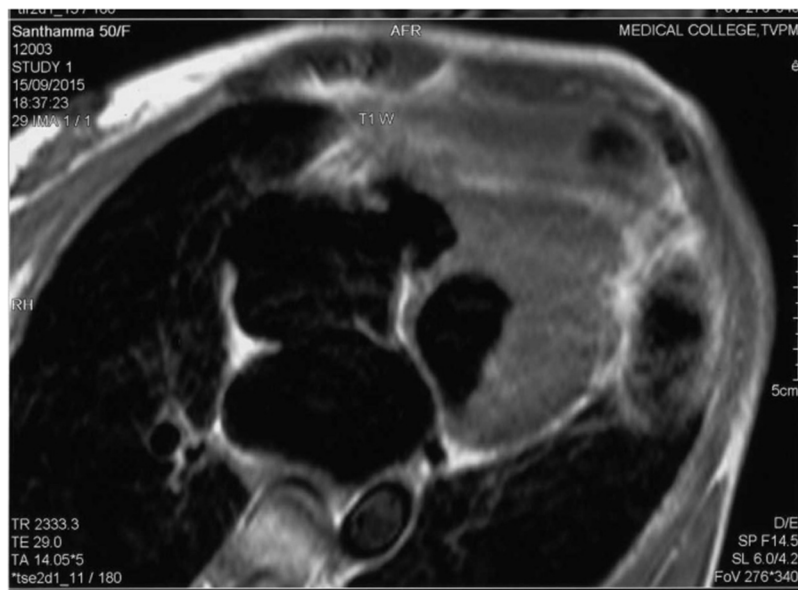


Fig. 2. An MRI image of a patient with endomyocardial fibrosis showing obliteration of the cavity of both the left ventricle and right ventricle.



Fig. 3. The map of Kerala showing both the Trivandrum District and the Alleppey district.



Fig. 4. The map of Kerala showing the water ways.

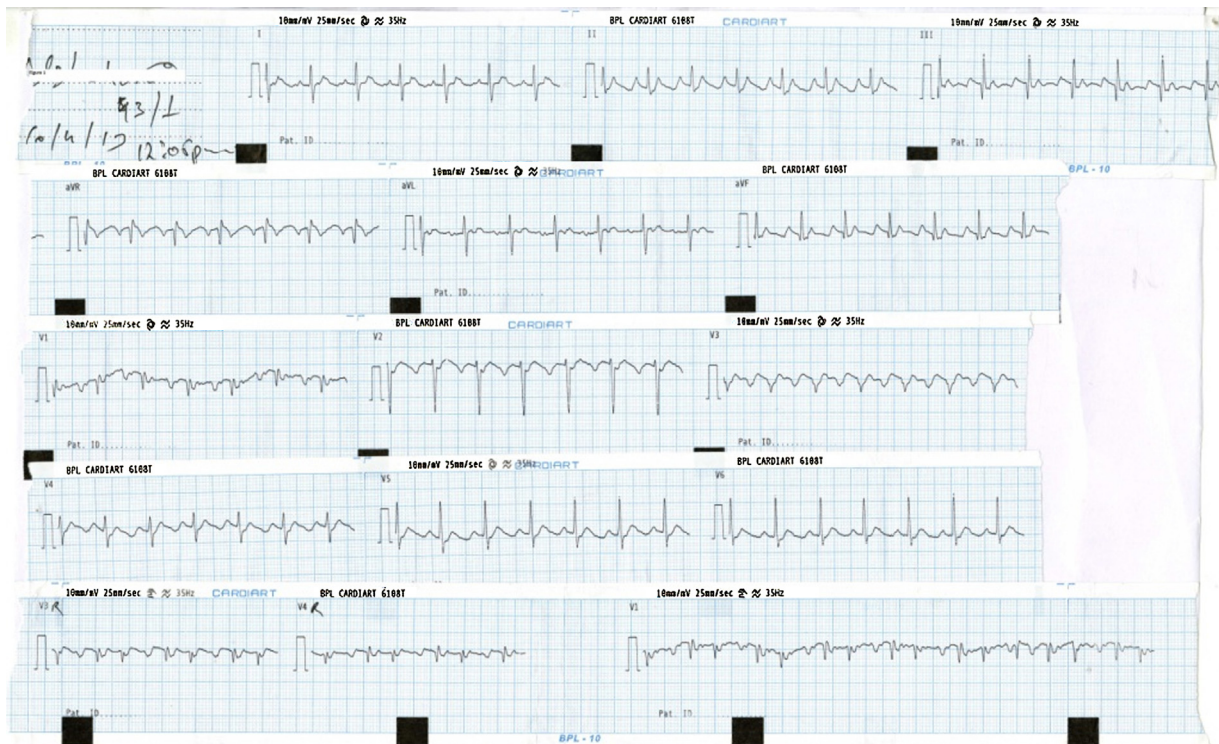


Fig. 5. An electrocardiogram of atrial flutter in an emf patient that reverted after treatment.

Table 1
Comparison of Alappuzha Patients versus Trivandrum Patients with endomyocardial fibrosis.

Variable	Alappuzha(49)	Trivandrum(154)	p-Value
Age Mean (SD)	51.33 (11.9)	51.9 (14.3)	0.796
Min – Max	25–74	14–80	
Sex			
Male	18	56	1.00
Female	31	98	
EMF			
LV	12	49	0.001
RV	30	51	
BV	7	54	
Functional class			
I + II	43	90	0.0001
III + IV	6	64	
Rhythm code			
SR	41	86	0.0001
AF	8	68	
Hemoglobin			
Mean (S.D)	11.9 (1.9)	11.7 (2.0)	0.615
Min – max	6 – 16	4–17	
Total Count			
Mean (S.D)	7530.1 (3494.9)	7711.9 (2859.4)	0.729
Min – max	925 – 25600	3300– 25,500	
Blood Urea			
Mean (S.D)	24.9 (6.3)	26.8 (5.2)	0.045
Min – max	16 – 40	15–43	
Polymorph			
Mean (S.D)	68.5 (9.2)	62.6 (12.5)	0.005
Min – max	45 – 90	30–96	
Lymphocytes			
Mean (S.D)	28.3 (8.6)	34.9 (12.5)	0.002
Min – max	5 – 45	4–70	
Eosinophil C			
Mean (S.D)	3.2 (3.2)	2.5 (2.0)	0.132
Min – max	1 – 15	0–10	
ESR			
Mean (S.D)	11.3 (7.6)	15.1 (20.5)	0.248
Min – max	2 – 45	1–140	

had Haemoglobin levels above 10 gm/dl . ($p < 0.003$) There was significantly more inflammation (by lymphocyte counts) in Trivandrum compared to Alleppey patients.(28.3+ 8.6% in Alleppey, 34.9+ 12.5% Trivandrum) ($p < 0.002$) Alleppey patients had more patients with Total counts below 7000 cells/mm³ compared to those from Trivandrum.(30.6% vs 44.8%) $p < 0.001$.

The distribution of the types of endomyocardial fibrosis were different in Alleppey and Trivandrum . Alleppey had significantly more right ventricular endomyocardial fibrosis than Trivandrum. (61% vs 33%) $p < 0.001$.Trivandrum had significantly more biventricular endomyocardial fibrosis. $p < 0.001$ (64.9% versus 14.3%). More Trivandrum patients had an elevated blood urea.(59% vs 32%) $p < 0.001$ (Tables 2 and 3).

There was a significant difference in the percentage of patients presenting with the first symptom below the age of 30 years. Alleppey had many younger patients when this parameter was examined. (Table 4).

The comorbidities in both Trivandrum patients and Alleppey patients, that could independently cause atrial fibrillation are given in Table 5.

Only 41/49 patients from Alleppey had an elevated eosinophil count, the mean percentage of eosinophil count was $3.2 \pm 3.11\%$. In Trivandrum, the mean eosinophil count was $2.5 \pm 1.66\%$. This was seen in 94 patients from Trivandrum. This was not significantly different from the eosinophil counts in Alleppey.(NS)

The survival of patients from Alleppey seemed to be much better than the patients from Trivandrum (Fig. 6)

Survival of both groups are shown in Fig. 1.

Briefly the 1 year, 3 years and 6 years survival of Alleppey patients was 100%, 95% and 91.5% respectively while the survival from Trivandrum at the same intervals was 93.5% at 1 year, 72.2% at three years and 61.7% at six years. ($p < 0.0001$)

Table 2

The difference in the various variables in patients with endomyocardial fibrosis in Alappuzha and Trivandrum.

	Alappuzha		Trivandrum		P_Value
	#	%	#	%	
Age in years					
Below 60	37	75.5	106	68.8	0.473
Above 60	12	24.5	48	31.2	
Gender					
Male	18	36.7	56	36.4	1.000
Female	31	63.3	98	63.6	
Diagnosis					
LV	12	24.5	49	31.8	1.000
RV	30	61.2	51	33.1	
BV	7	14.3	54	35.1	
Functional Class					
I + II	43	87.8	90	58.4	0.001
III + IV	6	12.2	64	41.6	
Rhythm Code					
Sinus	41	83.7	86	55.8	0.001
AF	8	16.3	68	44.2	
Hemoglobin					
<10	6	12.2	23	14.9	0.003
>= 10	37	75.5	129	83.8	
Total Count					
<7000	15	30.6	69	44.8	0.001
>= 7000	27	55.1	83	53.9	
LV					
LV yes	12	24.5	49	31.8	0.375
LV No	37	75.5	105	68.2	
RV					
RV yes	30	61.2	51	33.1	0.001
RV No	19	38.8	103	66.9	
BV					
BV yes	7	14.3	100	64.9	0.001
BV no	42	85.7	54	35.1	
Blood Urea (mg/dl.)					
<=25	27	55.1	62	40.3	0.001
>25	16	32.7	91	59.1	
Polymorph (%)					
<= 65	16	32.7	103	66.9	0.001
> 65	25	51	49	31.8	
Lymphocytes (%) Count					
<= 30	24	49	46	29.9	0.001
>30	17	34.7	106	68.8	

4. Discussion

Recent papers on endomyocardial fibrosis seem to show that endomyocardial fibrosis is slowly vanishing and is aging^{18–20}. But no other study had compared the pattern of endomyocardial fibrosis presenting to two centres separated by a distance.

Why should the survival of patients from Alleppey be so much better than the patients from Trivandrum. This is surprising in that, the mean age of both groups was the same, further the male/female ratio was also the same. But the proportion of patients with biventricular endomyocardial fibrosis patients was definitely less in the Alleppey population. It is possible that this group is a high risk group.

Further the Trivandrum patients had a significantly higher incidence of atrial fibrillation compared to the Alleppey population. Atrial fibrillation has previously been described as a marker for increased mortality in endomyocardial fibrosis. (Described below) This is probably because the ventricles are obliterated, and the only forward output from the heart either to the systemic or pulmonary circulation is mainly driven by the atria. When they fibrillate the patient rapidly dies.

It is possible that since the prevalence of patients in whom the first symptom started below the age of 30 years was more in the Alleppey group (approximately 50%) these patients received care earlier and hence survived longer.

Further Trivandrum patients had a higher number of patients with comorbidities like thyroid disease, systemic hypertension and chronic obstructive pulmonary disease and so this may have contributed to the higher incidence of atrial fibrillation.

Alternatively, the atrial fibrillation was the result of more severe or more biventricular endomyocardial fibrosis in the Trivandrum patients.

Previous studies with endomyocardial fibrosis have linked tropical endomyocardial fibrosis to tuber consumption leading to low magnesium and high cerium in the heart^{1,6–10}. In the absence of magnesium deficiency, less damage occurs, either to the person or the plant grown in tissue culture.

Magnesium deficiency definitely worsens the absorption of Cerium. Eapen and Valiathan have demonstrated increased Cerium levels in the blood of endomyocardial fibrosis patients compared to controls¹².

Since Alleppey is a district ridden with back waters and sea water, the consumption of fish seems to be higher than in Trivandrum²¹. They have a season called “Chakara” where they are suddenly swamped with large quantities of fish and prawns. The “Chakara” is scientifically known as the “mud bank” phenomenon. The “mud bank” phenomenon according to the scientists is a “region of calm and highly turbid waters that occurs along certain parts of the Kerala coast.” This has been reported from as early as 1678 CE. At the time of ‘chakara’ large numbers of fish are available along the Alleppey Coast, near Punnappra. In the 80’s “mud banks” were reported from as many as 28 locations in Kerala, but now this phenomenon seems to be reducing. Prawns are a good source of magnesium²². This may be one factor preventing the worsening of the health of patients with endomyocardial fibrosis from Alleppey.

In contrast the Trivandrum population tends to eat sardines, and other locally available fish and a larger quantity of tubers like cassava, high in carbohydrate and low in protein diets²³. Due to the high rainfall, the soil is laterite, that is inherently deficient in magnesium. So this population tends to be more malnourished and probably has more severe endomyocardial fibrosis. The magnesium content of sardines, mackerel and anchovies are less than that found in prawns²⁴. Tuna also has been found to have higher quantities of mercury that is harmful, but this does not have any relationship to endomyocardial fibrosis.

One more interesting finding in this study is the range of the total counts of the patients. In general the total counts were normal and not significantly different in Trivandrum or Alleppey. But if the range of the total count (WBC count) are taken some patients had very low total counts like 800/cmm or 950/cmm (See Table 3). Workers have previously reported this finding in endomyocardial fibrosis²⁵. But we were not the first to notice this, Andrade and Guimaraes had already commented on the same²⁶. We believe this, and the presence of anaemia reflect the toxicity of cerium or some unknown toxin on the bone marrow.

Of note is another survey by British workers²⁷. They studied the cerium levels in various populations in Uganda. In this study the Cerium and magnesium levels in the soil and water were studied in areas where endomyocardial fibrosis was prevalent. The region chosen was Mukuno, near Kampala. 200 separate foods were studied and 150 soil samples from 50 sites were studied. Children in Uganda have been found to eat soil regularly ‘geophagy’ (habitual soil eating) This population eats a lot of Cassava. These workers found that cassava was dried on the ground, thus it got contaminated with Cerium. They found poorer people, and most endomyocardial fibrosis patients drank from shallow wells. The shallow wells had more cerium content than deep wells. Autopsy analysis of cerium in heart tissues did not show elevated levels but these were paraffin preserved specimens (not the correct tissue to estimate cerium) But they did study the deciduous teeth of young children that analyses cerium levels in life. They found that

Table 3
 (a) The distribution of variables in patients – Left Ventricular endomyocardial fibrosis in Alappuzha and Trivandrum. (b) The distribution of variables in patients – RV –ventricular endomyocardial fibrosis in Alappuzha and Trivandrum. (c) The distribution of variables in patients – Biventricular endomyocardial fibrosis in Alappuzha and Trivandrum.

(a)					
Variables	Alappuzha(49)		Trivandrum(12)		P_Value
	#	%	#	%	
Age in years					
Below 60	32	65.3	6	50.0	0.342
Above 60	17	34.7	6	50.0	
Gender					
Male	15	30.6	6	50.0	0.309
Female	34	69.4	6	50.0	
Functional Class					
I + II	37	75.5	10	83.3	0.715
III + IV	12	24.5	2	16.7	
Rhythm Code					
Sinus	33	67.3	11	91.7	0.151
AF	16	32.7	1	8.3	
Blood urea					
<= 25	21	42.9	5	41.7	0.104
> 25	27	55.1	5	41.7	
No data	1	2.0	2	16.7	
Polymorph					
<= 65	32	65.3	2	16.7	0.001
> 65	16	32.7	7	58.3	
No Data	1	2.0	3	25.0	
Lymphocytes Count					
<= 30	13	26.5	9	75.0	0.001
> 30	35	71.4	0	0.0	
No Data	1	2.0	3	25.0	

(b)					
Variables	Alappuzha(51)		Trivandrum(30)		P_Value
	#	%	#	%	
Age in years					
Below 60	41	80.4	25	83.3	1.000
Above 60	10	19.6	5	16.7	
Gender					
Male	21	41.2	10	33.3	0.636
Female	30	58.8	20	66.7	
Functional Class					
I + II	22	43.1	28	93.3	0.001
III + IV	29	56.9	2	6.7	
Rhythm Code					
Sinus	26	51.0	25	83.3	0.004
AF	25	49.0	5	16.7	
Blood urea					
<= 25	26	51.0	20	66.7	0.126
>25	25	49.0	9	30.0	
No Data	0	0.0	1	3.3	
Polymorph					
<= 65	36	70.6	11	36.7	0.005
> 65	15	29.4	17	56.7	
No Data	0	0.0	2	6.7	
Lymphocytes Count					
<= 30	15	29.4	15	50.0	0.019
> 30	36	70.6	13	43.3	
No Data	0	0.0	2	6.7	

(c)					
Variables	Alappuzha(54)		Trivandrum(7)		P_Value
	#	%	#	%	
Age in years					
Below 60	33	61.1	6	85.7	0.405
Above 60	21	38.9	1	14.3	
Gender					
Male	20	37.0	2	28.6	1
Female	34	63.0	5	71.4	
Functional Class					
I + II	31	57.4	5	71.4	0.689
III + IV	23	42.6	2	28.6	
Rhythm Code					
Sinus	27	50.0	5	71.4	0.429
AF	27	50.0	2	28.6	

Table 3 (Continued)

(c) Variables	Alappuzha(54)		Trivandrum(7)		P_Value
	#	%	#	%	
Blood urea					
<=25	15	27.8	2	28.6	0.001
>25	39	72.2	2	28.6	
No Data	0	0.0	3		
Polymorph					
<=65	35	64.8	3	42.9	0.001
>65	18	33.3	1	14.3	
No Data	1	1.9	3		
Lymphocytes Count					
<=30	18	33.3	0	0.0	0.001
>30	35	64.8	4	57.1	
No Data	1	1.9	3	42.9	

Table 4

The distribution of patients reporting the first symptom below 30 years of age.

Type of treatment	Alappuzha	Trivandrum	P_value
RV dominant	10(38.5%)	9(56%)	<0.05
LV dominant	7(26.9%)	2(22%)	
BV dominant	9(34.6%)	5(31.3%)	
Total	26/49(53.6%)	16/154(10.4%)	

Note: Only 3 patients presented under the age of 15 years. 2 from Trivandrum & 1 from Alappuzha.

Table 5

Assosiated Co- morbidites of endomyocardial fibrosis patients in Alappuzha and Trivandrum.

Co morbidity	Alappuzha(49)	Trivandrum(154)
Systematic hypertension	3(6.1%)	11(7.1%)
COPD ^a	0(0.0%)	3(1.9%)
Diabetes Mellitus	3(6.1%)	3(1.9%)
Gall stones	0(0.0%)	1(0.6%)
Pullmonaty Tuberculosis	0(0.0%)	2(1.2%)
Rheumatic mitral stenosis	0(0.0%)	1(0.6%)
Multinodular goitre	1(2.0%)	1(0.6%)
Deep venous thrombosis	0(0.0%)	1(0.6%)
Ventricular septal defect	1(2.0%)	0(0.0%)
Inguinal Hernia	1(2.0%)	0(0.0%)
Alcoholic Liver Disease	2(4.0%)	0(0.0%)
Myasthenia Gravis	1(2.0%)	0(0.0%)
Atrial Septal Defect	1(2.0%)	0(0.0%)
Total	23(15.0%)	13(26.5%)

^a COPD- Chronic Obstructive Pulmonary Disease.

Ugandans are exposed to high levels of Cerium and this was found in the outer 25 micrometres of their teeth.

Endomyocardial fibrosis is supposed to be a disease caused by poor diet, low protein and exposure to toxins(cerium). It has been believed to be more common in those who eat regular tubers like cassava. So a recent report from Cameroon is of interest. Chelo studied the hospital records of the Mother and Child Centre of the Chantal Biya Foundation (MCC/CBF) in Cameroon. (Yaonade)²⁸. He examined the hospital records of consultations and echocardiography between January 2006 and December 2014. During this period he surveyed 273117 consultations and detected 1666 cases of heart disease and 54 cases of endomyocardial fibrosis. All these consultations were done in children below the age of 16 years. The percentage of endomyocardial fibrosis was only 3.24% of all heart diseases seen. Most of the patients came from 3 regions in Cameroon and 76% were from rural areas. The age range was from 2 years to 17 years. Most of the patients ate Cassava more than 6 times a week, rarely ate vegetables or fish. The other food they ate were plantains and coco-yams. No family had a car. Only 8.3% had a

fridge. Only 8.3% had running water. 66% had no electricity. From 2006, 32/54 patients died. (59%) No fish consumption at all was noted by the workers. 7/54 (12.96%) had atrial fibrillation and 2 had atrial flutter. This population is akin to the Trivandrum population reported by us.

Previous studies in endomyocardial fibrosis have shown that atrial fibrillation, or atrial arrhythmia is an important factor contributing to early mortality^{29,30}. Since the mean age of both Alleppey and Trivandrum patients was identical it is surprising the incidence of atrial fibrillation was higher in the Trivandrum population. However as previously discussed it is possible that the higher incidence of Biventricular endomyocardial fibrosis is responsible for the higher atrial fibrillation and the higher mortality of Trivandrum patients.

Barretto et al studied one hundred and sixty patients with endomyocardial fibrosis²⁹. Of these 58 had atrial fibrillation. He found that the presence of atrial fibrillation correlated with worse disease. The patients with atrial fibrillation had more dyspnoea, more oedema, lower ejection fractions(left ventricular) and more tricuspid regurgitation. Atrial fibrillation patients also had a significantly higher mortality (p < 0.01).^{29,30}.

What is the relevance of this paper?

Endomyocardial fibrosis is becoming scarcer, it may be because the overall general nutrition of the Kerala population is improving, the economic status is improving. Better food and better living conditions can possibly eradicate the disease. Now most Kerala children are fed nutritious, protein rich food in the midday meal programmes.

What does this study add?

This definitely shows that the overall types of endomyocardial fibrosis found in Medical College Trivandrum differed from those found in Alleppey. It is possible that the increased biventricular endomyocardial fibrosis found in Trivandrum patients and the increased atrial fibrillation represent the later stage, or more severe disease. It is well known that atrial fibrillation increases the mortality in endomyocardial fibrosis, and it is possible that biventricular endomyocardial fibrosis is the more severe disease.

How does this study affect day to day practice?

Possibly better nourished endomyocardial fibrosis patients live longer. It would be important to preserve sinus rhythm in endomyocardial fibrosis to prolong life as only a rate control strategy would not work. So a rhythm control strategy would be the better option. Actively trying to preserve sinus rhythm has

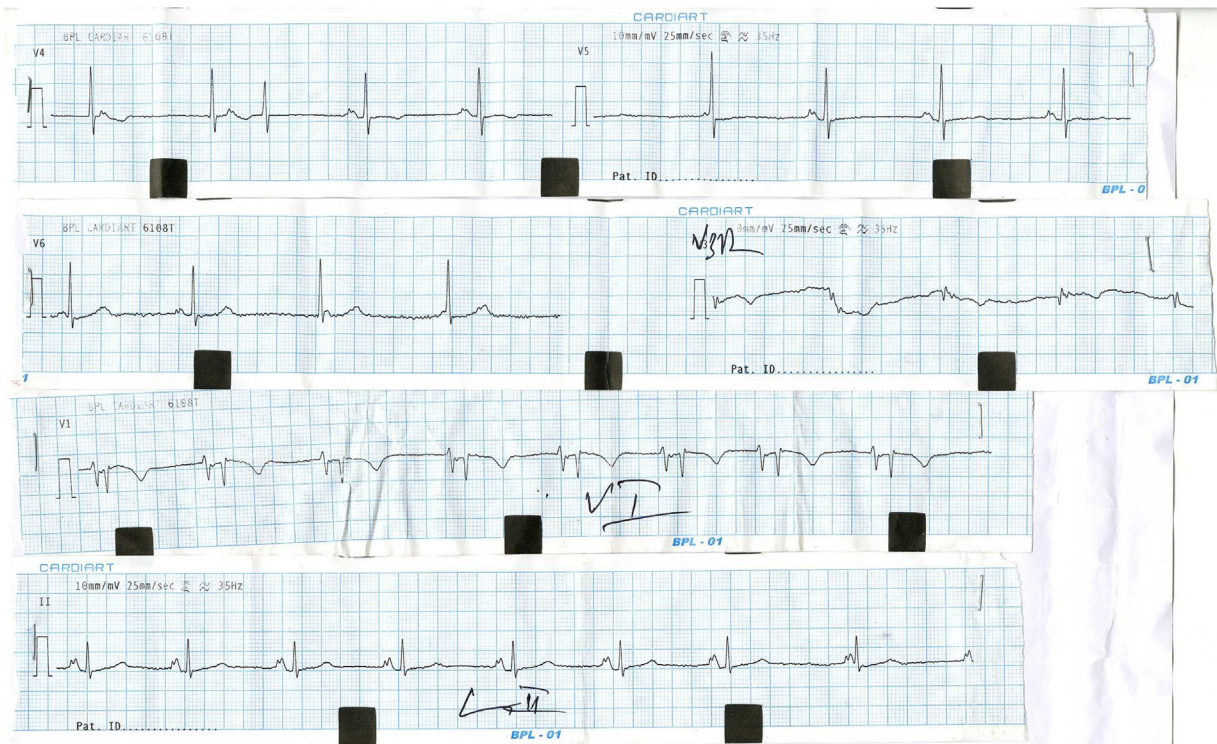


Fig. 6. The sinus rhythm ECG of the same patient with atrial flutter reverted with treatment.

never been recommended in endomyocardial fibrosis before. We now recommend this. In endomyocardial fibrosis, the ventricles are obliterated and the atria are dilated. After a while the only forward propulsion of blood is by the strong atrial contraction, hence atrial fibrillation is not well tolerated. Hence we recommend all measures including unloading the atria with diuretics and maintaining sinus rhythm with drugs (beta-blockers and calcium channel blockers.) should be actively pursued in Endomyocardial fibrosis.

We had a patient with atrial flutter and right ventricular endomyocardial fibrosis (Figs. 5 and 6). She was put on verapamil 40 mg 6th hourly and metoprolol 25 mg half twice a day. She was also put on torsemide 10 mg daily and warfarin. She reverted to sinus rhythm as is doing well. (after a period of 6 months.)

Another patient of ours was on a combination of metoprolol and Ramipril. This patient also had excellent rate control and finally reverted to sinus rhythm (after a while.) It is possible the Ramipril causes atrial remodelling and reverted her to sinus rhythm over a period of time.

The main strengths of the study

*This is a relatively large cohort of patients with tropical endomyocardial fibrosis from Kerala.

*The patients have been followed up by us as a group, and they tend to avoid travel to far off places for treatment.

*We did not expect to find any difference in the two cohorts. But the differences are probably true, as the mean age at presentation and the sex ratio are identical in both groups.

*Both mean age and the sex ratio are absolute facts, that cannot change due to author bias.

*Since the influence of the presence of atrial fibrillation in causing mortality in endomyocardial fibrosis has been previously reported by Barretto, this deserves mention in our patients.

The main limitations of the study:

*This is a hospital based study. But as mentioned above, these patients present repeatedly to us in the same hospitals.

*We have only assumed the dietary pattern from what is easily available and from our knowledge of the diet of socioeconomically backward Keralites.

*This assumption is akin to assuming most Hindus do not eat beef, and most north Indians do not eat much coconut. (This is not available in the north) (These are facts but cannot be proven retrospectively directly.)

*We only sought to explain the differences in the two populations.

Disclosures

No author has any relationship with the industry. Even though we have 3 open access publications we have not paid for any of them.

Contributorship statement

Dr PNG wrote the paper. Dr SMK collected both the Alleppey and the Trivandrum data. Dr Baijiu collected some of the Trivandrum data. Dr AGK and Dr SV both reviewed the protocols of both Trivandrum data and Alleppey data and both contributed patients from Trivandrum and Alleppey.

Dr PV follow-up some of the Trivandrum patients and treated them. Dr PSG analysed the data.

Competing interests

There are no competing interests and no author has any relationship to the industry. Though we have 3 open access papers we have not paid any money for any of them.

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Data sharing statement

There is no more data. There is no data sharing.

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