International Journal of Health Sciences and Research
www.ijhsr.org ISSN: 2249-9571

Original Research Article

Structural Equation Modeling of Health Related Quality of Life of Lymphatic Filariasis Patients

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ABSTRACT

Health Related quality of Life (HRQoL) assess the perceived well being of the individuals in their physical, mental and social well being of their daily life. The items in the HRQoL measures are interrelated and the relationship between them is complex in nature and the domains, which are the constructs of the HRQoL cannot be observed or measured directly. One of the major challenges in the modeling of HRQoL is related to the complexity and collinearities of the relationships among the variables, which cannot be unraveled by standard statistical analysis. Structural Equation Modeling (SEM) is a powerful statistical tool, which combines factor analysis and mathematical modeling to test hypotheses consisting of interacting variables and pathways with reference to substantive theory. The HRQoL of patients with filarial lymphoedema was assessed by using SF-36 and the Structural Equations Model was used to model the HRQoL data. Structural Equation Models consist of two interrelated components, a measurement model and a structural model. The measurement model, which specifies how the latent constructs are indicated by their observed variables, describes these observed variables measurement properties and is analogous to confirmatory factor analysis (CFA). The structural equation model specifies causal relationships among the latent variables, describes their direct and indirect effects, and allocates explained and unexplained variance of the dependent constructs. The present study developed a SEM of HRQoL with 16 indicator/measured variables of SF-36, 4 first order latents, 2 second order latents and one third order latent. This model was developed from the HRQoL data of filarial lymphoedema patients and it is novel in HRQoL among lymphoedema patient in our population. This model is highly useful to understand the inter relationship of the variables related to different health domains in HRQoL and it will help in the planning and implementing a comprehensive morbidity management program to improve the HRQoL in lymphatic filariasis patients.

Keywords: Health Related Quality of Life (HRQoL), Lymphatic Filariasis, Structural Equations Model

INTRODUCTION

Health related quality of life has emerged as an important component of clinical research in the context of outcomes research and the measurement of quality of care. It is a multidimensional construct, becoming more frequently used in clinical trials and health services research, as both primary and secondary end points. [1] HRQoL can quantify the impact of a disease and its treatment on the individual and is increasingly used as an important outcome measure in chronic diseases. Health Related quality of Life assess the perceived well being of the individuals in their physical, mental and social well being in their daily

life. The items in the HRQoL measures are interrelated and the relationship between them is complex in nature and the domains, which are the constructs of the HRQoL cannot be observed or measured directly.

One of the major challenges in the modeling of HRQoL is related to the complexity and collinearities of the relationships among the variables, which cannot be unraveled by standard statistical analysis. Structural Equation Modeling (SEM) is a powerful statistical tool, which combines factor analysis and mathematical modeling to test hypotheses consisting of interacting variables and pathways with reference to substantive theory. This method was widely used in different disciplines, [2,3] but this method was not been used extensively in biomedical and epidemiological research. In biological system, it is often the norm rather than exception that there are complex interactions between variables. Hence, structural equation modeling can be a useful research tool to identify the complex relationship between the variables in studies related to biological systems and also in HRQoL studies. Structural Equation Modeling has the advantages of dissecting these relationships, assessing the total effects of variables on one another as well as providing its directions and estimating the strengths of such relationships in an integrated model. [4]

Structural Equations Model was developed in the early 1900s as a result of Spearman's [5] development of factor analysis and the geneticist Wright's [6,7] invention of path analysis. SEM is a powerful multivariate analysis technique and its applications range from analysis of simple relationships between variables to complex analyses of measurement equivalence for first and higher-order constructs [8,9] Perhaps its greatest advantage is the ability to manage measurement error, which is one of the greatest limitations of most of the traditional statistical methods. Measurement error is the difference between a measured value of a variable and its true value. We expect that the latent variables will not perfectly predict the observed variables and in SEM, this is modeled by specifying a specific error factor for each observed variables. These measurement errors are also unobserved factors in SEM.

Structural Equation Models combine factor analysis principles with path analysis and other path modeling methods in specifying a set of linear equations representing hypothesized relations among latent constructs and their multiple indicators. Structural equation models consist of two interrelated components, a measurement model and a structural model. The measurement model, which specifies how the latent constructs are indicated by their observed variables, describes these observed variables measurement properties and is analogous to confirmatory factor analysis (CFA). Confirmatory factor analysis is a statistical technique used to verify the factor structure of a set of observed variables and test the relationship between observed variables and their underlying latent constructs. In CFA, the predicted factor structure of a number of observed variables is translated into the complete covariance matrix over these variables and this matrix is compared with the actual covariance matrix. The structural equation model specifies causal relationships among the latent variables, describes their direct and indirect effects, and allocates explained and unexplained variance of the dependent constructs.

Lymphatic filariasis (LF) caused by filarial parasites remains an important public health problem and is one of the most debilitating neglected tropical diseases. This infection leads to permanent lymphatic dysfunction in virtually all infected individuals and clinical disease in a subset of these infected individuals. [10] The major clinical manifestations of lymphatic filariasis are lymphoedema of the limbs and hydrocele. The World Health Assembly resolution on Global programme to Eliminate Filariasis highlights the need for

health indicators that capture the entire profile of people with this health condition. Since the advanced stages of lymphoedema are not reversible and have a substantial impact on health, Global Programme to Eliminate Lymphatic Filariasis (GPELF) launched in early 2000 following the World Health Assembly Resolution 50.29 in 1997 [11] incorporated Morbidity Management and Disability Prevention Activities (MMDPA) to reduce LF-related disability in those, already affected by chronic manifestations of the disease. Since the aim of MMDPA is to reduce the morbidity due to disease and to improve the quality of life of the patients, HRQoL can be used as a tool to assess the impact of morbidity management programme. [12] The proper understandings about the domains of health which are adversely affected by the disease and how it related to each other are very essential for the planning of intervention strategies and also its implementation. This study is proposed to develop a Structural Equation Model of the HRQoL of patients with lymphatic filariasis which will provide the underlying latents (factors) in HRQoL, demonstrates the relationships among observed variables (individual items), the relationships between latents and observed variables that are not factor indicators and also the relationship between the latents. The findings of this study are expected to provide detailed knowledge on the real impact in physical, mental and social well being in their daily life and the relationship between them. The results of this study will help the policy makers to broaden the existing morbidity management programme by incorporating the programmes to improve the quality in all the aspects of the daily life of the patients.

MATERIALS & METHODS

The study was carried out in Puducherry district of the Union territory of Puducherry and in two Lymphatic filariasis endemic villages in Villupuram District of Tamil Nadu state in South India. A total of 239 lymphatic filariasis patients with the clinical manifestation of filarial lymphoedema identified through the line listing of cases as part of morbidity management programme were included in the study. The present study included only the filariasis patients with different grades of lymphoedema. Acute attack of adenolymphangitis (ADL), which is the recurrent attacks of fever associated with inflammations of the lymph nodes and/or lymph vessels associated with chronic manifestation were considered as co-morbidity. The HRQoL was assessed by using the Short Form-36 (SF-36) questionnaire. The SF-36 is a 36-item scale constructed to survey health status and quality of life and is widely used as a generic HRQoL instrument. SF-36 questionnaire contains the items pertaining to the limitations in physical activities because of health problems; limitations in social activities because of physical or emotional problems; limitations in usual role activities because of physical health problems; bodily pain; psychological distress and well-being; limitations in usual role activities because of emotional problems; vitality (energy and fatigue); and general health perceptions. [13-17] The possible range of overall HRQoL scores was ranging from 0 (indicating the worse health status and equivalent to death) to 100 (indicating the best health status) which indicate higher the score higher the quality of life. [13,18] The SF-36 questionnaire was administered and the data was collected from patients in their domestic settings after explaining the purpose of the study and obtaining informed written consent. A recall period of 30 days was considered as ideal to recollect the sufferings experienced in each of the 36 items due to their chronic problem due to lymphatic filariasis.

Structural Equation Modeling was used to model the HRQoL data collected from lymphoedema patients. Although SEM is capable of testing the measurement model and structural model simultaneously, the recommendation is that the measurement model should be tested separately to detect

any inadequate fits prior to testing the full Model. [19] As recommended by Anderson and Gerbing, [20] measurement model was analyzed first followed by the structural model using AMOS software. This analysis involved a two- step process. First, confirmatory factor analysis (CFA) was used to describe the relationships between the latent constructs and their measured variables (measurement model). Then, SEM was performed to test the hypothesized relationships among all latent constructs (structural model). Unstandardized and Standardized regression coefficients for all paths were estimated. Unstandardized regression coefficient represents the amount of change in the dependent variable per single unit change in the predictor variable. The standardized regression weights represent the amount of change in the dependent variable that is attributable to a single standard deviation unit's worth of change in the predictor variable.

The conceptual model for SF-36 developed by Reed PJ *et al* 2000 [21] was considered. This model consists of 8 first order latents and 2 second order latents. The model was fitted with these 8 latents and 35 indicator variables of SF-36 and it was not fitting well and we modified the model by excluding the variable whose factor loading are less than 0.50. Fit indices are used to determine how well *a priori* model fits the sample data. These measures provide the most fundamental indication of how well the proposed theory fits the data. The goodness of fit of the model were assessed by using all the commonly used fit indices of SEM such as $\frac{\chi 2}{df}$ with cutoff value for the goodness of fitness as $\leq$5, Comparative Fit Index-CFI (>0.90), Root Mean Square Error of Approximation-RMSEA (<0.08),Tucker Lewis Index-TLI ($\geq$0.90), Normated Fit Index-NFI ($\geq$0.90), Incremental Fit Index-IFI (approached 1) and Goodness of Fit Index-GFI (>0.90) [22-25]

RESULTS

The modified first order model consists of 16 indicator variables under 4 latent variables such as *Physical Function, General Health, Social Function and Emotional Well- being* and structure (path) of the first order model is given in figure-1 and the details of the measured/observed variables in the modified SEM structure are given in Table- 1

Table-1: The details of the measured/observed variables in SEM

Abbreviations	Item/Question Number in SF-36	Questions in SF 36	Latent variable
PF-1	3	Problems in Vigorous activities	*Physical Function*ing
PF-2	4	Problems in Moderate activities	
PF-4	6	Problems in Climbing several flights of stairs	
PF-5	7	Problems in Climbing one flight of stairs	
PF-6	8	Problems in Bending, kneeling or stooping	
PF-7	9	Problems in Walking more than a mile	
PF-8	10	Problems in Walking several blocks	
EM-1	24	Have you been a very nervous person	*Emotional Well Being*
EM-2	25	Have you felt so down in the dumps that nothing could cheer you up	
EM-3	26	Have you felt calm and peaceful	
EM-4	28	Have you felt downhearted and blue	
S-1	20	To what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors' or groups	*Social Function*ing
S-2	32	How much of the time has your physical health or emotional problems interfered with your social activities	
GH-1	1	In general would you say your health	*General Health*
GH-3	34	I am as health as anybody I know	
GH-4	35	I expect my health to get worse	

The model fit indices of the single factor model are given in Table-2. The standard value of $\frac{\chi 2}{df}$ for assessing the goodness of fit of SEM $\leq$ 5.0, Comparative Fit Index CFI > 0.90, goodness of fit index (GFI) > 0.90, Normative fit Index (NFI) $\geq$ 0.90, Incremental fit Index (IFI) approaches 1, Tucker Lewis Index (TLI) is $\geq$ 0.90 and

Root mean Square Error of Approximation (RMSEA) is < 0.08. The estimate of $\frac{\chi^2}{df}$ in single factor model is 2.289, the estimate of Comparative Fit Index CFI is 0.983, Goodness of Fit index GFI is equal to 0.905, Normated fit Index (NFI) is 0.971, Incremental fit Index (IFI) is 0.983, Tucker Lewis Index (TLI) is 0.977 and the Root mean Square Error of Approximation (RMSEA) is 0.074. This shows that the single factor model developed has shown good fit as per all these fit indices.

Table-2: Model Fit indices of the single factor Structural Equations Model

Fit Indices	Results
Chi-square/degree of freedom (x2/d.f.)	2.289
Comparative Fit index (CFI)	0.983
Goodness of Fit Index (GFI)	0.905
Normated Fit Index (NFI)	0.971
Incremental Fit Index (IFI)	0.983
Tucker Lewis Index (TLI)	0.977
Root mean square error of approximation (RMSEA)	0.074

The unstandardized coefficients and associated test statistics are given in Table-3. The amount of change in the dependent or mediating variable for each one unit change in the variable predicting it is symbolized by the unstandardized regression coefficient. The Table-3 provides the unstandardized estimate, its standard error (SE), Critical ratio (CR) and the statistical significance. It shows that all the regression weights of the fitted model was found to be statistically significant (P<0.001)

This model consists of 16 indicator variables under 4 latent variables. The latent variables are *Physical Functions, General Health, Social Functions and Emotional Well being*. The first latent variable is *Physical Function*, the corresponding 7 measured variables are PF_1, PF_2, PF_4, PF_5, PF_6, PF_7 and PF_8. The second latent variable is *General Health*, the corresponding measured variables are GH_1, GH_3 and GH_5. The third latent variable is *Social Function* with the measured variables S_1 and S_2 and the measured variables corresponding to the fourth latent variable *Emotional Well- being* are EM_1, EM_2, EM_3 and EM_4.

The factor loadings of *Physical Function* with PF_1, PF_2, PF_4, PF_5, PF_6 and PF_7 were respectively 0.998, 0.655, 1.00, 0.566, 0.888 and 1.00. All these factor loadings were statistically significant (P< 0.01). The factor loadings of *General Health* with GH_1, GH_3 and GH_5 were 1.349, 1.00 and 0.941 respectively. The factor loading of *Social Function* with S_1 and S_2 were -0.601 and 1.00 respectively and the factor loadings of *Emotional Well-being* with EM_1, EM_2, EM_3 and EM_4 were 0.832, 0.981, -0.503 and 1.00 respectively. All these factor loadings were found to be statistically significant. The details of the factor loadings are given in Table-3 and the path diagram is given in Figure-1

Table-3: Factor Loadings (Regression Weights) of first order SEM

Indicator variable		Latent factor	Estimate	S.E.	C.R.	P
PF_8	<---	*Physical Function*	1.000			
PF_7	<---	*Physical Function*	1.004	.005	194.843	***
PF_6	<---	*Physical Function*	.888	.027	32.563	***
PF_5	<---	*Physical Function*	.566	.027	21.017	***
PF_4	<---	*Physical Function*	1.000	.007	137.572	***
PF_2	<---	*Physical Function*	.655	.031	20.895	***
PF_1	<---	Physical Function	.998	.009	112.368	***
EM_3	<---	Emotional Well being	-.503	.047	-10.804	***
EM_2	<---	Emotional Well being	.981	.042	23.639	***
EM_1	<---	Emotional Well being	.832	.052	16.043	***
S_2	<---	Social Function	1.000			
S_1	<---	Social Function	-.601	.042	-14.461	***
GH_3	<---	General Health	1.000			
GH_1	<---	General Health	1.349	.086	15.627	***
GH_5	<---	General Health	.941	.033	28.302	***
EM_4	<---	Emotional Well being	1.000			

***Statistically significant.

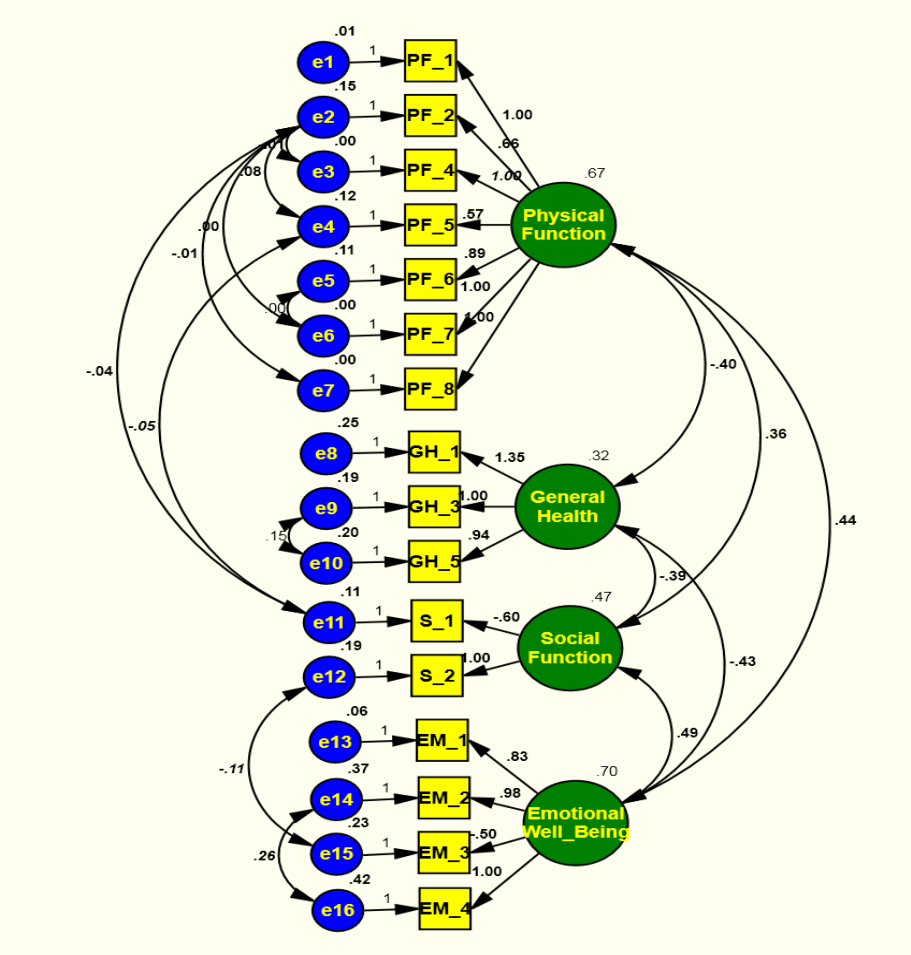

Figure-1: First order factor loadings of SEM (Unstandardized Estimates)

The standardized regression weights of the first order SEM are given Table-4. The standardized regression weights of *Physical Function* with PF_1, PF_2, PF_4, PF_5, PF_6, PF_7 and PF_8 were respectively 0.994, 0.811, 0.997, 0.799, 0.906, 1.00 and 0.997. The standardized regression weights of *General Health* with GH_1, GH_3 and GH_5 were 0.840, 0.797 and 0.768 respectively. The standardized regression weights of *Social Function* with S_1 and S_2 were -0.766 and 0.844 respectively and the standardized regression weights of Emotional well-being with EM_1, EM_2, EM_3 and EM_4 were 0.943, 0.802, -0.661 and 0.790 respectively.

The covariance of *Physical Function* with *General Health*, *Social Function* and Emotional well-being were -0.397, 0.362 and 0.444 respectively. The covariance of *Emotional Well-being* with *General Health* and *Social Function* were -0.427 and 0.493 respectively and the covariance between the *Social Function* and *General Health* was -0.397. All these covariance between the latent were found to be statistically significant (P<0.01). It was also observed that there was significant covariance between the measurement errors

Table-4: Standardized Factor Loadings (Regression Weights) of first order SEM

Indicator variable		Latent factor	Estimate
PF_8	<---	*Physical Function*	.997
PF_7	<---	*Physical Function*	1.000
PF_6	<---	*Physical Function*	.906
PF_5	<---	*Physical Function*	.799
PF_4	<---	*Physical Function*	.997
PF_2	<---	*Physical Function*	.811
PF_1	<---	*Physical Function*	.994
EM_3	<---	*Emotional Well-being*	-.661
EM_2	<---	*Emotional Well-being*	.802
EM_1	<---	*Emotional Well-being*	.943
S_2	<---	*Social Function*	.844
S_1	<---	*Social Function*	-.776
GH_3	<---	*General Health*	.797
GH_1	<---	*General Health*	.840
GH_5	<---	*General Health*	.768
EM_4	<---	*Emotional Well-being*	.790

The structure of the second order SEM is given in Figure-2 and the model fit indices of the second order SEM are given in Table-5. The estimate of $\frac{\chi^2}{df}$ is 2.342, the estimate of Comparative Fit Index CFI is 0.982, Goodness of Fit index GFI is equal to 0.904, Normative fit Index (NFI) is 0.970, Incremental fit Index (IFI) is 0.982, Tucker Lewis Index (TLI) is 0.976 and the Root mean Square Error of Approximation (RMSEA) is 0.075. This shows that the two factor model developed has shown good fit as per all these fit indices.

Table-5: Model Fit indices of the Second order Structural Equations Model

Fit Indices	Results
Chi-square/degree of freedom (x2/d.f.)	2.342
Comparative Fit index (CFI)	0.982
Goodness of Fit Index (GFI)	0.904
Normated Fit Index (NFI)	0.970
Incremental Fit Index (IFI)	0.982
Tucker Lewis Index (TLI)	0.976
Root mean square error of approximation (RMSEA)	0.075

The unstandardised estimates of the second order SEM are given in Table-6. This model consists of 16 indicator variables in 4 first order latents *(Physical Functions, General Health, Social Functions and Emotional Well being)* and two second level latents (*Physical Health and Mental Health*). The *Physical Health* latent was described by two first order latents *Physical Function* and *General Health* and the *Mental Health* latent was described by two first order latents *Social Function* and *Emotional Well-being*. The factor loading between the latents *Physical Function* and *General Health* was -1.004 and between *Social Function* and *Mental Health* as 0.928. The *Physical Function* is explained by 7 indicator variables (PF_1, PF_2, PF_4, PF_5, PF_6, PF_7 and PF_8), *General Health* is explained by 3 indicator variables (GH_1, GH_3 and GH_5), *Social Function* is explained by 2 indicator variables (S_1 and S_2) and Emotional well-being is explained by 4 indicator variables (EM_1, EM_2, EM_3 and EM_4). The factor loadings of *Physical Function* with PF_1, PF_2, PF_4, PF_5, PF_6, PF_7 and PF_8 were respectively 0.998, 0.661, 1.00, 0.573, 0.888, 1.004 and 1.00. All these factor loading were statistically significant (P< 0.01). The factor loadings of *General Health* with GH_1, GH_3 and GH_5 were 1.340, 1.00 and 0.943 respectively. The factor loadings of *Social Function* with S_1 and S_2 were -0.607 and 1.00 respectively and the factor loadings of Emotional well-being with EM_1, EM_2, EM_3 and EM_4 were 0.825, 0.982, -0.507 and 1.00 respectively. All the factor loadings were found to be statistically significant (P<0.01). The details of the path analysis and factor loadings are given in Figure-2

Table-6: Factor Loadings (Regression Weights) of second order SEM

Indicator variable/ Latents			Estimate	S.E.	C.R.	P
Physical Function	<---	Physical Health	1.000			
General Health	<---	Physical Health	-1.004	0.078	-13.321	***
Emotional well-being	<---	Mental Health	1.000			
Social Function	<---	Mental Health	0.928	0.076	12.263	***
PF_8	<---	*Physical Function*	1.000			
PF_7	<---	*Physical Function*	1.004	.005	194.844	***
PF_6	<---	*Physical Function*	.888	.027	32.555	***
PF_5	<---	*Physical Function*	.573	.027	21.263	***
PF_4	<---	*Physical Function*	1.000	.007	137.721	***
PF_2	<---	*Physical Function*	.661	.031	21.090	***
PF_1	<---	*Physical Function*	.998	.009	112.440	***
EM_3	<---	Emotional Well being	-.507	.046	-10.929	***
EM_2	<---	Emotional Well being	.982	.042	23.624	***
EM_1	<---	Emotional Well being	.825	.052	15.948	***
S_2	<---	*Social Function*	1.000			
S_1	<---	*Social Function*	-.607	.042	-14.375	***
GH_3	<---	*General Health*	1.000			
GH_1	<---	*General Health*	1.340	.087	15.438	***
GH_5	<---	*General Health*	.943	.033	28.423	***
EM_4	<---	Emotional Well being	1.000			

***Statistically significant

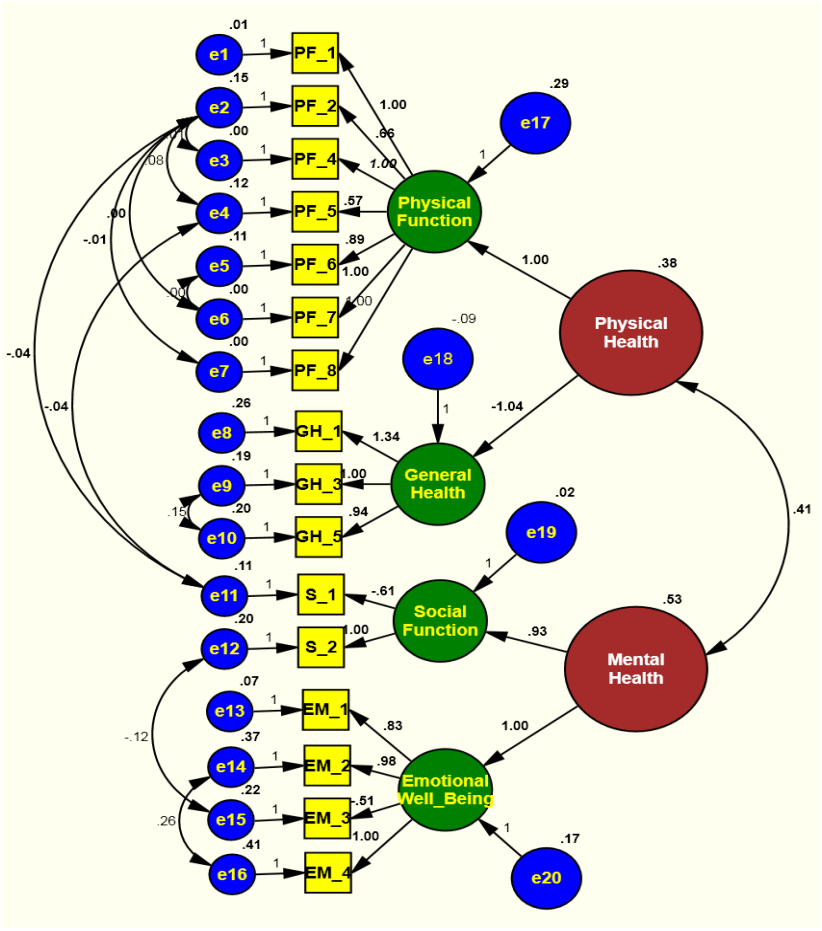

Figure-2: Second order factor loadings in SEM (Unstandardised Estimates)

The standardized regression weights of the second order SEM are given in Table-7. The Physical Health latent was described by two first order latents *Physical Function* and *General Health* and the *Mental Health* latent was described by two first order latents *Social Function* and *Emotional Well being*. The standardized regression weights of Physical Health with *Physical Function* and *General Health* were 0.754 and -1.138 and Mental Health with Emotional well-being and *Social Function* were 0.873 and 0.983 respectively. The standardized regression weights of *Physical Function* with PF_1, PF_2, PF_4, PF_5, PF_6, PF_7 and PF_8 were respectively 0.994, 0.814, 0.997, 0.803, 0.906, 1.00 and 0.997. The standardized regression weights of *General Health* with GH_1, GH_3 and GH_5 were 0.832, 0.795 and 0.767 respectively. The standardized regression weights of *Social Function* with S_1 and S_2 were -0.782 and 0.837 respectively and the standardized regression weights of *Emotional Well-being* with EM_1, EM_2, EM_3 and EM_4 were 0.937, 0.805, -0.668 and 0.792 respectively. All these factor loadings were found to be statistically significant (P<0.001).

Table-7: Standardized Factor Loadings (Regression Weights) of second order SEM

Observed variables/ latents			Estimate
Physical Function	<---	Physical Health	0.754
General Health	<---	Physical Health	-1.138
Emotional Well being	<---	Mental Health	0.873
Social Function	<---	Mental Health	0.983
PF_8	<---	*Physical Function*	.997
PF_7	<---	*Physical Function*	1.000
PF_6	<---	*Physical Function*	.906
PF_5	<---	*Physical Function*	.803
PF_4	<---	*Physical Function*	.997
PF_2	<---	*Physical Function*	.814
PF_1	<---	*Physical Function*	.994
EM_3	<---	Emotional Well being	-.668
EM_2	<---	Emotional Well being	.805
EM_1	<---	Emotional Well being	.937
S_2	<---	*Social Function*	.837
S_1	<---	*Social Function*	-.782
GH_3	<---	*General Health*	.795
GH_1	<---	*General Health*	.832
GH_5	<---	*General Health*	.767
EM_4	<---	Emotional Well being	.792

The covariance between the second order latents, *Physical Heal*th and *Mental Health* was 0.411 and it was found to be statistically significant (P<0.001). It was also observed that there was significant covariance between the measurement errors.

Table-8: Model Fit indices of the Third order Structural Equations Model

Fit Indices	Results
Chi-square/degree of freedom (x2/d.f.)	2.236
Comparative Fit index (CFI)	0.981
Goodness of Fit Index (GFI)	0.900
Normated Fit Index (NFI)	0.967
Incremental Fit Index (IFI)	0.981
Tucker Lewis Index (TLI)	0.975
Root mean square error of approximation (RMSEA)	0.072

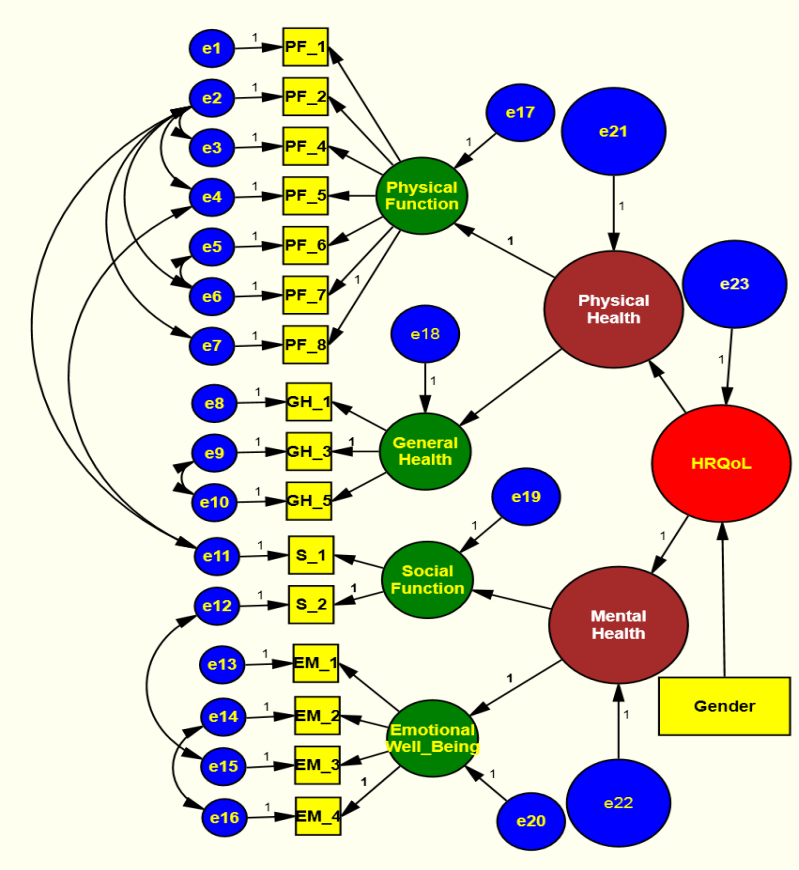

Figure- 3: Third order SEM structure.

The structure of the third order SEM is given in Figure-3 and the model fit indices of the second order SEM are given in Table-8. The third order factor is HRQoL with the second order factors as *Physical Health* and *Mental Health*. The relationship of the socio-demographic factors with HRQoL is also probed. The socio-demographic factors considered for the model was age, gender, education status and income and among theses only with gender the model shows good fit. The value of $\frac{\chi 2}{df}$ for this third order SEM was 2.236, Comparative Fit Index CFI is 0.981, Goodness of fit index IS 0.900, Normative fit Index (NFI) IS 0.967, Incremental fit Index (IFI) is 0.981, Tucker Lewis Index (TLI) is 0.975 and Root mean Square Error of Approximation (RMSEA) is 0.072. This shows that the third order SEM in Figure-3 shown good fit as per all these fit indices.

The unstandardized estimates of the third order SEM (regression weights) are given in Table-9. This model consists of 16 indicator variables in 4 first order latents (*Physical Functions, General Health, Social Functions and Emotional Well-being*) and two second order latents (*Physical Health* and *Mental Health*) and one third order latent HRQoL. The *Physical Health* latent was described by two first order latents *Physical Function* and *General Health* and the *Mental Health* latent was described by

two first order latents *Social Function* and *Emotional Well being*. The third order latent HRQoL was described by the two second order latents such as *Physical Health* and *Mental Health*. The socio demographic and clinical characteristics such as age, gender, marital status, education status, type of house were considered as observed exogenous variables. The third order SEM was found to be good fit with gender as observed exogenous variables. The factor loading between the latents *Physical Health* and HRQoL was 1.767 and it was not found to be statistically significant even though the overall model shows good fit. The factor loading between the observed exogenous variables gender was -0.04 and also not found to be statistically significant even though the overall model shows good fit. The factor loadings between all other latents and observed variable with latent were found to be statistically significant.

Table-9: Factor Loadings (Regression Weights) for Third order SEM

Observed variables/ latents			Estimate	S.E.	C.R.	P
HRQoL	<---	Gender	-.040	.106	-.374	.709
Physical Health	<---	*HRQoL*	*1.767*	*3.139*	*.563*	*.573*
Mental Health	<---	*HRQoL*	*1.000*			
Physical Function	<---	*Physical Health*	*1.000*			
General Health	<---	*Physical Health*	*-1.048*	*.079*	*-13.277*	***
Emotional Well Being	<---	*Mental Health*	*1.000*			
Social Function	<---	*Mental Health*	*.930*	*.076*	*12.255*	***
PF_8	<---	*Physical Function*	*1.000*			
PF_7	<---	*Physical Function*	*1.004*	*.005*	*194.869*	***
PF_6	<---	*Physical Function*	*.888*	*.027*	*32.552*	***
PF_5	<---	*Physical Function*	*.574*	*.027*	*21.278*	***
PF_4	<---	*Physical Function*	*1.000*	*.007*	*137.709*	***
PF_2	<---	*Physical Function*	*.662*	*.031*	*21.097*	***
PF_1	<---	*Physical Function*	*.998*	*.009*	*112.430*	***
EM_3	<---	*Emotional Well-Being*	*-.507*	*.046*	*-10.927*	***
EM_2	<---	*Emotional Well-Being*	*.983*	*.042*	*23.621*	***
EM_1	<---	*Emotional Well -Being*	*.825*	*.052*	*15.930*	***
S_2	<---	*Social Function*	*1.000*			
S_1	<---	*Social Function*	*-.608*	*.042*	*-14.414*	***
GH_3	<---	*General Health*	*1.000*			
GH_1	<---	*General Health*	*1.341*	*.087*	*15.424*	***
GH_5	<---	*General Health*	*.945*	*.033*	*28.479*	***
EM_4	<---	*Emotional Well-Being*	*1.000*			

***Statistically significant

The standardized regression weights of the Third order SEM are given in Table-10.

Table 10: Standardized Factor Loadings (Regression Weights) for Third order SEM

Observed variables/ latents			Estimate
HRQoL	<---	Gender	-.040
Physical Health	<---	HRQoL	1.381
Mental Health	<---	HRQoL	.660
Physical Function	<---	Physical Health	.753
General Health	<---	Physical Health	-1.140
Emotional Well Being	<---	Mental Health	.872
Social Function	<---	Mental Health	.985
PF_8	<---	*Physical Function*	.997
PF_7	<---	*Physical Function*	1.000
PF_6	<---	*Physical Function*	.906
PF_5	<---	*Physical Function*	.803
PF_4	<---	*Physical Function*	.997
PF_2	<---	*Physical Function*	.814
PF_1	<---	*Physical Function*	.994
EM_3	<---	Emotional Well-Being	-.668
EM_2	<---	Emotional Well-Being	.805
EM_1	<---	Emotional Well-Being	.937
S_2	<---	*Social Function*	.836
S_1	<---	*Social Function*	-.783
GH_3	<---	*General Health*	.794
GH_1	<---	*General Health*	.832
GH_5	<---	*General Health*	.768
EM_4	<---	Emotional Well-Being	.792

DISCUSSION & CONCLUSION

The present study demonstrated the Structural Equation Model of Health Related Quality of Life among filarial lymphoedema patients. This model was developed to identify the complex relationship between different items and domains in the HRQoL. HRQoL is the perception of the patients/individuals regarding their well being in their physical, mental and social aspects of their daily life. The items or the domains of HRQoL are inter-related and this relations and complex in nature. The domains of HRQoL which are the constructs/latents cannot be measured directly and the conventional statistical methods are not very efficient in

bringing the relationships of these variables more effectively.

The model initiated with the conceptual model developed by Reed PJ *et al* 2000 for SF-36 instrument. This conceptual model consists of 8 latent variables (*Physical Function, Role Physical, Role Emotional, Body Pain, Vitality, Social Function, General Health and Mental function (emotional well-being)*) with 35 indicator variables. The *Physical Function* corresponds to 10 measured variables, Role Physical corresponds to 4 measured variables, Role Emotional corresponds to 3 measured variables, Body Pain corresponds to 2 measured variables, Vitality corresponds to 4 measured variables, Emotional well-being corresponds to 5 measured variables, *Social Function* corresponds to 3 measured variables and *General Health* corresponds to 5 measured variables. However this conceptual model was not fitting well with the data of the HRQoL among lymphoedema patients. The model was modified by eliminating some of the measured variables whose factor loadings were found to be very poor. Modification indices were used to modify the model and a model with 4 latent variables with 16 indicator variables were developed. The first order latent variables are *Physical Function* with 7 measured variables (PF_1:Vigorous activities; PF_2: Moderate activities; PF_4: Climbing several flights of stairs; PF_5: Climbing one flight of stairs ; PF_6: Bending, kneeling or stooping; PF_7: Walking more than a mile ; PF_8: Walking several blocks), *General Health* with 3 measured variables (GH_1: Health in general; GH_3: healthy anybody I know; GH_4: Expect my health to get worst), *Social Function* with 2 measured variables (SF_1: Interference with normal social activities; SF_2: amount of time that has interfere) and Emotional well-being with 4 measured variables (EM_1: nervousness ; EM_2: feeling so down and nothing could cheer up; EM_3: Feeling calm and peaceful; EM_4: feeling down hearted and blue).

The model was developed in two stages as, firstly confirmatory factor analysis (CFA) was used to describe the relationships between the latent constructs such as *Physical Function, General Health, Social Function* and Emotional well-being with their measured variables (measurement model). Unstandardized and Standardized factor loadings were calculated for all the indicators (the higher, the better). Then, SEM was performed to test the hypothesized relationships among all latent constructs (structural model). The goodness of fit of the model were assessed by using all the commonly used fit indices of SEM such as $\frac{\chi 2}{df}$, Comparative Fit Index (CFI), Root Mean Square Error of Approximation (RMSEA) and the Tucker Lewis Index (TLI), the Normated Fit Index (NFI), Incremental Fit Index (IFI), and Goodness of Fit Index (GFI).

The first order SEM developed with 4 latents and 16 measured variables has shown good fit as per the fit indices. The estimate of the fit indices were $\frac{\chi 2}{df}$is 2.289, Comparative Fit Index CFI is 0.983, Goodness of Fit index GFI is 0.905, Normative fit Index (NFI) is 0.971, Incremental fit Index (IFI) is 0.983, Tucker Lewis Index (TLI) is 0.977 and the Root mean Square Error of Approximation (RMSEA) is 0.074. This suggests that the model shows good fit and all the estimates of the regression weights were found to be statistically significant ($P<0.01$). The model developed in the present study was slightly different from the conceptual model suggested for SF-36 by Reed PJ et al in terms of the number of latent and measured variables. The probable reason for this could be due to the level of sufferings in different aspects of health will be different for different health conditions. Lymphatic filariasis is chronic and disfiguring diseases which are irreversible in nature. This disease manifesting as different health states causes long-term suffering and morbidity as well as high physical, mental and psychological and social burden. The

patients were also facing high level of stigma and discrimination and the psychological and social stigma associated with disease are immense (WHO 1998). This disease adversely affected marriageability and marital life of the patients. Therefore the perception of the patients in different aspects of HRQoL may different when compared to other diseases. The conceptual model suggested by *Reed PJ et al* 2000 may not be universally true and need to be modified according to the disease conditions. The social and cultural settings may also play an important role in the relationship between the variables in the HRQoL studies. Since the relationship of variables in the HRQoL may vary according to the disease conditions and therefore Disease specific SEM for HRQoL has to be developed to understand the interrelationship of the variables more effectively. The SEM model developed in this study will be useful for modeling the HRQoL of diseases which are similar to lymphatic filariasis.

The present study was also developed a SEM with second order latents. The second order latents are; *Physical Health* with the corresponding first order latents *Physical Function* and *General Health* and *Mental Health* with corresponding latents *Social Function* and Emotional well being. The second order SEM has also shown good fit and the estimates of the fit indices are; $\frac{\chi 2}{df}$= 2.342, Comparative Fit Index CFI = 0.982, Goodness of Fit index GFI = 0.904, Normative fit Index (NFI) = 0.970, Incremental fit Index (IFI) = 0.982, Tucker Lewis Index (TLI) = 0.976 and the Root mean Square Error of Approximation (RMSEA) = 0.075 with statistically significant regression weights. This suggests that the second order SEM also fits well and the estimates of the fit indices are almost similar to the fit indices in single order SEM.

The third order Structural Equations Model was also developed with HRQoL as the third latent and the associated second order latents are *Physical Health* and *Mental Health*. The relationship of third order latent with the exogenous observed variables (age, gender, marital status, education status, type of house) was also attempted. Even though the model shows good fit, the factor loading between the third order latent and gender which is the exogenous observed variable was not found to be statistically significant.

The present study demonstrated structural equation modeling with first order, Second order and Third order latents for HRQoL of patients with lymphoedema. This model was developed from the HRQoL data from filarial lymphoedema patients and it is novel among lymphoedema patient in our population. This model is highly useful to understand the inter relationship of the variables related to different health domains and it will help in the planning and implementing a comprehensive morbidity management program to improve the HRQoL in lymphatic filariasis patients. The SEM has lot of potential but it was less explored in the field of epidemiology and health research and it could be due to the complexity of the model. The relationships between the variables in the biomedical sciences are very complex in nature and certain aspects, which are constructs, cannot be measures directly. Therefore the SEM is a better statistical model in biomedical sciences to explore those relationships more effectively. The present model has not considered the mediation effect of the variables with any of the latents. Further studies are required to assess the mediation effect of different clinical and social factors with the latents and it will be further useful in implementing the morbidity management programme according to the characteristics of the patients.

ACKNOWLEDGEMENT

The authors are grateful to the Director, Dean (Research) and Dean (Academics) of Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), Pondicherry for their constant support and encouragement. We express our sincere thanks to the patients who participated in this study.

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How to cite this article: Harichandrakumar KT, Kumaran M. Structural equation modeling of health related quality of life of lymphatic filariasis patients. Int J Health Sci Res. 2018; 8(7):245-258.

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