ORIGINAL ARTICLE

USING THYPRO 39 SCALE FOR PREDICTING THE QUALITY OF LIFE IN HYPOTHYROID PATIENTS AT LADY READING HOSPITAL

Mujeeb Ur Rehman, Sobia Sabir Ali, Nawaz Khan, Ibrar Ahmad, Irfan Ullah

Diabetes and Endocrinology Division, MTI Lady Reading Hospital, Peshawar-Pakistan

Background: Thyroid disorders are the second most common of the endocrine diseases. With regards to Hypothyroidism, it has a slow indolent course over the years, before its diagnosis. Most of the patient, on adequate treatment with biochemical euthyroid status, have generalised symptoms that affect their quality of life. Several tools to assess quality of life in thyroid disorders have been validated and recommended for use for those patients in clinical follow ups. ThyPRO 39 is one of a recently developed thyroid-specific quality of life (QoL) questionnaires applicable to patients with benign thyroid disorders (BTD). The purpose of this study was to predict the thyroid-related quality of life (QoL) instrument ThyPRO 39 in patients with Hypothyroidism, who were rendered euthyroid with thyroid replacement therapy prior to the administration of study tool and to assess the internal reliability of this scale in our population. **Methods:** A sample of 52 patients undergoing maintenance treatment for Hypothyroidism who visited the outpatient Endocrinology clinics at Lady Reading Hospital was studied. They were interviewed for their baseline demographic details and details on ThyPRO 39 questionnaire were recorded after a written informed consent. The data was entered and analysed using SPSS 25. The Internal reliability of the ThyPRO 39 scale was assessed for multi-item scales using Cronbach's alpha coefficient. **Results:** The ThyPRO 39 scale demonstrated good response across the whole range of QoL aspects in patients with hypothyroidism. Internal reliability for ThyPRO 39 scale was satisfactory. Cronbach's Alpha in our study was 0.928, which was comparable to the results of other studies. **Conclusion:** We suggest implementing this measurement tool as a patient-reported outcome in clinical studies in our indigenous population and further more to utilise it as a screening tool for QoL in clinical management of Hypothyroidism in our routine medical consultations.

Keywords: Thyroid disease; Hypothyroidism; Quality of life; ThyPRO 39 questionnaire.

Citation: Rehman M, Ali SS, Khan N, Ahmad I, Irfanullah. Using thyPRO 39 scale for predicting the quality of life in hypothyroid patients at Lady Reading Hospital. J Ayub Med Coll Abbottabad 2020;32(3):396–400.

INTRODUCTION

Thyroid diseases are common endocrine disorders, particularly with predilection in females. There is a spectrum of thyroid dysfunction from hypothyroidism to hyperthyroidism with a variety of nonspecific and systemic afflictions involving most of the body systems. However, in spite of its clear recognition, the diagnosis of thyroid diseases is delayed in many instances. The treatment of these disorders is much rationalized, with most of the patients having a decent outcome. In some cases, despite adequate therapy, the patients per se continue to remain symptomatic with poor quality of life.[1] There are various symptoms of hypothyroidism: physiological and psychological, that can profoundly affect the quality of life. Although the clinical features of hypothyroidism are addressed in great details, inadvertently the associated psychosocial affects may not be addressed as vigorously as appropriate.[2,3]

Patients with hypothyroidism if treated appropriately respond effectively to the treatment improvement of the symptoms to a greater extent. However, some of the patients' having a fair biochemical control persists to have symptoms of varying extent with obvious impairment of quality of life.[4] There is evidence indicating inability of levothyroxine (LT4) to render the cells totally euthyroid and that may be the confounding factor for poor psychological wellbeing and cognitive decline in hypothyroid patients with apparent euthyroid status.[5] Different studies have exhibited the fact that there is poor quality of life even with adequate treatment in hypothyroid patients but no valid explanation for that has been generated.[4]

To further explore such concerns in health-related quality of life with hindsight to improve treatment efficacy, patient reported outcomes have been recorded. Those efforts led to development of ThyPRO Scale 39 by Torquil Watt for benign thyroid disorders that explored the individual thyroid disorders that co-existed simultaneously (e.g., goitre and hyperthyroidism) or if the treatment of one disease entity may lead to another (e.g., removal of a goitre leading to hypothyroidism). In brief the content of the ThyPRO addressed the impact of all

benign thyroid diseases and could be utilized in daily clinical practices.[6]

In Pakistan, we do not have any specified tools for exploring health related quality of life in patients with thyroid disorders. With that consideration this study was designed to use the comprehensive Thyroid Specific Patient Reported Outcome 39 (ThyPRO 39) questionnaire measuring quality of life (QoL).[7] A thorough review of literature suggested no indigenous study ascertaining the QoL among hypothyroid patients in euthyroid state. This study was first of its kind in our local set up. The results generated from this study will be shared with other local health professionals and relevant authorities to formulate recommendations about effective management of QoL of such persons and similarly to ignite further research on this untended issue in our community.

MATERIAL AND METHODS

It was a cross sectional study, conducted from July 2018 to January 2019, at the Outpatient Clinics of Diabetes and Endocrinology Division, MTI Lady Reading Hospital Peshawar. Non-probability consecutive sampling was done and 52 patients were enrolled for study after a written informed consent prior to inclusion in study. Ethical approval was taken ahead of the study from Institutional Ethical Board of the hospital. The main purpose of the study was to explore QoL in hypothyroid persons who were rendered euthyroid biochemically on optimal thyroid replacement therapy with the help of ThyPRO 39 scale and to ascertain the extent of poor QoL in our population. The patients with confirmed hypothyroidism were included, with an age range of 18–60 years. The causes of hypothyroidism were categorized as primary hypothyroidism, post thyroidectomy, post radioactive iodine therapy, moreover they were rendered euthyroid on maintenance dose of Thyroxine for at least 6 months, that was confirmed and documented in their previous medical record. The patients who had underlying comorbidities such as chronic kidney disease, chronic liver disease, congestive cardiac failure, major psychiatric disorders, malignant diseases, immunosuppressive medications, pregnancy and lactation, acute medical conditions like myocardial infarction, cerebrovascular accident, and major surgery within the past 6 months were excluded.

Patients were interviewed in the Outpatient Endocrinology Clinics and demographic details, medical history and examination, investigation reports were recorded on a questionnaire and included; gender, age, education level, marital status, current employment status, BMI, menopausal status in women, causes of hypothyroidism etc. Furthermore, the details pertaining to quality of life were noted on ThyPRO-39 questionnaire. The Permission to use that scale in our study was sought from the authors, prior to undertaking that study. The patients completed the ThyPRO 39 scale in the presence of data collector, who dealt with HRQoL assessments, so there were no missing data, nor reading or writing problems or otherwise it was filled by the data collector, who was well versed with the scale.

ThyPRO39 is a short version of the ThyPRO consisting of 39 items grouped in 11 scales and one single item impact on overall QoL. Approximately 15-20 minutes were required to answer the scale. Each item was rated by the patient on a five-point Likert scale: 0 — not at all; 1 — a little; 2 — some; 3 — quite a bit; 4 — very much/completely. The scales were derived by averaging and linearly transforming these item scores into their respective 0–100 scale score, increasing scores indicating decreasing QoL (i.e., more symptoms or greater impact of disease) and lower scores indicating better QoL. Data was analysed using SPSS 25.0. Analysis of the basic variables was carried out using descriptive statistics. Cronbach Alpha Reliability was also calculated. Chi square test was applied to find out the gender and institutional differences and BMI and residential differences of patients among hypothyroid symptoms, quality of life, and composite scores of ThyPro39. Pearson correlation test was done to correlate the inter-correlation between ThyPRO39 and its subscales and relationship between ThyPRO39 and causes of hypothyroidism. The results of all the test of significance were considered significant at $p \leq 0.05$ level.

RESULTS

The mean age of the study participants (n=52) was 35.80±10.96 years with the age range of 19–60 years. The Cronbach's Alpha reliability of the ThyPRO39 was 0.928. Table-1 outlines data in this regard. Majority of the patients had better quality of life (n=29, 55.8%), fewer had symptoms of hypothyroidism (n=15, 28.8%) and half of the patients had Composite symptoms (n=27, 51.9%). Details are given in Table-2. Using Pearson correlation analysis between Quality of life, hypothyroidism and Composite scale of ThyPro39 is given in table-3.

Inter-scale correlation between hypothyroidism, quality of life and Composite score showed a positive correlation between hypothyroid symptoms, quality of life with composite scores of ThyPro39 ($p<0.000$), but showed non-significant relationship between quality of life and hypothyroid symptoms (Table-4).

There was no significant difference found between male and female patients with Hypothyroidism ($p=0.379$), similarly no significant gender difference was found on patient's Quality of life ($p=.086$). Patients

on composite scores of ThyPRO39 showed a non-significant gender difference (p=0.766). Similarly, a non-significant difference was found in patients of Urban and Rural areas with Hypothyroidism, quality of life and composite scores of ThyPRO39, however significant difference was found between Body Mass Index (BMI) and Composite scale of ThyPRO39 (p=0.038), whereas non-significant difference was found between quality of life, hypothyroidism and BMI. Similarly, no significant educational status differences were found with hypothyroid symptoms, quality of life and composite scale of ThyPRO39.

Table-1: Basic demographic details of the study (n=52)

Variables		Frequencies (%)
Gender	Male	7 (13.5)
	Female	45 (86.5)
Area of Residence	Urban	37 (71.2)
	Rural	15 (28.8)
Educational Status	Illiterate	15 (28.8)
	Higher secondary	22 (42.3)
	Graduation	15 (28.8)
Body Mass Index	Normal weight	17 (32.7)
	Overweight	15 (28.8)
	Obese	20 (38.5)
Pre/post-Menopausal	Pre-menopausal	38 (73.1)
	Post-menopausal	14 (26.9)
Causes of Hypothyroidism	Hashimoto Thyroiditis	39 (75)
	Post RAI/Post Thyroidectomy	13 (25)

Table 2: Basic details of ThyPro 39 and its sub-scales (n=52)

Variables	Mean (SD)	High/Low
Hypothyroid Symptoms	Mean 3.93±4.94	Low= 37 (71.2%) High= 15 (28.8%)
Quality of Life	Mean 55.29±24.9	Low= 29 (55.8%) High= 23 (44.2%)
Composite Scale	Mean 33.41±10.6	Low = 27 (51.9%) High = 25 (48.1%)
Goitre	Mean 4.35±5.47	Low = 42 (80.8%) High = 10 (19.2%)
Hyperthyroid	Mean 11.62±8.32	Low = 24 (46.2%) High = 28 (53.8%)
Eye	Mean 5.67±9.52	Low = 37 (71.2%) High = 15 (28.8%)
Tiredness	Mean 45.37±19.7	Low = 25 (48.1%) High = 27 (51.9%)
Cognition	Mean 33.15±20.07	Low = 29 (55.8%) High = 23 (44.2%)
Anxiety	Mean 42.88±24.38	Low = 26 (50%) High = 26 (50%)
Depression	Mean 41.25± 23.24	Low = 23 (44.2%) High = 29 (55.8%)
Emotional Susceptibility	Mean 31.40±17.72	Low = 28 (53.8%) High = 24 (46.2%)
Social Life	Mean 17.48±17.72	Low = 24 (46.2%) High = 28 (53.8%)
Daily life	Mean 30.10±21.4	Low = 25 (48.1%) High = 27 (51.9%)
Cosmetic complaints	Mean 28.77±17.4	Low = 31 (59.6%) High = 21 (40.4%)

Table-3: Summary of Pearson correlation to estimate the correlation and strength of linear relationship between Quality of life, hypothyroid and Composite scale of ThyPro39 with causes of thyroid (n=52)

Measures	I	II	III	IV
Hypothyroid Symptoms	-			
Quality of Life	.091 (.523)	-		
Composite Scale	.353* (.010)	.782** (.000)	-	
Causes of Hypothyroid	.169 (.231)	.011 (.937)	.047 (.742)	-

**Correlation is significant at the 0.01 level (2-tailed).
*Correlation is significant at the 0.05 level (2-tailed).

Table-4: Summary of Inter-scale correlation to estimate the correlation and strength of linear relationship between Hypothyroid symptoms, quality of life and composite scale of ThyPro 39 (n=52)

Measures	I	II	III
Hypothyroid Symptoms	-		
Quality of Life	.091 (.523)	-	
Composite Scale	.353* (.010)	.782** (.000)	-

**Correlation is significant at the 0.01 level (2-tailed).
*Correlation is significant at the 0.05 level (2-tailed).

DISCUSSION

Hypothyroidism is often diagnosed, and subsequently treated, due to health-related quality of life (HRQL) issues. The impact of hypothyroidism on QoL is gaining more attention by health care teams and could be appreciably detected by patient reported outcomes in the form of questionnaires. Although in the past such trends have not been instituted to assess QoL in a longitudinal design. The ThyPRO questionnaire has demonstrated good response across the whole range of QoL aspects in patients with hypothyroidism since it is only thyroid specific rather than having more generic details. It has been tested in many centres across the globe for its reliability and validity.[8,9]

In our study we found that majority of the study participants were female that is about 86.5%. That was not an un-anticipated finding, since the prevalence of thyroid disorders is much greater in females with a ratio of 4:1. Likewise most of those females were in the reproductive age group and were having their menstrual cycles and only 26.9% were post-menopausal. There were higher numbers of participants from the urban localities and with higher secondary education. There was another noticeable trait, that most of the participants were obese in terms of their BMI. That could be possibly and partly due to the tendency of weight gain in hypothyroidism, even though our enrolled patients were all

euthyroid biochemically. With regards to the cause of hypothyroidism, about 75% of the participants had auto-immune thyroiditis.

Cronbach Alpha in our study was 0.928, that was comparable to the results of Watt *et al* who reported a Cronbach`s alpha above 0.9.[8] That indicated that the scale was highly consistent and reliable. Generally, when Cronbach's Alpha exceeds 0.70, reliability is confirmed. Cronbach's alpha to be greater than .90 is indicative of a perfect result.[10]

Likewise, a Serbian study showed Cronbach alpha the range 0.83–0.95.[11] Our value however was slightly higher than a Romanian study, which assessed the reliability, and the cross-cultural validity.[12] In their study the range of reliability was found to be from 0.78 to 0.87. All these studies including ours although with slight differences, do confirm the reliability of ThyPRO. Although majority of the studies are done on ThyPRO scale rather than its shorter version, which we had used. Only one a study conducted on the Chinese population had failed to confirm the reliability with a value below 0.7.[13]

The predominant cause for hypothyroidism was Hashimoto Thyroiditis in our study. In comparison to our findings, the Romanian study[12] had a good proportion of patients with Hashimoto's disease, whereas in a Danish study majority of patients had non-toxic goitre. Hashimoto's thyroiditis has also been described as the commonest cause in a Greek Study.[14]

Our study showed that majority of the hypothyroid patients irrespective of the underlying cause once were rendered euthyroid, exhibited a better quality of life on ThyPRO. That emphasizes the relevance as well as dominant role of attaining normal hormone profile in the course of treatment. In the Serbian study[11], a significant inverse relationship was found between QoL scores and hormonal status.

Inter-scale correlation between hypothyroidism, quality of life and Composite score showed a significantly positive correlation between hypothyroid symptoms, quality of life with composite scores of ThyPro39. Strength of the study is that data was collected exercising rigor, however its weakness is a small sample size.

CONCLUSION

In conclusion, we found that ThyPRO has very good response to treatment across the range of benign thyroid diseases. We recommend it use in future clinical studies, trials, as well as in daily clinical practice. Such studies should further evaluate the relationships between clinical variables and Quality of life (QOL), as measured by ThyPRO. We recommend using this instrument if evaluations of changes and comparisons of differences in changes, as e.g., in randomized clinical trials, are important.

AUTHORS' CONTRIBUTION

MUR: Conception of study design, acquisition of data, data compilation and analysis, final approval of manuscript. SSA: Conception of study design, analysis and interpretation of data, drafting the work and revising and final approval of manuscript. NK: Final approval of manuscript IA: Final approval of manuscript. MRS: Analysis and interpretation of data, drafting the results. IU: Acquisition of data, final approval of manuscript

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Submitted: July 13, 2020	*Revised: --*	*Accepted: July 21, 2020*

Address for Correspondence:

Dr Sobia Sabir Ali, Divsional Head and Assistant Professor, Diabetes and Endocrinology, MTI, Lady Reading Hospital, Peshawar-Pakistan
Cell: +92 333 924 7104
Email: drsobias@hotmail.com