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Health-related quality of life among pulmonary tuberculosis patients in Pakistan

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Abstract

Purpose Health-related quality of life (HRQoL) of pulmonary TB patients has not been assessed in Pakistan. We assessed self-reported HRQoL of pulmonary TB patients in Karachi, Pakistan utilizing the EQ-5D and EQ-VAS prior to, during, and after completion of TB treatment.

Methods We enrolled 226 pulmonary TB patients in a longitudinal cohort study. Health-utility scores were estimated by the EQ-5D five dimensions and the EQ-Visual Analogue Scale (VAS) at baseline (month 0) and each monthly follow-up visit until treatment completion at month 6. Repeated-measures ANOVA was used to investigate effect of time into treatment on EQ-5D and EQ-VAS scores.

Results EQ-5D health utility and EQ-VAS scores increase with treatment progression. For the enrolled TB patients, the mean EQ-5D utility scores more than doubled from 0.43 to 0.88, $p < .001$, effect size $\eta^2 = 0.40$ from treatment initiation to treatment completion.

Conclusion Perceived HRQoL of TB patients improves with treatment progression. This can inform targeted treatment plans as well as TB policy and funding for high-burden countries.

Keywords Tuberculosis · Public health · Health-related quality of life · EQ-5D

Introduction

Tuberculosis (TB) is a global public health concern with approximately 10.4 million new TB cases worldwide and 1.4 million TB deaths in 2016 [1]. Traditionally, TB research has focused on clinical markers and drug therapy as TB is curable with adherence to the prescribed 6-month antibiotic drug regimen for new patients [2]. The first 2 months of treatment mark the intensive phase of treatment and the following 4 months mark the continuation phase [1]. The prolonged treatment period can have detrimental effects on the patient's health-related quality of life (HRQoL). Reduced HRQoL has been attributed to symptoms of TB, side effects of drug therapy, societal stigma, economic costs, anxiety, and depression during the treatment process [3].

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TB patients report worse HRQoL compared to control populations [4–6]. In a control study of 90 TB patients in India, the clinical population reported significantly lower mean HRQoL score on a World Health Organization Quality of Life tool than the control population [6]. Similarly in another control study of 64 TB patients using the using the Short Form SF-36 questionnaire, the patients reported lower HRQoL than the control population [5]. Longitudinal cohort studies of HRQoL assessment studies in TB patients show improvement in HRQoL scores after the intensive drug therapy period [3, 5, 7] and at treatment completion at 6 months [4]. Understanding patient's perception of health status during TB treatment can inform treatment protocol and counseling services for better treatment adherence [8].

Pakistan ranks 5th amongst the 22 countries with the highest burden of TB, approximately 518,000 new TB cases annually [1]. There has been limited research on the experience of diagnosis and treatment of TB in Pakistan. In a recent study, TB patients in Pakistan identified deficiency in treatment services rather than unwillingness to adhere to medication for failure to follow-up with treatment [3]. Whereas, another study reported access to treatment and

limited patient–clinician interaction as factors for lack of adherence to treatment [9]. Clinicians have been reported to underestimate the impact of TB diagnosis and treatment on patients' physical and psychological domains, therefore measures of patients' own perception of health can provide a more accurate picture [10]. While cross-sectional studies measuring HRQoL of TB patients in South Asia have been previously conducted [6], there have been no studies assessing longitudinal change in HRQoL with TB treatment completion in Pakistan. Improvement in HRQoL after the initial intensive period has been associated with loss to follow-up, therefore in this study treatment seekers were followed up till end of treatment assessing change during the continuation phase as well. High prevalence, limited available resources and social stigma associated with TB diagnosis in the region impacts patient's willingness to seek treatment [8, 9]. There is a need for HRQoL studies in the region which demonstrate an association between TB treatment completion and improved patient perception of health so that TB treatment planning in the region can become more patient-inclusive. This evidence can inform improvement in TB treatment provision by clinicians, counsellors, and public health professionals.

In this study, we assessed self-reported HRQoL of pulmonary TB patients in Karachi, Pakistan utilizing the EQ-5D and EQ-VAS (Urdu version) [11] prior to, during and after completion of treatment to investigate change in HRQoL during the course of TB treatment.

Methods

Study design

This was a longitudinal cohort study.

Study participants and data collection

The study took place from July 2015 to June 2016 at the outpatient TB clinic of The Indus Hospital in Karachi, Pakistan. Sample size of 226 was determined for 80% power after adjusting for attrition based on previous studies. New pulmonary tuberculosis patients between the age of 18 and 65 who could speak and read Urdu, planned to continue treatment at the clinic at the time of registration, and gave informed consent to participate before enrollment were included in the study. Before obtaining informed consent, participants were explained the purpose of the study and assured that refusal to participate would have no impact on their treatment as usual. TB patients with extra-pulmonary TB, drug-resistant TB, and other comorbid diseases were not included in the study. Extra-pulmonary TB and drug-resistant TB have different treatment courses of longer duration. Due to this, only patients diagnosed with drug-susceptible pulmonary at the clinic were approached to participate. Participants who became drug resistant over the course of treatment were excluded from the final analysis as their treatment course was changed.

Socio-demographic and clinical characteristics such as age, marital status, education status, bacteriological status, and comorbidities are collected for all new patients enrolled in the TB program at the clinic. A health-worker was trained to administer the EQ-5D and EQ-VAS. Eligible patients enrolled in the Susceptible TB program were explained the purpose and duration of the study. All participants included the study provided informed consent and completed the EQ-5D and EQ-VAS facilitated by the trained health-worker in a face to face interview at the clinic. The patient completed the form before treatment initiation, at month 2, and end of treatment (month 6).

EQ-5D (EuroQol five-dimension questionnaire)

HRQoL was assessed using the EuroQoL five-dimension questionnaire EQ-5D and the EQ-VAS as their feasibility and reliability in TB populations has been previously established [12]. The validated Urdu version of the questionnaire was obtained from the EuroQoL and the study was registered with the organization in January 2015 (ID: 7795). The survey had two parts; EQ-5D-3L provided a descriptive profile of five dimensions/questions: mobility, self-care, usual activity, pain, and anxiety. Each dimension had three levels; level 1: no problem, level 2: some problem, and level 3: extreme problem. The scores for each dimension can be combined to present a health state. For example, a response of 1 on each dimension (11111) refers to a perfect health state. The five health states of each patient can be summarized into a single health-utility value by using country-specific societal preference weights (or value sets). The health state of 11111 corresponds with a utility value of 1.0. Because the country-specific value set was not available for Pakistan, the UK-based value set was used in this study, which has also been applied in previous studies in Pakistan [13, 14].

The second part of the questionnaire, the EQ-VAS is a visual analogue scale from 0 to 100 on which the patient marked their perception of current health state with 0 being worst imaginable health state and 100 being best imaginable health state.

Ethical considerations

Approval for this study was given by the Institutional Review Board (IRB) at Interactive Research and Development (IRD) that oversees research activities at The Indus Hospital (OHRP Registration No. 00005148).

Statistical analysis

Data were analyzed using SPSS version 24 [15]. Descriptive statistics of demographic variables are provided with mean and standard deviation. Unadjusted repeated-measures ANOVA was used to compare the change in EQ-5D utility values and EQ-VAS scores of TB patients before, during, and after completing treatment (months 0, 2 and 6). The Greenhouse-Geisser F was used to adjust for violation of sphericity. Repeated-Measures ANOVA was used as we were interested in specific time-points of months 2 and 6 of TB treatment due to their clinical relevance to treatment. p value $< .05$ was considered statistically significant.

Results

A total of 226 participants completed the EQ-5D and EQ-VAS forms before starting treatment, 165 of them completed the survey again at month 2 (end of intensive phase), and 176 of them completed the surveys at month 6 (end of treatment). The overall attrition rate in the study was 22.1%. Reasons for attrition included conversion to drug-resistant TB (3.1%), failure to hand over completed forms to health workers at treatment follow-up (13.3%), transfer to another health facility (3.1%), and death (2.7%). The male to female ratio was approximately 1:1 with approximately 60% of the study population between the ages of 18 and 35 years. Of the 226 patients at baseline, 12 patients did not indicate their marital and employment status at data collection. They were included in the final analysis as it was not stratified by subgroups (Table 1).

Before treatment initiation, more than 50% of the patients reported some or extreme problems in mobility, usual activities, pain, and anxiety/depression. Extreme problems were reported by 42% of patients in usual activities and by 20% in pain and anxiety (Fig. 1). By month 2, 18% reported extreme problems in usual activities and 7% in pain and anxiety. By end of treatment, no patients reported extreme problems in mobility, self-care, pain, or anxiety and only 1% experienced extreme problems in usual activities.

The mean EQ-5D utility value increased from 0.43 before starting treatment to 0.88 at end of treatment and the EQ-VAS increased from 54.7 to 76.6 in the same time frame. Repeated-measures ANOVA showed a significant effect of time on EQ-5D utility value, F (1.62, 265.07) = 111.06, $p < .001$, $\eta^2 = 0.40$ as well as on EQ-VAS, F (1.70, 278.96) = 186.36, $p < .001$, $\eta^2 = 0.53$. Pairwise comparisons found a significant improvement from month 0 to month 2 in EQ-5D, 95% CI [0.33, 0.19]; as well as EQ-VAS scores 95% CI [12.56, 7.17] (Table 2; Figs. 2, 3).

Table 1 Demographic characteristics of TB patients enrolled at the Indus Hospital TB Clinic from June to December 2015 and eligible for this study ($N = 226$)

Characteristics	*n*	%
Sex		
Male	116	51.3
Female	110	48.7
Age in years		
18–25	85	37.6
26–35	54	23.9
36–45	46	20.4
> 46	41	18.1
Marital status		
Single	63	29.4
Married	137	60.6
Widowed/divorced	14	6.2
Employment status		
Employed	79	35.0
Unemployed	135	59.7
Bacteriological status of sputum smear		
Smear positive	172	76.1
Smear negative	54	23.9

Discussion

This is the first longitudinal cohort study to assess change in HRQoL in TB patients in Pakistan, to our knowledge. We found that TB affects physical as well as psychological domains of HRQoL, which is consistent with reports from previous results [6, 16–21]. Higher proportion of problems were reported in the physical domains compared to psychological, particularly in the usual activities and pain category, also reported previously [21, 22]. Our results show a significant improvement in EQ-5D and EQ-VAS scores with time into treatment, in keeping with previous studies [17–20]. While the greatest increase in EQ-5D scores was observed in the first 2 months of treatment, consistent with previous reports [4, 8], the EQ-5D scores continued to improve in the 4 months of the treatment continuation phase for both males and females. Although females reported lower scores before treatment initiation than males, by the end of treatment males and females reported similar scores.

Psychological domains impacted by the diagnosis and treatment of TB are understudied. Problems were reported by 55.5% of patients in the anxiety depression category before treatment initiation and 6.8% still reported some problems at the end of treatment in our study. This is comparable to a previous study in Pakistan which reported 46% of TB patients had anxiety and/or depression, and higher than the 34% average prevalence of depression and anxiety in Pakistan [23]. The same study also identified

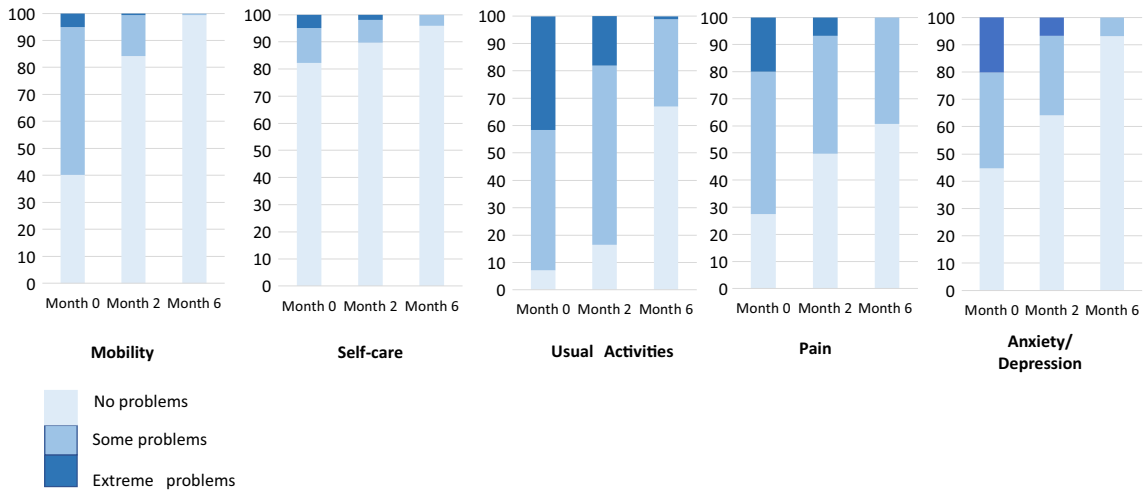

Fig. 1 Trend for the level of problems reported (%) before treatment initiation (month 0), at end of intensive phase (month 2) and at treatment completion (month 6) by TB patients enrolled in the study

Table 2 Mean EQ-5D and EQ-5D VAS scores at baseline, month 2 and end of treatment of TB patients enrolled in the study

	EQ-5D utility score	EQ-VAS
Month 0	0.43 (0.37)	54.73 (12.65)
Month 2	0.68 (0.28)	63.47 (10.41)
Month 6	0.88 (0.11)	76.56 (7.50)

Values in () denotes standard deviations

perception of greater physical symptoms as a contributing factor for psychological symptoms. These results indicate that psychological problems experienced by TB patients should be addressed as a component of standard treatment provision. It has been found that healthcare programs that include holistic assessment of social and psychological aspects of treatment in physical disorders are more likely to be successful [24].

We used EuroQol measures for HRQoL assessment [11]. HRQoL can be measured using disease specific or generic QoL measurement tools such as the EQ-5D [25]; generic tools allow for comparison of patient groups from different health conditions [12]. For example, our scores of 0.43 and 54.73 on the EQ-5D and EQ-VAS were worse in comparison to a study of diabetic patients in Pakistan, 0.47 and 64.77 [14]. This can be useful for public health policy and funding consideration by utilizing patient-reported measures to provide the evidence base for public health resource allocation. Currently in Pakistan, prioritization of resource allocation towards public health interventions is largely conducted on an ad hoc basis. The EQ-5D-3L has been previously evaluated and found to be a reliable measure of HRQoL [12]. Ceiling effects have been reported as a concern with EQ-5D [26], particularly the ceiling effect observed in the self-care category [27]. However, it has been found to be more respondent-friendly as it is time-effective and

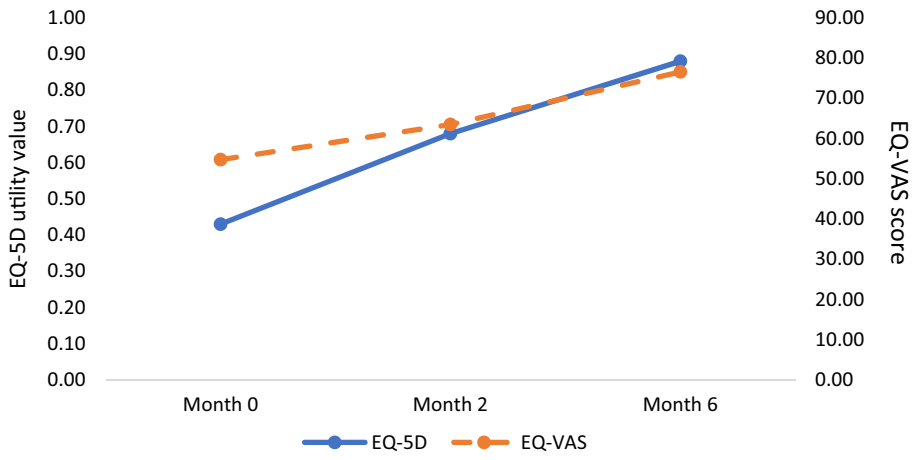

Fig. 2 Mean EQ-5D utility sores and EQ-VAS scores through course of treatment of TB patients enrolled in the study

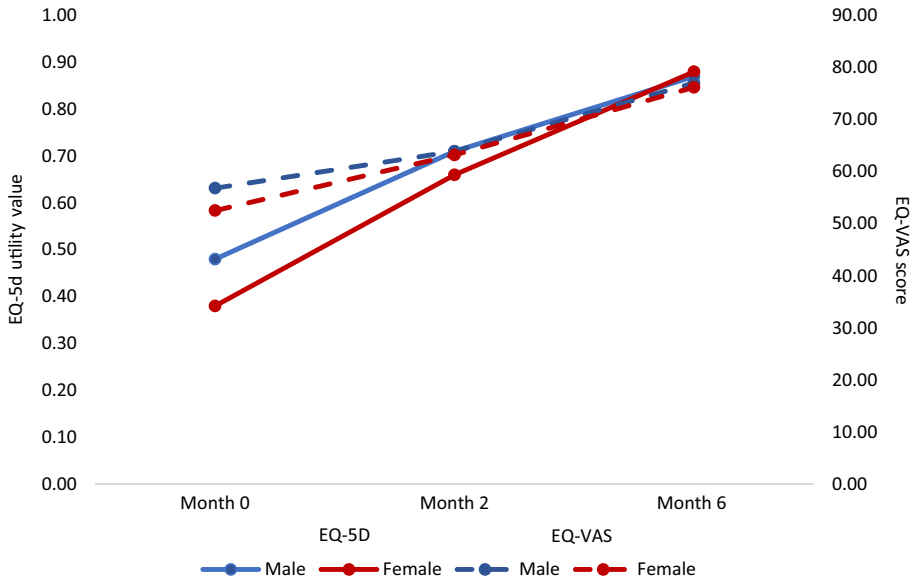

Fig. 3 Mean EQ-5D utility sores and EQ-VAS scores through course of treatment of TB patients enrolled in the study by gender

easy to comprehend compared to other HRQoL measurement tools [28]. EQ-5D also provides a single health-utility measure, which can be used for cost-effectiveness and cost-utility analysis in the future for development of public health policy and budget considerations [29]. In Pakistan, only 7% of TB funding is provided domestically [1], significant gain in quality of life associated with completion of treatment can be used to provide an evidence base to justify higher amount of government funding towards treatment interventions. As a generic HRQoL tool, the EQ-5D provides utility values which can be used to calculate Quality-adjusted life years (QALY). The QALY can be used for economic evaluation of healthcare interventions and cost-effectiveness of treatments for different public health diseases and inform public health budget considerations [30].

A strength of this study is that it was the first longitudinal assessment of change in EQ-5D scores of TB patients on treatment in Pakistan, a TB high-burden country [1]. Moreover, treatment was provided free of cost to our sample population ensuring that treatment costs would not be a deterrent for participation. Participants were ensured before each data collection that refusal to participate would not have any impact on their treatment as usual so that they would not feel obligated to participate in the study. However, there are some limitations that should be noted. First, we utilized EQ-5D health-utility value set based on the UK general population, although this has been used in previous studies in Pakistan [13, 14], there is a need to calculate utility values based on the general population in Pakistan for use in clinical studies to provide a more accurate assessment of HRQoL in future studies. Second, due to attrition, we were not able to follow-up with all the enrolled patients at baseline; 13% did not return to complete the survey at follow-up visits. Follow-up with patients who opt not to complete HRQoL surveys can inform change in HRQoL future study designs. Third, the requirement of fluency in Urdu limited the respondent pool. Many people with TB who visit the clinic come from other cities and speak regional languages and had to be excluded from the study.

Future directions

While this study focused on QoL during the treatment period, future studies with long-term follow-up in a high-burden country like Pakistan are warranted as research indicates that it can take up to 2-years post treatment for TB patients to have HRQoL scores comparable to people without TB [31]. Building on this study, future studies to identify factors associated with change in HRQoL during TB treatment in Pakistan should be undertaken. HRQoL should also be assessed in especially vulnerable populations such as children with TB and people with HIV/TB co-infection. Future studies with control group comparison of change in HRQoL of adherent patients with low adherence patients during treatment can help identify factors associated with adherence and HRQoL.

A World Health Organization report on adherence to long-term therapies identified a need to address time-points during TB treatment for targeted approach to caregiving efforts [32]. The results of this study suggest that increased vigilance at the end of the intensive phase is warranted due to rapid change in patient's perceived health state which can influence health behaviors [17, 33]. HRQoL scores can be predictive of TB treatment outcomes, monitoring HRQoL scores at the end of the intensive phase period can also help identify patients who need targeted treatment efforts for better treatment outcomes [4].

In conclusion, self-reported HRQoL improves significantly with time into treatment. This can inform current TB treatment practices as well as policy with a focused approach on the initial months of treatment by including patient-reported outcomes along with clinical outcomes to be utilized by clinicians, counsellors, and public health professional for TB-treatment planning and provision.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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