

Original**Nutritional Assessment Tools in Patients with Pulmonary Tuberculosis:
A Cross-Sectional Study**

Badder Hina Afnan¹, Sahar Soomro², Saba Mughal³, Syed Afnan Omer Ali⁴,
Madiha Patel⁵, Nadeem Ahmed⁶

¹*Dow University Hospital, Dow University of Health Sciences, Karachi, Pakistan*

²*School of Nursing and Midwifery, Dow University of Health Sciences, Karachi, Pakistan*

³*School of Public Health, Dow University of Health Sciences, Karachi, Pakistan*

⁴*Manager Information Technology, Hilal Foods. Pvt., Karachi, Pakistan*

⁵*Health Admin Referral Administrator, HESA Medical Centre, London, United Kingdom*

⁶*Tuberculosis Unit, Ojha Institute of Chest Diseases, Dow University of Health Sciences, Karachi, Pakistan*

ABSTRACT Background: Nutritional counseling is a highly recommended part of the treatment plan for Pulmonary Tuberculosis (PTB), as predominantly patients present clinically with malnourished status. However, scarce evidence exists on the prevalence of malnourishment among patients with PTB, particularly in Pakistan. This study therefore aims to report on the prevalence of malnutrition status, as documented using universal nutritional assessment tools on patients with PTB, receiving first-line drug (FLD) and second-line drug (SLD) therapies. Methods: A cross-sectional study enrolled 315 participants diagnosed with PTB, receiving FLD or SLD treatment, recruited from a tertiary-care hospital and clinic in Karachi, Pakistan. Inclusion criteria encompassed both genders, 18 to 55 years of age, with either new or relapsed PTB cases. A structured questionnaire composed of various methods for assessing nutritional parameters was conducted by a registered dietitian. The statistical analysis was carried out using SPSS, with data expressed as percentages, mean and standard deviation (SD), and statistically significant associations using p-value. Results: From 312 patients, 54.2% (n=169) were females and 61.2% (n=191) patients were on FLD therapy. Average Body Mass Index (BMI) (kg/m²) of the patients was 17.72 ± 3.15 (SD), whereas average calorie intake (kcal) of the patients was 1321.77 ± 506.19 (SD). Patients who received FLD had lower average BMI and MAMC (mm) in comparison to those on SLD. Mean differences were found to be statistically significant between both treatment groups for BMI (p-value=0.044) and MAMC (p-value= <0.001). Average BMI (p-value <0.001) and calorie intake (p-value=0.030) were significantly different when compared with the duration of treatment. Conclusion: The study reveals that patients diagnosed with PTB are presented with varying degrees of malnourishment, despite being on either drug therapy as indicated through data collected using validated tools specific for nutritional assessment. Based on the results, the extent of time on drug therapy is associated with the outcome of improvement in nutritional status in the patient.

Keywords: pulmonary tuberculosis, nutritional assessment, malnutrition, anthropometric measurements, Pakistan

INTRODUCTION

Tuberculosis (TB) has been featured as a health emergency globally over the last two decades according to World Health Organization (WHO), along with being one of the major community health concerns weighing on the developing country of Pakistan (1,2). Pakistan presently ranks 6th among 22 countries with the highest reported burden of TB worldwide, with incidence drastically escalating, of which approximately 44% of the tuberculosis burden in the Eastern Mediterranean region (1, 3). Within developed or high-income countries, patients with TB have been linked with

poverty and low socioeconomic status (4). Low-income neighborhoods are negatively impacted from overcrowding and malnutrition, therefore, are prone to develop TB (5, 6). Pakistan has a spectrum of urbanization ranging from affluent to low-income neighborhoods with minimal access to healthcare services and treatment (6).

Studies have reported that patients with TB are malnourished as indicated by reduction in visceral proteins, anthropometrics indexes and macronutrients status (7). Strong evidence shows underweight body mass index (BMI) is exclusively a risk factor in developing TB (8). Although body weight has been seen to decrease during TB treatment, recovery can be slow and significant wasting can persist for months

*To whom correspondence should be addressed:
badder_hina@hotmail.com

after the start of effective tuberculosis treatment (9, 10). The breakdown of protein and other reserves due to fever may also worsen nutrition parameters and weaken resistance against the infection (11). There is strong evidence that underweight body mass index (BMI) is exclusively a risk factor in developing TB (12). Wasting, or loss of bodily weight, has long been recognized as a main feature of tuberculosis, owing to a combination of decrease in appetite, loss of fat and lean tissue, as a result of decreased energy intake, complicated by altered metabolism as part of the bodily inflammatory responses.

Presently, international guidelines identify two treatment pathways to overcome TB: First-line drug (FLD) and second-line drug (SLD) therapy. To inhibit the resistant or slow-growing strains of TB, the continuation phase of the treatment is effectively controlled by using first-line drugs (FLD) (13). However, FLD therapy often fails to cure TB, causing further spread of the disease, leading to the emergence of drug-resistant bacteria. The emergence of multi-drug resistant TB (MDR-TB) is on the rise and a serious concern within the healthcare community (17). As a result, SLD drugs are utilized, however, they are more toxic and expensive than FLDs (14).

Nutritional assessment is fundamental in the management of Pulmonary TB (PTB) patients, requiring clinical expertise in history-taking and physical assessment, with the duties ideally being fulfilled by a registered dietician (RD), as the evaluation is multi-faceted (15). Bhargava et al. (2017) simplified the tools comprising the nutritional evaluation, through abbreviation of tools utilized in the form of "ABCD," with "A" standing for anthropometry, "B" signifying biochemical assessment, "C" being clinical assessment, and "D" comprising of dietary assessment.

Anthropometry involves measurements such as height, weight, and BMI of patients. Biochemical, or laboratory, assessment involves evaluation of serum hemoglobin and complete blood count (CBC), and serum electrolytes to further evaluate for undernutrition status in patients of PTB. Clinical evaluation is often performed by a healthcare professional with expertise to identify signs of nutritional abnormalities, often represented as pallor, oedema, muscle wasting, flaky skin, and loss of buccal pad of fat along with numerous often clinical indicators of malnutrition (15). Lastly, a significant component of nutritional assessment includes the dietary assessment, involving gathering data based on the patient's dietary recall of food intake within the past 24 hours (15). All these tools are important to aid in determining the prevalence of malnutrition of an individual with PTB on drug therapy.

There is limited and lack of relevant data documented on the prevalence of nutritional status gathered using proper nutritional assessment tools specifically on TB patients within indigenous society of Pakistan. Therefore, this study is designed to provide a perspective on the prevalence of nutritional status of malnutrition among pulmonary TB patients. The aim of the study is to assess the nutritional status of pulmonary TB patients on FLD and SLD treatment utilizing universally recognized tools of nutritional assessment for patients receiving both types of drug therapy.

METHODS

The research design involves a cross-sectional study, by enrolling 315 patients admitted for treatment of PTB, with either FLD or SLD, between December 2018 to March 2019. Setting of study was a public-sector, tertiary-care hospital located in Karachi, an urban city in Pakistan. A structured questionnaire was verbally administered by a registered dietician in the official language of Urdu, taking approximately 20-30 minutes to administer.

The inclusion criteria for the study subjects was as follows: patients of either gender giving informed consent, between the ages of 18-55 years, who are admitted & diagnosed with pulmonary TB, either as new or relapsed cases. The exclusion criteria were participants who were either pregnant, lactating, or on oral food supplements. Furthermore, if the patients were undergoing any other treatment or were diagnosed with other cross-infections, such as HIV, were excluded. The sample size for this study was calculated by a statistician, which encompasses an incremental 5% for participants to account for loss of follow-up and unwilling to participate in the study.

Data collection

A quantitative, structured questionnaire with physical assessment parameters was conducted by a trained, registered dietitian (R.D.). Demographics such as age, gender, type of treatment, educational level, ethnicity, and occupational level was documented upon consent. After consent, anthropometric measurements were assessed and the participant's blood samples were withdrawn and sent for laboratory biochemical analysis. For anthropometric measurements of weight were measured to the nearest 0.1 kg without shoes using an electronic platform on a model weighing scale. For height, data was documented to the nearest 0.1 cm. Body mass index (BMI) was calculated (kg/m²) and the patients will be classified into categories of BMI based on the WHO population cut-offs for Asians (16). Mid-upper Arm Muscle Circumference (MAMC) were measured with a flexible, measuring tape. Triceps and sub-scapular skin folds aided in determining Mid-upper Arm Muscle Circumference (MAMC) by a skin fold tool and was calculated (17). Blood samples were collected to determine Hemoglobin (Hgb) and Albumin levels of each participant. Nutritional clinical assessment was conducted to evaluate for physical signs of malnutrition. Dietary history was documented by interviewing the participant about recalling their 24-hour dietary intake to calculate energy in kilocalories and protein in grams from Diabetic Exchange list (18). Based on the PTB treatment international guidelines, data related to nutritional assessment was collected at initial visit (<1 month), at an interval where treatment regimen was followed-up (<2 months), after the treatment was completed (<6 months), and a follow-up visit (<6 months) (19).

Statistical Analysis

The statistical analysis was carried out using SPSS version 21.0. Percentage and frequency were reported for categorical variables whereas mean and standard deviation were reported for continuous variables.

Assumption of normality was checked by using Shapiro-wilk test of the continuous variables. Chi-square test was run to check association between categorical variables and type of treatment. Mann-Whitney U-test and Kruskal-wallis test were applied to check mean differences between type of treatment and duration of treatment. All test results having p-values less than or equal to 0.05 level of significance were considered statistically significant.

Ethical Issues

The study was conducted with the highest respect and dignity for participants. This study underwent ethical review through institutional review committee of Dow University at the beginning of the

study and data collection being initiated upon IRB approval.

RESULTS

A total of 312 pulmonary tuberculosis patients were included in the study and 3 patients had loss of follow-up during the study. Among all the patients 45.8% (n=143) were males and 54.2% (n=169) were females. Patients who were married were 56.4% (n=176). There were 44.6% (n=139) patients who were uneducated. Majority of the patients were Urdu speaking (31.7%, n=99) and then those who belonged to Sindhi ethnicity (26.9%, n=84). There were 61.2% (n=191) patients who were on FLD and 38.8% (n=121) patients who received SLD. None of the demographic variable showed any significant association with the type of treatment. See Table 1.

Table 1. Socio-Demographic characteristics of pulmonary tuberculosis patients by type of treatment (n=312)

Variables	Total	Type of Treatment		p-value*
		FLD (n=191)	SLD (n=121)	
		n (%)	n (%)	
Gender				
Male	143	92 (64.3)	51 (35.7)	0.299
Female	169	99 (58.6)	70 (41.4)	
Marital status				
Unmarried	136	91 (66.9)	45 (33.1)	0.070
Married	176	100 (56.8)	76 (43.2)	
Education level				
Uneducated	139	79 (56.8)	60 (43.2)	0.353
Up to secondary	135	88 (65.2)	47 (34.8)	
Intermediate and above	38	24 (63.2)	14 (36.8)	
Ethnicity				
Sindhi	84	49 (58.3)	35 (41.7)	0.083
Punjabi	44	31 (70.5)	13 (29.5)	
Balochi	10	8 (80.0)	2 (20.0)	
Pashto	29	16 (55.2)	13 (44.8)	
Urdu	99	66 (66.7)	33 (33.3)	
Others	46	21 (45.7)	25 (54.3)	
Number of family members				
≤ 4	66	46 (69.7)	20 (30.3)	0.056
5 – 9	196	110 (56.1)	86 (43.9)	
≥ 10	50	35 (70.0)	15 (30.0)	

*p-value has been calculated using Chi-square test.

Anthropometric measurements were assessed of all patients. Average age of the patients was 34.91 years with SD ± 14.62 years and ranged between 18 and 60 years. It was found that in all patients average BMI (kg/m^2) was 17.72 with SD ± 3.15 and ranged between 11.03 and 31.92. It was evaluated in biochemical characteristics and dietary history that average hemoglobin (g/dl) was 10.34 with SD ± 1.02 whereas average calorie intake (kcal) of the patients was 1321.77 with SD ± 506.19 which was ranged between 365 and

2550. It was reported that patients who received FLD had lower average BMI (kg/m^2) and MACU (mm) in comparison with those who were on SLD. Mean differences were found to be statistically significant between both treatment groups for BMI (Mean difference=0.73, p-value=0.044) and MACU (Mean difference=18.22, p-value= <0.001). It was found that on average calorie (kcal) and protein (grams) intake was also lower in those patients who received FLD. See Table 2.

Table 2. Comparison of nutritional status of pulmonary tuberculosis patients stratified in first-line drug (FLD) and second-line drug (SLD)

Characteristics	Overall Mean	SD	Range
Anthropometric measurements			
BMI (kg/m^2)	17.72	3.15	11.03 - 31.92
MACU (mm)	220.49	40.6	127.0 - 330.2
Biochemical characteristics			
Hemoglobin (g/dl)	10.34	1.02	7.8 - 13.6
Albumin (g/dL)	2.33	0.52	1.0 - 3.6
Dietary history (24-hour recall)			
Calories (kcal)	1321.77	506.19	365 – 2550
Protein (grams)	49.91	23.68	10 – 112
	FLD (n=191)	SLD (n=121)	p-value*
	Mean \pm SD	Mean \pm SD	
Age (years)	35.56 \pm 15.25	33.89 \pm 13.56	0.377
BMI (kg/m^2)	17.44 \pm 3.15	18.17 \pm 3.12	0.044
MAMC (mm)	21.34 \pm 3.95	23.16 \pm 3.96	< 0.001
Hemoglobin (g/dl)	10.33 \pm 1.04	10.35 \pm 1.00	0.826
Albumin (g/dL)	2.35 \pm 0.52	2.31 \pm 0.53	0.334
Calories (kcal)	1298.71 \pm 515.19	1358.16 \pm 491.56	0.347
Protein (grams)	48.59 \pm 22.32	51.98 \pm 25.65	0.451

*p-value has been calculated using Mann-Whitney U Test.

Mean differences were also calculated among four different durations of treatment. A clear increment in BMI was seen as the duration of treatment increases and highest significant mean BMI difference was found in between the patients who received treatment for less than a month and those whose duration of treatment was more than six months (Mean difference=3.79, p-value= <0.001). Calorie intake (p-value=0.030) was also found to be statistically significantly different among the groups of duration of treatment. See Table 3.

Clinical examination data pertaining to nutritionally deficiencies in PTB patients were also gathered. Out of all the patient participants, a mere 1.3% reported night-blindness, dry with yellow or white spots

in eyes was reported in 7.7% of the participants. Dry, dull, or rough appearance of eyes was observed in 21.8%, while pale conjunctive was stated in 19.6%. Softening of cornea was reported in 2.6%, while 10.6% were examined to have cracked and reddened cornea of eyes. Bilateral cracks or redness of lips was observed in 9.9%, vertical cracks (cheilosis) were assessed in 13.1% of participants. In clinical examination of tongue features, magenta was observed in 28.5%, smooth or slick or loss of papillae was observed in 19.6%. Beefy, red-color or red/swollen mucosa was observed in 23.1%, while decreased taste was reported by 18.9% of patients. Clinical data observed for nails included the observation of spoon-shaped nails was seen in 43.9%, dull or lack-

luster was seen in 30.8%, pale or mottled appearance was observed in 21.2%. Clinical assessment of pallor appearance was seen in 33% out of total patient participants. Muscle-wasting was seen in 26.0%, difficulty in walking was reported by 26.6% of

participants. Musculoskeletal problems, such as pain in calf or thighs were reported in 18.3%, joint pain or swelling was reported in 37.8%, while a mere 10.9% of total participants stated difficulty in walking. (See Table 4).

Table 3. Nutritional status of pulmonary tuberculosis patients by duration of FLD treatment (n=312)

Variables	During Drug Treatment		After Drug Treatment		p-value*
	< 1 month (n=191)	< 2 months (n=191)	< 6 months (n=191)	> 6 months (n=191)	
	Mean ± SD				
BMI (kg/m ²)	16.15 ± 1.89	17.53 ± 2.82	18.86 ± 3.31	19.94 ± 4.05	<0.001
MAMC (mm)	21.74 ± 3.65	22.195 ± 4.51	22.21 ± 3.9	22.06 ± 3.86	0.826
Hemoglobin (g/dl)	10.27 ± 1.02	10.33 ± 1.12	10.39 ± 0.98	10.42 ± 0.83	0.828
Albumin (g/dL)	2.34 ± 0.47	2.27 ± 0.51	2.37 ± 0.54	2.43 ± 0.59	0.484
Calories (kcal)	1264.24 ± 491.16	1420.53 ± 525.12	1327.92 ± 508.70	1167.10 ± 436.52	0.030
Protein (grams)	46.88 ± 21.35	53.71 ± 24.06	50.70 ± 26.69	44.85 ± 21.13	0.119

*p-value has been calculated using Kruskal-wallis test.

Table 4. Nutrition based clinical assessment of pulmonary tuberculosis patients (n=312)

Physical Signs	N		%	
Eyes	Yes	No	Yes	No
Night Blindness	4	308	1.3	98.7
Dry with yellow or white spot	24	288	7.7	92.3
Dry, dull, rough appearance	68	244	21.8	78.2
Pale conjunctive	61	251	19.6	80.4
Softening of cornea	8	304	2.6	97.4
Cracked and reddened corners of eyes	33	279	10.6	89.4
Lips				
Bilateral cracks or redness of lip	31		9.9	
Vertical cracks (cheilosis)	41		13.1	
N/A*	240		76.9	
Tongue				
Magenta	89		28.5	
Smooth, slick or loss of appetite	61		19.6	
Beefy red color mucosa, red and swollen	31		9.9	
Decreased taste	72		23.1	
N/A*	59		18.9	
Nails				
Spoon-shaped	137		43.9	
Dull, lackluster	96		30.8	
Pale, mottled	66		21.2	
N/A*	13		4.2	
Pallor				
Yes	103		33.0	
No	209		67.0	
Muscle Wasting				
Yes	81		26.0	
No	231		74.0	
Difficulty in Walking				
Yes	83		26.6	
No	229		73.4	
Musculoskeletal				
Pain in calves or thighs	57		18.3	
Joint pain or swollen	118		37.8	
Difficulty in walking	34		10.9	
N/A*	89		28.5	

*N/A=Not Available

DISCUSSION

Nutritional assessment is a core component, yet an often rarely applied aspect, of a pulmonary tuberculosis patient's treatment plan. This study noted there is no significant difference between gender and nutritional status in patients on either FLD or SLD. In addition, this research demonstrated that most (20-22). Newly diagnosed adult TB patients were underweight based on BMI and MAMC at the time of initiating drug therapy, with majority of the participants being moderate to severely malnourished. Numerous evidence-based researches have observed malnourishment being evident in TB patients at the time of enrollment, in a spectrum of both developing and developed countries WHO (2013). This study found PTB patients had reported lower cut-offs for BMI, mid-arm muscle circumference (MAMC), and lower ranges of serum albumin, despite being maintained on FLD or SLD therapy. Similarly, a study conducted in India revealed that TB patients were 11 times more likely to have a BMI of less than 18.5, indicating a borderline underweight status (Shetty, 2006) (23).

Based on the results of this study, significantly lower serum albumin levels were noted in patients taking either treatment for PTB, which is similar to findings of an Iranian study conducted on 120 patients (Sultan et al., 2012) (24). A study by Kumar et al. (2014) (25) highlighted the necessity for protein consumption in patients with multi-drug resistant PTB as findings showed lower serum protein, serum albumin and blood hemoglobin levels. Low albumin could be attributed to hepatic production of acute phase reactant proteins due to cytokines, such as interleukin-6 and tumour necrosis factor (TNF), which inhibits the creation of serum albumin in the blood vessels, causing severe fluctuations in the plasma concentrations of certain essential micro-nutrients and albumin.

Skin-fold thickness measures the amount of fat under the skin. Patients with lower than mean averages of skin-fold thickness within this research were considered under-nourished. In comparison, a study conducted by Nthiga et al. (2017) (26) in a referral hospital in Kenya indicated the mean and percentages of skin-fold thicknesses were lower declaring undernourishment among PTB patients. Body wasting is a pronounced and characteristic feature among PTB patients, which is linked with lower caloric intake due to loss of appetite and lack of food consumption (Schwenk et al., 2000) (27). The study's findings show lower ranges of MAMC in TB patients taking either FLD or SLD. In Uganda, Mupere and colleagues (2010) (28) reported when compared to individuals negative for TB, patients with TB displayed lower body mass index (BMI), body weight, body cell mass, and fat mass, regardless of gender (29). This research showed patient's mean hemoglobin concentrations were significantly lower as compared to normal physiologic levels.

This study's results showed the caloric intake was found to be statistically significant based on the duration of treatment, with a longer duration of drug treatment being associated with greater caloric and protein intake among the PTB patients (see Table 3). According to WHO (2013) guidelines, approximately 40kcal/kg and

proteins 1.2-1.5 grams should be ideally consumed by patients diagnosed with TB diseases (30). This effort is to fill the gap in knowledge since there are few studies conducted in Pakistan previously. To the best of the authors' awareness, there have been no previous studies conducted to fill the gap in knowledge and clinical practice to best determine calories and protein consumption, specifically addressing TB patient's nutrition needs within Pakistan. Based on the results of our study, inadequate intake of calories and protein are associated with the diseased state of PTB, as the patient recovers with the disease, similarly, causing improvement in the patient's dietary intake. Inadequate dietary intake is due to patients' inability to access adequate nutritious foods, thus, causing malnutrition. The use of the 24-hour dietary recall as an instrument presents as a limitation in this study. The dietary recall tool introduces social desirability bias and recall bias, in which patients may not be able to fully recollect or under-report their past dietary intake or possibly provide responses which will be favored by the interviewer.

CONCLUSION

The study reveals that patients diagnosed with PTB are overall nutritionally malnourished, despite treatment with either FLD or SLD therapy, due to the pathophysiological impact of the disease on the patient's body. Based on the results of this study, it is understood that the duration of the drug therapy is associated with the outcome of improvement in nutritional status. Thus, it is advised to initiate drug therapy with immediate effect to hinder the malnourished state of the PTB patient. Nutritional counseling is often undervalued as a part of the treatment regime for PTB, especially in the developing country practices of Pakistan. However, literature and research have determined that the true nutritional parameters are assessed based on validated tools, such as anthropometric measurements of BMI or muscle arm circumference, biochemical laboratory factors such as albumin, 24-dietary recall and clinical physical assessment, and have been found as strong predictors to evaluate the nutritional trajectory in patients with PTB. Majority of the patients with pulmonary TB in this study were categorized as severely underweight accompanied by low caloric intake based on the 24-hour dietary recall.

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