Association of Nutritional Factors with Tuberculosis Treatment Outcome

Harshita Gupta
Department of Pulmonary Medicine, King George's Medical University, Lucknow, Uttar Pradesh, India

Surya Kant
Department of Pulmonary Medicine, King George's Medical University, Lucknow, Uttar Pradesh, India

Amita Jain
Department of Microbiology, King George's Medical University, Lucknow (UP)

Savita Ahluwalia
Department of Home Science, M.V.PG University, Lucknow, Uttar Pradesh, India

S.M. Natu
Department of Pathology, King George's Medical University, Lucknow, Uttar Pradesh, India

ABSTRACT

Macro and micro-nutrient deficiencies and diminished nutritional status are common features of pulmonary tuberculosis.

To determine the association of nutritional factors with pulmonary tuberculosis treatment outcome in newly diagnosed patients. A hospital based prospective follow-up cohort study design.

Two urban Directly Observed Treatment Short-course (DOTS) centers in Lucknow District of Uttar Pradesh, India.

Newly diagnosed sputum smear-positive cases for Acid-fast Bacilli (AFB) before and after treatment were included in the study. Outcomes were evaluated by clinical, radiological and mycobacterial culture and drug-susceptibility testing in sputum smear positive patients. The parameters used to assess the nutritional status were body mass index (BMI) and mid upper arm circumference (MUAC). Nutrients intake was assessed by 24- hour dietary recall method.

A total of 185 newly diagnosed patients with pulmonary tuberculosis were recruited. Out of these, 14 patients were lost to follow up after treatment and remaining 171 patients were analyzed. The mean (±SD) age of the study population was 29 (±12) years. Significant ($p<0.0001$) increase was observed in nutrients intake with the clinical, radiological and bacteriological outcomes at six month treatment. Protein ($p=0.04$) and retinol ($p=0.01$) intake were significantly associated with the conversion of clinical outcomes, i.e. symptomatic to asymptomatic. Intake of energy ($p=0.04$), protein ($p=0.04$) and fat ($p=0.008$) were significantly associated with complete radiological clearance. In case of drug-related outcomes, energy ($p=0.01$) and protein ($p=0.02$) intakes were associated significantly with drug resistance. Among all the nutrients, protein intake was closely associated with clinical, radiological and bacteriological outcomes.

Protein intake was related with different clinical, radiological and bacteriological outcomes. Increased intake of protein was probably associated with rapid clinical recovery and weight gain, complete radiological clearing and early bacteriological conversion.

Keywords

Tuberculosis, drug-susceptibility testing, nutrients

1. INTRODUCTION

Tuberculosis (TB) is a contagious disease caused by the bacillus Mycobacterium tuberculosis (M.tb) (WHO, 2012). It is one of the major public health problem in India. India is the highest TB burden country throughout the world, accounting for approximately one-fifth of the global incidence- an estimated 2 million cases annually (ATS, 2000). In India, more new TB cases are seemed annually than any other country. It is estimated that about 40% of Indian population is infected with TB bacillus (but who are not infected with human immunodeficiency virus) (WHO, 2012). In all the infected cases, active TB does not develop because of the infected person's immune system halts growth of the bacteria (ATS, 2000). It is well established that impaired immune function is associated with nutritional deficiencies (Perronne C, 1999). While malnutrition limits cell mediated immunity and increases host susceptibility to infection, infection can lead to nutritional stress and weight loss, thereby weakening immune function and nutritional status (Chandra RK, 1991; Karien Cilliers, 2011). Malnutrition comprises macro and micronutrient deficiency (Cegielski JP, Mc. Murray DN et al, 2004). Nutritional status is one of the most important determinants of resistance to infection (Karyadi E, Schultink W et al, 2000; Paton et al, 2006). Patients with active TB generally have lower BMI, skin-fold thicknesses, MUAC and the proportion of fat than healthy adults (Karyadi E, Schultink W et al, 2000).

People with active TB are often malnourished and suffer from micronutrient deficiencies as well as weight loss and decreased appetite (WHO, 2012). In active TB, catabolic processes leading to wasting usually begin before the patient is diagnosed; the basal metabolic rate or resting energy expenditure is increased, resulting in increased energy needs to meet the basic demands for body function (Cegielski JP, Mc. Murray DN et al, 2004). At the same time, energy intakes are likely to decline as a result of illness-associated anorexia (Macallan, Margaret A. Mcnurlan et al, 1998). This combination of conditions resulting weight loss with ultimately wasting. Apart from macronutrient deficiency, deficiency of micronutrients has been shown to be an important determinant of TB outcome. The most frequent cause of secondary immunodeficiency is considered to be the micronutrients deficiency and morbidity due to infection, including TB. Two important micronutrients, vitamin A and zinc deficiencies are common features of pulmonary TB (Karyadi E, Schultink W et al, 2000; Van Lettow M, Harries AD et al, 2004; McMurray DN, Bartow RA et al; 1990). Vitamins A, zinc and iron have key roles in metabolic pathways, cellular function, and immune competence (Karyadi E, Schultink W et al, 2000). The concentration of these may have a role in host defense against TB (Surya Kant, Harshita Gupta et al, 2011). Deficiency of single or multiple nutrients can reduce an individual's resistance to any infection (Crowle AJ, Ross EJ et al, 1989).

To the best of my knowledge, none of the study is available to determine the association of nutritional factors with TB treatment outcome, which appeared to be an important determinant of clinical, radiological and bacteriological outcomes in newly diagnosed pulmonary TB patients.

2. METHODOLOGY

2.1. Study design and setting

A prospective follow-up cohort study was conducted between January 2010 to March 2011 at the two urban Directly Observed Treatment Short-course (DOTS) centers of Lucknow Medical University and a TB Hospital located near to Medical University, Lucknow District of Uttar Pradesh, India.

2.2. Study population

The study consisted of 185 newly diagnosed sputum smear positive for AFB in pulmonary TB patients of both sexes and between the age group of 12 to 65 years at the time of interview and were about to be registered for treatment. Patients were excluded if they fulfilled any of the following exclusion criteria: previous history of anti-tuberculosis treatment (ATT); pregnant and lactating women; subjects known to be HIV positive/ or suffering from any immuno-deficient state; and use of corticosteroids or supplements containing vitamin A, zinc, iron etc. during the earlier month. All subjects were free from alcoholism.

2.3. Ethical considerations

The study was ethically approved by the institutional ethics committee of a medical university, Lucknow, U.P., India. All eligible patients were informed about the study and signed an informed consent form from each subject before the beginning of the study.

2.4. Data collection

2.4.1. Personal interview and clinical examination

Structured questionnaire was used to collect the information regarding socio-demographic background and data about family history. Socioeconomic status was assessed by Kuppuswamy's socioeconomic status (SES) scale (SSL Parashar, 2012). Subsequently, patients were thoroughly examined by medical doctors at both the hospitals.

2.5. Assessment of clinical outcomes

Clinical outcomes were assessed at baseline and after six month of ATT. Following symptoms were clinically assessed included fever, cough, expectoration, chest pain breathlessness, wheezing, hemoptysis, dyspnea, night sweat, loss or improve of appetite and weight loss or gain.

2.6. Assessment of bacteriological outcomes

Bacteriological outcomes were assessed by RNTCP guidelines, 2006 included AFB smear examination and grading, AFB culture and drug susceptibility test. All specimens were carried to the accredited Intermediate Reference Laboratory (IRL) at the Department of Microbiology, Medical University, Lucknow where further processing was done.

2.7. Specimen collection

The diagnosis of TB was done in accordance to the RNTCP guidelines, 2006. At the time of enrolment; three sputum specimens on two consecutive days from each patient were collected in properly labeled screw capped, sterile disposable plastic bottles after oral gargling with normal water. Thus, there were three samples: SPOT - EARLY MORNING - SPOT. Specimen contained mucoid or mucopurulent material with minimum amounts of oral or nasal material into the McCartney bottles, and volume was of approximately 5ml.

2.7.1. AFB smears examination and grading

An AFB smear examination was carried out by direct microscopy using the Ziehl-Neelsen Method. Sputum smear result was examined and interpreted according to the AFB grading (RNTCP, 2009).

2.7.2. AFB culture and drug-susceptibility test

Culture examinations were done on all diagnostic specimens, regardless of AFB smear positive. Sputum specimens from each patient were processed with Sodium Hydroxide (NaOH) Method- Modified Petroff's procedure and cultured on Lowenstein-Jensen (L-J) slopes (RNTCP, 2009). All inoculated L-J drug and control media were incubated at 37ºC. All cultures were examined 48-72 hours after inoculation to detect gross contaminants. Thereafter, cultures were examined weekly, up to eight weeks on a specified day through the week. Typical colonies of M.tb were rough, crumbly, waxy, non-pigmented (buff-coloured) and slow-growers, i.e., only appeared two to three weeks after inoculation ((RNTCP, 2009)). The colony was confirmed by Z-N staining.

Drug resistance was expressed in proportion method, where a strain was considered to be drug resistance if the number of colonies that grew on a drug containing media was 1% or more of the colony that grew on a control drug free media. The drug containing media and media concentration for streptomycin, isoniazid, rifampicin, ethambutol were 4 µg/ml, 0.2 µg/ml, 40 µg/ml and 2 µg/ml respectively (RNTCP-Mannual of SOPs, 2009). The control (drug free) media showed good growth at least 50 to 100 colonies (RNTCP, 2009).

2.8. Assessment of radiological outcomes

Radiological outcomes were assessed by chest x-ray examination. Chest radiographs (CXR) were made of all the patients at the time of diagnosis and after six-month treatment. Patients were evaluated by judging the site of lesions, zone of involvement, the nature of the lesion (visible cavitary and non-cavitary area) in both lungs as well as classified as the extent of the lesion having mild, moderate and far advanced lesion as per American Thoracic Society classification (ATS, 2000). Radiological clearance was observed in terms of complete radiological clearance (complete clearance of residual radiological lung lesions) and incomplete radiological clearance (degree of residual radiological lung lesion clearance), graded as Grade I (more than 25% radiological clearance); Grade II (between 25-50% radiological clearance); Grade III (between 50-75% radiological clearance); Grade IV (more than 75% radiological clearance) in the chest x-rays (Vimlesh Seth, S.K.

Kabra et al, 2008). The chest x-rays (postero-anterior view) were appraised by a radiologist.

2.9. Nutritional assessment

24-hour dietary recall method was used to collect the data regarding nutrients intake of an individual patient. It was based on the foods and amounts actually consumed by the patient on three specific days. The patients were asked to recall as much detail as possible the food intake for the past 24- hour (recorded in the questionnaire). Special efforts were made to include all foods eaten in the preceding 24-hour by asking what the patient had eaten in the morning, at lunch, during the afternoon, at dinner, in the evening and during the night. Portion size was assessed by asking the patients with the help of digital photographs to facilitate more accurate portion size estimation and the nutrients content of meals (Rosalind S. Gibson, Elaine L. Ferguson et al, 2008). Portion size was estimated by using the proportion size booklet of National Health and Nutrition Examination Survey (NHANES, 2010). Nutrients content of meals was compared with the Recommended Dietary Allowances (RDA) of respective age, sex, occupation and body weight of an individual patient (ICMR, 2009). The percent nutrients intake of the RDA was calculated. The association of nutrients intake was done with tuberculosis treatment outcomes.

2.10. Anthropometric measurements

Anthropometric measurements were taken before and after ATT. Patients were assessed by anthropometric parameters such as height, weight, BMI and MUAC. Standard protocol for anthropometric measurement was followed by the National Centre for Health Statistics (National Health and Nutrition Examination Survey III Anthropometric Procedures) for various age groups (NHANES, 2007). Measurements were taken three times consecutively and mean values were observed. To eliminate the inter-examiner error, only one person took all the anthropometric measurements.

2.11. Statistical analysis

The data collected was entered into Microsoft Excel computer program and checked for any inconsistency. The descriptive statistics such as percentage, and mean (±SD) were calculated. The unpaired t-test was used to test the significance between the two means. The paired student t-test was used to compare the changes in nutritional status and nutrients intake from baseline to six- month treatment. Multivariate logistic regression analysis was used to determine the factors associated with treatment outcomes. The p-value less than 0.05 was considered as significant. All the analysis was carried out by using SPSS 15.0 version.

3. RESULTS AND ANALYSIS

A total of 185 newly diagnosed patients with pulmonary TB were recruited. Out of these, 14 (7.6%) patients were lost to follow up at the end of the treatment. Remaining 171 (92.4%) patients, 57.3% were males and 42.6% were females. The most frequent age group in the present study was 21-30 years consisted of 38% patients and 26.9% patients were below 21years. The mean (±SD) age of the study population was 29 (±12) years. Sputum positivity grade +3 was most prevalent (35.1%). The majority of the patients were Muslims (52.6%). Most of the patients (77.7%) belonged to the upper lower income group. Majority (74.8%) of the patients were non-vegetarian and 65.5% were smokers (Table 1).

Table 1. Characteristics and radiographic presentation of the TB patients

Variables	n=171
Age (years)*	29(±12)
Gender (n, %)	
Male	98(57.3)
Female	73(42.6)
Religion (n, %)	
Hindu	81(47.3)
Muslims	90(52.6)
Socio-economic status (n, %)	
Upper	1(0.5)
Upper Middle	2(1.2)
Lower Middle	34(19.8)
Upper Lower	133(77.7)
Lower	1(0.5)
Eating Habits (n, %)	
Vegetarian	32(18.7)
Non-vegetarian	128(74.8)
Eggarian	11(6.43)
Family History of TB (n, %)	
Yes	41(23.9)
No	130(76.0)
Smoking (n, %)	
Yes	112(65.5)
No	59(34.5)
Chest Radiographic (nature of lesion) (n, %)	
Cavitary	57(33.3)
Non-cavitary	114(66.6)
Type of Lesions	
Mild	15(8.8)
Moderate	115(67.2)
Far Advanced	55(32.7)

In nutritional assessment, significant ($p<0.0001$) increase was observed in intake of all the nutrients where the percent nutrients intake was inadequate when compared to RDA in all the patients from baseline to six month (Figure 1).

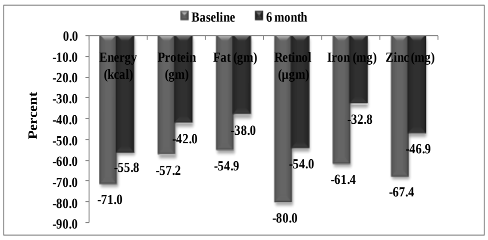

Figure 1: Percent nutrients intake of RDA from baseline to 6 month (*p<0.0001 Baseline to 6 months (McNemar test))

During clinical assessment at baseline, all patients were symptomatic and after six-month treatment, 69.6% became asymptomatic. Significant difference was reported in protein (p=0.03) and zinc (p=0.02) intake at six month between symptomatic and asymptomatic patients. However, the energy, fat, retinol and iron intake was similar at six month between symptomatic and asymptomatic patients (Table 2).

With relation to radiological assessment at baseline, 171 (92.4%) AFB positive patients were depicted residual radiological shadows in the chest x-ray. After six months ATT, 73.1% patients showed complete radiological clearing and 26.9% patients showed residual radiological shadows in the chest x-ray. The grade-wise residual radiological shadows were Grade I (0.0%), Grade II (2.3%), Grade III (4.7%), Grade IV (19.9%) (Table not shown). The energy intake was significantly (p<0.0001) increased from baseline (719.18±200.19) to six month (1109.41±279.07) among the patients with complete radiological clearance. Similar observation reported in the patients with residual radiological shadows in the chest x-ray. There was no significant difference between nutrients intake and complete and incomplete radiological clearance at six month (Table 3).

Out of 171 sputum smear positive patients for AFB, 156 (91.2%) isolates of patients were culture positive and subjected to drug-susceptibility test. Of these, 129 (82.6%) isolates were sensitive to all the drugs and 27 (17.3%) isolates were resistant to any drug. A significant (p<0.0001) increase was established in the intake of nutrients and drug sensitive and drug resistant isolates of patients from baseline to six month. None of the significant difference was observed with nutrients intake between drug sensitive and resistant outcomes at six month (Table 4).

The difference between symptomatic and asymptomatic in BMI at 6 month was insignificant. However, there was significant (p=0.02) difference in MUAC at 6 month between symptomatic (8.07±0.93) and asymptomatic patients (8.61±1.02) in clinical outcomes. The BMI was significantly (p<0.0001) increased among the patients with complete radiological clearance and not clearance in chest x-ray from baseline to 6 month. Similar observation was found for MUAC. In drug-susceptibility test, the BMI was significantly (p<0.0001) increased from baseline to 6 month in both drug sensitive (Baseline=16.45±2.52, 6 month=18.68±3.01) and resistant (Baseline=16.17±2.04, 6 month=17.14±2.59) patients. Almost similar findings were observed for MUAC. There was no significant (p>0.05) difference in BMI and MUAC at 6 month (Table 5).

Multivariate logistic regression analysis revealed that the protein (p=0.04) and retinol (p=0.01) intake were significantly associated with the conversion of clinical outcomes, i.e. symptomatic to asymptomatic. Energy (p=0.04), protein (p=0.04) and fat (p=0.008) intake were significantly associated with complete radiological clearance. In case of drug-related outcomes, energy (p=0.01) and protein (p=0.02) intake were significantly associated with drug resistance. Among the nutrients, protein intake was closely associated with clinical, radiological and bacteriological outcomes (Table 6).

Table 2: Association of clinical outcome (presence or absence of any one of the symptoms) with nutrients intake

Nutrients		Clinical outcome	Mean±sd		p-value[1]
			Baseline	6 month	
Energy (kcal)	Baseline	Symptomatic (n=171)	717.38±199.24	1088.09±287.69	<0.0001*
		Asymptomatic (n=0)	NA	NA	NA
		p-value[2]	NA	NA	
	6 month	Symptomatic (n=52)	685.42±199.54	1042.97±255.72	<0.0001*
		Asymptomatic (n=119)	731.35±198.33	1107.80±299.47	<0.0001*
		p-value[2]	0.17	0.18	
Protein (gm)	Baseline	Symptomatic (n=171)	24.58±7.70	33.26±9.11	<0.0001*
		Asymptomatic (n=0)	NA	NA	NA
		p-value[2]	NA	NA	
	6 month	Symptomatic (n=52)	22.56±6.30	31.03±8.16	<0.0001*
		Asymptomatic (n=119)	25.47±8.10	34.24±9.36	<0.0001*
		p-value[2]	0.02*	0.03*	
Fat (gm)	Baseline	Symptomatic (n=171)	13.56±2.54	18.59±2.57	0.0001
		Asymptomatic (n=0)	NA	NA	NA
		p-value[2]	NA	NA	
	6 month	Symptomatic (n=52)	13.72±2.33	18.16±2.49	0.0001*
		Asymptomatic (n=119)	13.49±2.62	18.77±2.59	0.0001*
		p-value[2]	0.58	0.14	
Retinol (μgm)	Baseline	Symptomatic (n=171)	120.58±85.15	186.28±103.11	<0.0001*
		Asymptomatic (n=0)	NA	NA	NA
		p-value[2]	NA	NA	
	6 month	Symptomatic (n=52)	130.25±79.97	193.96±100.82	<0.0001*
		Asymptomatic (n=119)	116.36±88.72	182.92±104.34	<0.0001*

		p-value[2]	0.33	0.52	
Iron (mg)	Baseline	Symptomatic (n=171)	7.49±2.52	13.11±3.13	<0.0001*
		Asymptomatic (n=0)	NA	NA	NA
		p-value[2]	NA	NA	
	6 month	Symptomatic (n=52)	7.12±1.98	12.65±3.34	<0.0001*
		Asymptomatic (n=119)	7.65±2.71	13.31±3.02	<0.0001*
		p-value[2]	0.42	0.26	
Zinc (mg)	Baseline	Symptomatic (n=171)	3.62±1.27	5.88±1.63	<0.0001*
		Asymptomatic (n=0)	NA	NA	NA
		p-value[2]	NA	NA	
	6 month	Symptomatic (n=52)	3.40±1.21	5.45±1.68	<0.0001*
		Asymptomatic (n=119)	3.71±1.28	6.07±1.58	<0.0001*
		p-value[2]	0.13	0.02*	

Table 3: Association of radiological outcome with nutrients intake (1Paired t-test, 2Unpaired t-test, *Statistically significant)

Nutrients	**Radiological clearance**	**Mean±sd**		**p-value[1]**
		Baseline	**6 month**	
Energy (kcal)	Complete cleared (n=125)	719.18±200.19	1109.41±279.07	<0.0001*
	Not cleared (n=46)	712.51±198.76	1030.13±305.68	<0.0001*
	p-value[2]	0.85	0.11	
Protein (gm)	Complete cleared (n=125)	25.09±8.09	33.84±9.28	0.001*
	Not cleared (n=46)	23.21±6.41	31.69±8.53	<0.0001*
	p-value[2]	0.16	0.17	
Fat (gm)	Complete cleared (n=125)	13.39±2.62	18.63±2.60	0.001*
	Not cleared (n=46)	14.04±2.29	18.50±2.49	<0.0001*
	p-value[2]	0.14	0.77	
Retinol (µgm)	Complete cleared (n=125)	120.24±88.54	185.40±103.54	0.001*
	Not cleared (n=46)	121.52±80.24	188.66±103.03	<0.0001*
	p-value[2]	0.93	0.86	
Iron (mg)	Complete cleared (n=125)	7.54±2.65	13.38±2.98	0.001*
	Not cleared (n=46)	7.34±2.14	12.38±3.40	<0.0001*
	p-value[2]	0.63	0.06	
Zinc (mg)	Complete cleared (n=125)	3.70±1.31	6.03±1.60	0.001*
	Not cleared (n=46)	3.38±1.13	5.48±1.65	<0.0001*
	p-value[2]	0.52	0.14	

4: Association of drug-susceptibility outcome with nutrients intake (1Paired t-test, 2Unpaired t-test, *Statistically significant)

Nutrients		**Drug-susceptibility outcome (n=156)**	**Mean±sd**		**p-value[1]**
			Baseline	**6 month**	
Energy (kcal)	Baseline	Sensitive (n=129)	723.88±197.23	1099.08±298.41	<0.0001*
		Resistant (n=27)	716.04±225.99	1071.13±285.14	<0.0001*
		p-value[2]	0.86	0.66	
Protein (gm/day)	Baseline	Sensitive (n=129)	25.05±8.03	34.08±9.38	0.001*
		Resistant (n=27)	22.60±5.27	30.43±7.50	<0.0001*
		p-value[2]	0.13	0.06	
Fat (gm/day)	Baseline	Sensitive (n=129)	13.71±2.52	18.86±2.51	<0.0001*
		Resistant (n=27)	13.32±2.13	18.03±2.59	<0.0001*
		p-value[2]	0.46	0.12	
Retinol (µgm/day)	Baseline	Sensitive (n=129)	122.34±87.02	188.42±101.84	0.001*
		Resistant (n=27)	113.57±80.92	181.81±113.08	<0.0001*
		p-value[2]	0.63	0.76	
		Sensitive (n=129)	7.47±2.64	13.13±2.9	<0.0001*

Iron (mg/day)	Baseline			4	
		Resistant (n=27)	7.35±1.98	12.46±3.75	<0.0001*
		p-value[2]	0.82	0.31	
Zinc (mg/day)	Baseline	Sensitive (n=129)	3.63±1.29	5.97±1.57	0.001*
		Resistant (n=27)	3.43±1.23	5.36±1.87	<0.0001*
		p-value[2]	0.46	0.08	

Table 5: Association of nutritional status with clinical, radiological and bacteriological outcomes (1Paired t-test, 2Unpaired t-test, * Statistically significant)

	Nutritional status		Outcomes	Mean±sd		p-value[1]
				Baseline	6 month	
Clinical	BMI (kg/m²)	Baseline	Symptomatic (n=171)	16.40±2.39	18.48±2.94	<0.0001*
			Asymptomatic (n=0)	NA	NA	NA
			p-value[2]	NA	NA	
		6 month	Symptomatic (n=52)	16.31±2.51	18.20±3.46	<0.0001*
			Asymptomatic (n=119)	16.45±2.35	18.60±2.70	<0.0001*
			p-value[2]	0.72	0.42	
	MUAC (cm)	Baseline	Symptomatic (n=171)	7.64±0.86	8.44±1.02	<0.0001*
			Asymptomatic (n=0)	NA	NA	NA
			p-value[2]	NA	NA	
		6 month	Symptomatic (n=52)	7.39±0.77	8.07±0.93	0.001*
			Asymptomatic (n=119)	7.75±0.88	8.61±1.02	0.001*
			p-value[2]	0.01*	0.02*	
Radiological	BMI (kg/m²)	6 month	Complete cleared (n=125)	16.53±2.46	18.81±2.97	<0.0001*
			Not cleared (n=46)	16.08±2.19	17.59±2.71	<0.0001*
			p-value[2]	0.28	0.02*	
	MUAC (cm)		Complete cleared (n=125)	7.73±0.81	8.59±1.02	0.001*
			Not cleared (n=46)	7.39±0.95	8.05±0.93	<0.0001*
			p-value[2]	0.02*	0.02*	
Bacteriological	BMI (kg/m²)	Baseline	Sensitive (n=129)	16.45±2.52	18.68±3.01	<0.0001*
			Resistant (n=27)	16.17±2.04	17.14±2.59	<0.0001*
			p-value[2]	0.60	0.20	
	MUAC (cm)		Sensitive (n=129)	7.66±0.87	8.51±1.06	0.001*
			Resistant (n=27)	7.59±0.83	8.13±0.81	<0.0001*
			p-value[2]	0.68	0.08	

Table 6: Significant associated nutritional factors with clinical, radiological and bacteriological outcomes (Results of multivariate logistic regression)

Outcomes	Nutritional factors	Beta coefficient	S.E.	OR	95%CI of OR	p-value
Clinical	Protein (gm)	-0.064	0.032	0.93	0.88-0.99	0.04*
	Retinol (μgm)	0.007	0.003	1.007	1.002-1.01	0.01*
Radiological	Energy (kcal)	-0.004	0.002	0.99	0.95-0.99	0.04*
	Protein (gm)	0.106	0.052	1.11	1.01-1.23	0.04*
	Fat (gm)	-0.220	0.083	0.80	0.68-0.94	0.008*
Bacteriological	Energy (kcal)	-0.006	0.002	0.99	0.98-0.99	0.01*
	Protein (gm)	0.132	0.072	1.14	1.01-1.32	0.04*
No.	ID (Pubchem/chEMBL)	Molecular weight	No. of H Bond acceptors	No. of H Bond Donors	XLogP	No. of violations
1	CID 21680727	350.389	6	2	0.2	0
2	Ampicillin (CID	349.404	5	3	-1.1	0

	6249)					
3	Sigma_c3416	376.383	9	3	0.679	0
4	Stock1n-13321	333.382	7	2	1.098	0
5	Stock1n-31653	458.467	10	4	0.503	0
6	CID 50909816	351.397	5	2	0.2	0
7	CID 2174	349.404	5	3	-1.1	0
8	CID 4084	361.415	5	2	3	0
9	CHEMBL1232898	441.543	5	4	0.1	0
10	CHEMBL1235251	437.466	9	3	-3.1	0
11	CHEMBL55731	403.493	7	4	-1.7	0
12	CHEMBL1231663	380.415	7	4	-1.4	0
13	CID 31161	316.26	7	4	2.3	0
14	CID 4478475	320.25	8	6	1.1	0
15	CID 44399514	238.193	6	2	0.8	0

SE-Standard error, OR-Odds Ratio, CI-Confidence interval, *statistically significant

4. DISCUSSION

Malnutrition and TB are both the problem of considerable magnitude in most of the underdeveloped region of the world. TB remains a major public health problem in India. Malnutrition enhances the development of active TB, and active TB makes malnutrition worse (Van Lettow M, Harries AD et al, 2004). Malnutrition causes significant impairment of several important mechanisms of immune protection, including phagocytic function, cell-mediated immunity, antibody concentration, and cytokine production in TB. An impaired immune function is associated with nutritional deficiency; thereby weight loss and poor nutritional status (Cegielski JP, Mc. Murray DN, 2004). Nutrient intake was one of the most important host factor which responsible for treatment outcomes in TB. An improvement in nutrient intake lead to rapid clinical recovery and weight gain, early bacteriological conversion, complete radiological clearing and no future complications or sequelae, i.e. good treatment outcome. Present study highlights the association of nutritional factors with TB treatment outcome.Our finding showed the association between nutrients intake and clinical, radiological and bacteriological outcomes. Before ATT, nutrients intake was lowered with respect to RDA in all age group of patients. After six month treatment, nutrients intake, BMI and MUAC were significantly improved (Figure 2).

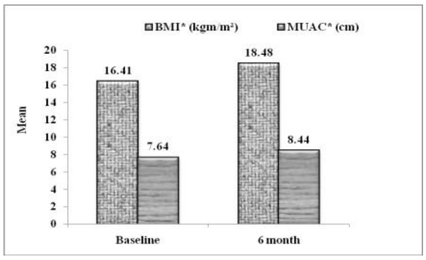

Figure 2: Changes in BMI and MUAC from baseline to 6 month

After treatment, 42.6% patients were achieved the normal range (18.50-24.99 kg/m2) of BMI. Improvement in nutritional status included variety of reasons like improved appetite, food intake and metabolic efficiency along with ATT (Surya Kant, Harshita Gupta, 2011).

Present study revealed that protein intake was probably associated with TB treatment outcomes. Before treatment of active TB, protein metabolism and nutritional status effects through multiple mechanisms. Due to the presence of pro-inflammatory cytokines, utilization of amino acids and may be inhibition of protein synthesis (Surya Kant, Harshita Gupta, 2011). Protein accretion increased the production of the tumor necrosis factor- alpha and interferon-gamma, may selectively compromise portion of cell-mediated immune response that is important for restricting TB (Crowle AJ, Ross EJ, 1989). After six months ATT, level of macro-nutrients specifically energy, protein, fat and appetite were significantly improved and thereby gain in weight. Reduction in bacilli load or negative sputum smear denoted melioration in intake of micro-nutrients, particularly retinol and zinc, which strengthen the immune system (McMurray DN, Bartow RA, 1990). Adequate macro and micronutrient intake during TB care and recovery is needed to fully restore nutritional status during and following TB treatment and microbial cure. Daily multiple micronutrient supplementations may represent a novel approach and add benefit among the patients. Multiple micronutrient supplementations may strengthen the immune system which decreases the burden of Mycobacterium and letting them for faster recovery leads to better treatment outcome. In addition, raising nutritional status of population may prove to be an effective measure to control TB. Thus, nutritional assessment and regular monitoring of the nutritional status by a dietician are essential for the successful management of TB patients and should be an essential part of tuberculosis control programmes.

One of the limitation of this study might be perception of patients towards no previous history of ATT because sometime patients did not recognize their previous history of ATT due to social phenomenon. Another limitation might be the duration of study period which leaded to fewer sample size, thus, a study with larger sample size needed for better inference about the outcome.

5. CONCLUSION

Findings of this study indicated that protein intake was closely associated with clinical, radiological and bacteriological outcomes. Increased intake of protein was responsible for better treatment outcomes. Adjunctive protein supplementation may accelerate the beneficial therapeutic effect of TB chemotherapy and allowing them for faster recovery, which lends to better treatment outcome.

6. REFERENCES

[1] World Health Organization, 2012. Available at: http://www.who.int/topics/tuberculosis/en/

[2] ATS/CDC. (2000) Targeted Tuberculin Testing and Treatment of Latent Tuberculosis Infection. Am J Resp Crit Care Med. 161(4):S221-S247. http://ajrccm.atsjournals.org/cgi/content/full/161/4/S1/S221

[3] Perronne C. (1999) Tuberculosis, HIV infection, and malnutrition: an infernal trio in central Africa. Nutrition. 15(4), 321-322.

[4] Chandra RK. (1991) McCollum Award lecture. Nutrition and immunity: lessons from the past and new insights into the future. Am J Clin Nutr. 53(5), 1087-1101.

[5] Karien Cilliers. (2011) The Pharmacokinetics and Toxicity of Antituberculosis Agents and other Co-Administered Drugs in Children with Tuberculosis, with and Without HIV Infection, and their Relationship to Nutritional Status. Available at:http://scholar.sun.ac.za/bitstream/handle/10019.1/6864/cilliers_pharmacokinetics_2011.pdf?sequence=1

[6] Cegielski JP, Mc. Murray DN. (2004) The relationship between malnutrition and tuberculosis: evidence from studies in humans and experimental animals. Int J Tuberc Lung Dis. 8(3), 218-26.

[7] Karyadi E, Schultink W et al. (2000) Poor Micronutrient Status of Active Pulmonar Tuberculosis patients in Indonesia. J. Nutrition. 130, 2953-2958.

[8] Paton, N.I., Ng. (2006) Body composition studies in patients with wasting associated with tuberculosis. Nutrition. 22(3), 245-251.

[9] Cegielski JP, Mc. (2004) Murray DN. The relationship between malnutrition and tuberculosis: evidence from studies in humans and experimental animals. Int J Tuberc Lung Dis. 8(3), 218-26.

[10] Macallan, Margaret A. Mcnurlan, Anura V. Kurpad et al. (1998) Whole body protein metabolism in human pulmonary tuberculosis and undernutrition: evidence for anabolic block in tuberculosis. Clinical Science. 94, 321–331.

[11] Van Lettow M, Harries AD et al. (2004) Micronutrient malnutrition and wasting in adults with pulmonary tuberculosis with and without HIV co-infection in Malawi. BMC Infect Dis. 4, 61.

[12] McMurray DN, Bartow RA et al. (1990) Micronutrient status and immune function in tuberculosis. Ann N Y Acad Sci. 587, 59-69.

[13] Surya Kant, Harshita Gupta. (2011) Nutrition and Tuberculosis. Lucknow Medical Journal. 1, 79-83.

[14] Crowle AJ, Ross EJ. (1989). Inhibition of retinal acid of multiplication on virulent tubercle bacilli in cultured human macrophages. Infect Immun. 57:840-4.

[15] S S L Parashar. Social, Behavioral and Communication Sciences. Available at: http://www.whoindia.org/LinkFiles/Human_Resources_Section4Textbook_on_Public_Health_and_Community_Medicine.pdf

[16] Revised National Tuberculosis Control Programme. Training Module for Medical Practitioners, 2006. Available at: www.tbcindia.nic.in/pdfs/Financial%20Training%20Module.pdf.

[17] Revised National TB Control Programme Training Manual for Mycobacterium tuberculosis Culture & Drug susceptibility testing, 2009. Available at: http://www.tbcindia.nic.in/pdfs/Training%20manual%20M%20tuberculosis%20C%20DST.pdf

[18] Revised National TB Control Programme. Manual of Standard Operating Procedures (SOPs), 2009. Available at: http://www.tbcindia.nic.in/pdfs/standard%20operating%20procedures%20for%20C&DST%20labs.pdf

[19] American Thoracic Society and Centers for Disease Control and Prevention. (2000) Diagnostic standards and classification of tuberculosis in adults and children. Am J Respir Crit Care Med. 161, 1376–1395.

[20] Vimlesh Seth, S.K. Kabra. (2008) Essentials of tuberculosis in children.3rd edition.

[21] Rosalind S. Gibson, Elaine L. Ferguson. (2008) An interactive 24-hour recall for assessing the adequacy of iron and zinc intakes in developing countries. Available at: www.ifpri.org/sites/default/files/publications/tech08.pdf

[22] National Health and Nutrition Examination Survey 1999-2001. (2010) Available at: http://www.cdc.gov/nchs/nhanes/measuring_guides_dri/measuringguides02.htm

[23] Nutrient Requirements and Recommended Dietary Allowances for Indians. (2009) National Institute of Nutrition, Indian Council of Medical Research. Available at: http://icmr.nic.in/final/RDA-2010.pdf

[24] National Health and Nutrition Examination Survey III Anthropometric Procedures-Anthropometry procedures manual, 2007. Available at: http://www.cdc.gov/nchs/data/nhanes/nhanes_07_08/manual_an.pdf

[25] Macallan DC. (1999) Malnutrition in tuberculosis. Diagn Microbiol Infect Dis. 34(2), 153-157.PolyMedix PMX-30063 Effective Against NDM-