Nutrition and Tuberculosis

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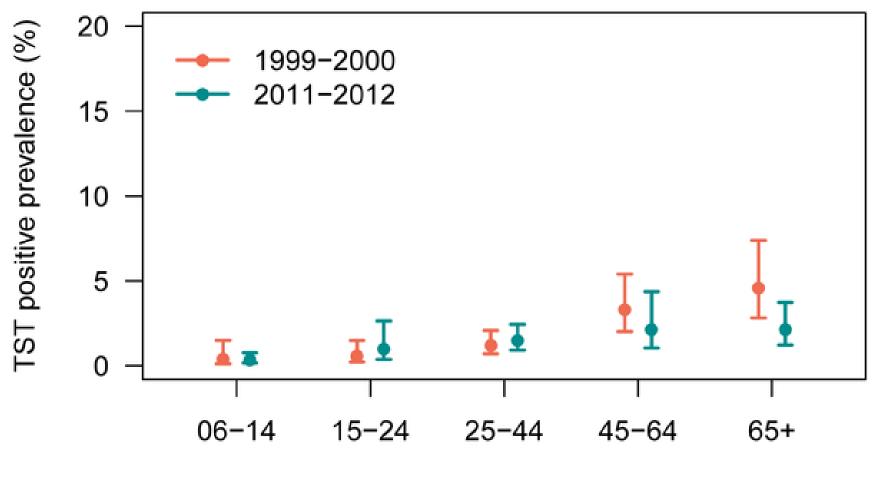
Tuberculosis

- TB is one of the top ten causes of illness, death, and disability worldwide
- The leading cause of death from a curable infectious disease
- It is estimated that approximately one-third of the world's population is infected with Mycobacterium tuberculosis
- 8.8 million new cases during 2005 alone
- About 10% of those with latent TB are expected to develop active TB disease

Epidemiology

- More than 80% of TB patients live in Asia and sub-Saharan Africa
- Sub-Saharan Africa has the highest incidence of the disease
- India, China, Indonesia, Bangladesh, and Pakistan together account for more than half of the global estimate of active TB
- Approximately 1.6 million people died from TB in 2005
- Deaths from active TB are expected to increase to five million a year by 2050

Tuberculin skin test positive prevalence estimates from the civilian, noninstitutionalized U.S.-born population aged 6 years or older, by age group.



age group

Miramontes R, Hill AN, Yelk Woodruff RS, Lambert LA, Navin TR, et al. (2015) Tuberculosis Infection in the United States: Prevalence Estimates from the National Health and Nutrition Examination Survey, 2011-2012. PLOS ONE 10(11): e0140881. https://doi.org/10.1371/journal.pone.0140881

https://journals.plos.org/plosone/article?id=10.1371/journal.pone.014

Pathophysiology

- Mycobacterium tuberculosis (latent TB) from an individual with active TB is spread through airborne droplets dispersed via coughing, sneezing, singing, or talking
- TB infection occurs when the droplets are inhaled and lodge in passageways in the lungs
- The infection is usually controlled and active disease does not develop unless the immune function is weakened
- Active TB disease can be caused by a recent infection, activation of latent TB, or a relapse following earlier treatment

Clinical presentation Diagnosis

- Bacteriology remains the recommended method for diagnosing active TB, first through sputum smear microscopy and then culture testing
- Culturing TB bacteria is expensive and results are not immediately available
- TB smears detect 65-80% of infections

Active TB disease

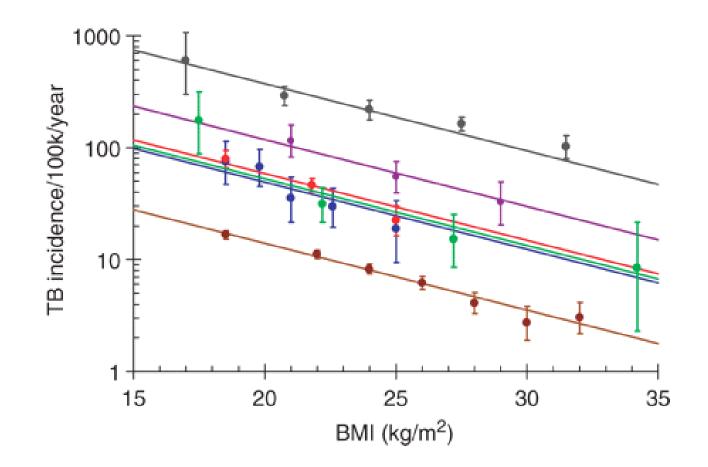
- TB bacteria grow in almost any organ system but infection occurs most often in the mid to lower lung
- Symptoms of active TB include persistent cough, fever, night sweats, weight loss, shortness of breath, coughing up blood, and chest pain



Risk factors for TB

- Poverty
- HIV-infection
- Sharing a home with someone who has active TB
- Exposure to smoke from domestic stoves and cigarettes
- Poorly controlled diabetes
- Vitamin D deficiency
- Malnutrition
- Chemotherapy
- Gender (Male)

Dose–response relationship in the reviewed cohort studies on the association between BMI and TB incidence. ...



Int J Epidemiol, Volume 39, Issue 1, February 2010, Pages 149–155, https://doi.org/10.1093/ije/dyp308



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Effect sizes of low serum vitamin D in tuberculosis patients and controls

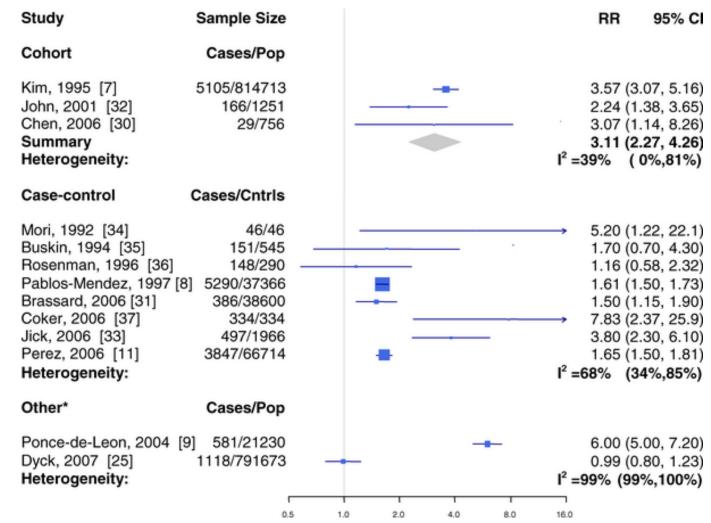
Study or sub-category	Cases N	Control N	Effect Size (SE)	Effect Size (random) 95% Cl	Weight %	Effect Size (random) 95% Cl
Davies, UK	40	40	0.8600 (0.2300)	+	16.69	0.86 (0.41, 1.31)
Grange, Indonesia	40	38	0.1800 (0.2300)	+	16.69	0.18 [-0.27, 0.63]
Davies, Kenya	15	15	1.0400 (0.3900)		8.34	1.04 [0.28, 1.80]
Davies, Thailand	51	51	0.9600 (0.2100)	+	18.31	0.96 [0.55, 1.37]
Chan, Hong Kong	24	24	0.3300 (0.3000)		12.14	0.33 [-0.26, 0.92]
Wikinson, UK	103	42	0.5900 (0.2300)	+	16.69	0.59 [0.14, 1.04]
Sasidharan, India	35	16	0.9400 (0.3200)		11.13	0.94 (0.31, 1.57)
Total (95% CI)	308	226		•	100.00	0.68 [0.43, 0.93]
Test for heterogeneity: Cha	= 10.14, df = 6(P =			,		
Test for overall effect Z =						
			-4	-2 0 2	4	
			1	Lower in Controls Lower in Case	10	

Alcohol

- More than 40 g alcohol per day, and/or have an alcohol use disorder
- Increased risk of infection
- Influence on the immune system

Alcohol use as a risk factor for tuberculosis – a systematic review •Knut Lönnroth, Brian G Williams, Stephanie Stadlin, Ernesto Jaramillo &Christopher Dye <u>BMC Public Health</u> volume 8, Article number: 289 (2008)

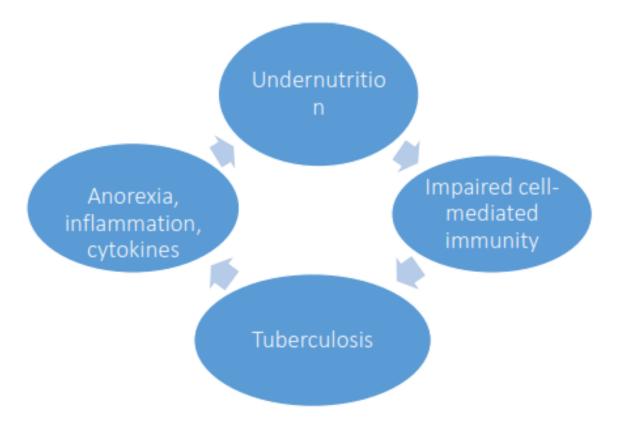
Forest Plot of the 13 Studies That Quantitatively Assessed the Association between Diabetes and Active Tuberculosis by Study Designs



Jeon CY, Murray MB (2008) Diabetes Mellitus Increases the Risk of Active Tuberculosis: A Systematic Review of 13 Observational Studies. PLOS Medicine 5(7): e152. https://doi.org/10.1371/journal.pmed.0050152

https://journals.plos.org/pdicite/article?id=1371/is_l.pmed.6550152 EDICINE

Box 3. Vulnerability factors related to progression of disease (Adapted from ²⁴)							
Individual	Household/community	Environment/institution					
Age	Socioeconomic status	Geography/physical terrain					
Sex	Migration	Availability of health services					
Nutritional status	Access to treatment	Quality of health care					
Immunity		Availability of appropriate					
Genetics		treatment					
Interactions with other diseases		Emergence of drug resistance					
(such as HIV, diabetes)		Development of infrastructure/					
Behavior		other services					
Poverty		Public policy					
Education							
Knowledge							
Diet							
Livelihood							
L							



Malnutrition and immunity

 It is well established that nutritional deficiency is associated with impaired immune functions

Malnutrition weakening immune function

- Malnutrition enhances the development of active TB, and active TB makes malnutrition worse
- Decreased appetite and food intake, and increased losses and altered metabolism associated with the inflammatory and immune response

Body Mass Index (BMI) and Regulatory Cytokines

- Individuals with low BMI have diminished circulating levels of proinflammatory (IFN-γ, TNF-α, IL-22, IL-1α, IL-1β, and IL-6) cytokines but elevated levels of regulatory cytokines (IL-10, TGF-β, IL-5, IL-13).
- A positive correlation between the circulating levels of pro-inflammatory cytokines and high BMI (between 25 and 29.9) and a negative correlation between the circulating levels of anti-inflammatory cytokines and low BMI
- These data suggest a protective mechanism of BMI against progression of TB infection to disease by altering the cytokines of an individual.

Malnutrition and immunity

- Utilization of amino aids and protein synthesis may be inhibited due to the presence of pro-inflammatory cytokines
- A study in UK:
- 66% of patients had a BMI <18.5 (6 times more frequent than in controls). weight, skin-fold thicknesses, mid-upper arm circumference (MUAC), fat mass, and fat free mass were all significantly lower in those with active TB
- Wasting is associated with increased mortality in those with active TB

Malnutrition and immunity

- Among individuals with latent TB, the occurrence of malnutrition may be an important trigger for active TB development
- One longitudinal study conducted in the United States found the incidence of active TB was 2.2 times higher in children with low subcutaneous fat stores (skin-fold thicknesses between 0 and 4mm) compared with those with 10mm subcutaneous fat

Nutritional status changes during TB treatment

- Treatment of active TB without supplementary nutrition, nutritional status usually improves: (improved appetite and food intake, reduced energy/nutrient demands, and improved metabolic efficiency)
- Most improvements, however, are limited to increases in fat mass
- Recovery from TB does not guarantee protein mass restoration, even though weight gain is significant
- After 12 months 32% of males and 19% of females considered cured of their TB continued to have a BMI <18.5, indicating malnutrition continued after TB treatment

Nutritional status and TB relapse

- Relapse risk was increased amongst those who were ≤90% of ideal body weight at the time of diagnosis
- Weight gain of less than 5% between diagnosis and completion of the initiation phase of therapy is significantly associated with relapse
- Additional study is needed to determine whether nutritional support to underweight patients with active disease prevents relapse following anti-TB treatment

Serum albumin levels and TB

- The normal range is 3.5 to 5.5 g/dL
- Many studies have reported low concentrations of serum albumin (<35g/L), an indicator of protein status, at the time of active TB diagnosis
- However, cytokines present during the acute phase response to active infection down-regulate serum albumin levels
- Low levels of albumin may reflect the presence of inflammation rather than a protein deficient state
- After anti-TB treatment, mean serum albumin will increase significantly to the level of the healthy controls

Serum electrolytes

- Measurement of serum potassium and magnesium is desirable, if patient has severe undernutrition and has been admitted for inpatient management.
- This is because patients with severe undernutrition are deficient in these, and low levels of potassium and magnesium are risk factors for re-feeding syndrome

Malnutrition and TB/HIV co-infection in adults

- TB and HIV infections are both independently associated with malnutrition
- TB/HIV co-infection poses an additional metabolic, physical, and nutritional burden, resulting in potential further increase in energy expenditure, malabsorption, micronutrient deficiency, and increased production of proinflammatory cytokines resulting in breakdown of body lipids and proteins
- The combination of TB/HIV co-infection and malnutrition has been termed "triple trouble
- Co-infected patients also had significantly lower mean serum albumin compared with HIV-negative TB patients

Objectives

- Nutritional assessment
- Clinical assessment of nutritional status
- nutrition-oriented history and nutrition-oriented examination
- Anthropometric measurements in children and classification of nutritional status using WHO recommended cut-offs
- Anthropometric measurements in adults and classification of nutritional status according to ranges of BMI appropriate for Asian populations
- Use of mid upper arm circumference for classification of nutritional status in patients who are unable to stand or in whom BMI is inappropriate (pregnant women, patients with oedema)
- Clinical and nutritional indicators of need for inpatient care (red flags)



- Nutritional counselling
- Concept of healthy balanced diet
- Understanding the impact of TB on nutritional status and importance of nutritional recovery in patients with TB
- Advice on increasing energy intake of diet by using locally available nutrient-rich food
- Understanding foods and practices to avoid, and clarifying myths and misconceptions including expenses on costly fruits, costly tonics, commercial food supplements and IV fluid therapy
- Understanding the role of physical activity in strengthening muscles and improving appetite



- Nutritional management
- Recommended energy, protein and micronutrient intake in patients with active TB
- Management of moderate to severe undernutrition in patients with poor family or a food basket for the patient
- Management of severe undernutrition requiring hospitalization initial stabilization phase and rehabilitation phase
- Micronutrient supplementation in patients with active TB

Outcomes and indicators

- Direct nutritional and patient-important outcomes
 - Improved nutritional intake
 - Improved anthropometric measures and nutritional recovery at the end of treatment
 - Improved functional status
 - Improved health-related quality of life

Outcomes and indicators

• Clinical outcomes

- Reduction in TB related mortality
- Reduction in rates of adverse drug events
- Reduction in rates of relapse

Effect of TB on nutritional status

Wasting, which occurs because of 3 mechanisms

- Decreased intake because of anorexia and its severity correlates broadly with the severity of clinical disease.
- TB increases the basal metabolic rate because of fever, although this increase is offset by the decreased energy expenditure due to decreased activity before the clinical improvement starts as a result of treatment.
- Finally TB causes protein catabolism with a resultant negative nitrogen balance, with muscle breakdown under the influence of the acute phase response.

Mid upper arm circumference (MUAC)

- The left upper arm -measured midway between the tip of the shoulder (acromion) and elbow (olecranon)
- MUAC < 22 cm in women correlates with a BMI of < 18.5 kg/m2 and is suggestive of undernutrition
- MUAC < 19 cm: Severe undernutrition and MUAC 19–22 cm: Moderate acute malnutrition
- MUAC reflects of the effect of acute undernutrition more than BMI
- Patients with a MUAC less than 19 cm had 5 times the mortality rate of those with a MUAC > 24 cm

Nutritional indicator	Age group	Severe acute malnutrition (SAM)	Moderate acute malnutrition (MAM)
BMI for age	6 years to less than 18 years	Less than -3 z score (< -3 z score)	>-3 z score to < - 2 z score
MUAC	6 years to less than 10 years	Less than 11.5 cm (<11.5 cm)	>13.5-14.5 cm
	10 years to less than 18 years	Less than 16.0 cm (<16.0 cm)	≥16.0 &< 19.0 cm
Edema	6 years -18 years	Present	Absent

Effect of nutritional interventions on outcomes in patients with TB

Cochrane review

Insufficient research in the form of randomised trials on the effect of macronutrient and micronutrient supplementation, to either confirm or exclude a beneficial effect of nutritional supplementation on outcomes in patients with TB

Weight gains in patients in India

- In the absence of nutritional support:
 - RNTCP cohort: Mean weight gain =3.22 kg
 - Non-RNTCP cohort(Rural central India) Mean weight gain= 3.9 kg
- With nutritional support
 - Men: 7.8 kg (sanatorium treatment group) vs. 5.5 kg (domiciliary treatment group)
 - Women: 11.0 kg (sanatorium treatment group) vs. 4.8 kg (domiciliary treatment group)
- Nutritional support should aim at a weight gain of approximately 5% of body weight during the initial intensive phase of treatment.

Time of sputum smears or culture negativity

	Nutrit	ion sup	port	c	ontrol			Mean Difference	Mean Dit	fference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV. Random, 95% Cl	IV. Rando	m, 95% Cl
Adrian R Martineau 2011	86	23.37	62	93.5	21.94	64	8.3%	-7.50 [-15.42, 0.42]		
Cao hong 2013	12.6	1.3	24	19.2	1.2	24	45.4%	-6.60 [-7.31, -5.89]		
Trevino A Pakasi 2010	13.6	1.4	66	17.5	1.7	86	46.3%	-3.90 [-4.39, -3.41]	-	
Total (95% CI)			152			174	100.0%	-5.42 [-7.93, -2.92]	-	
Heterogeneity: Tau ^z = 3.46	; Chi# = 3	8.08, df	= 2 (P	< 0.000	01); 2 =	95%				
Test for overall effect: Z = 4	4.24 (P <	0.0001)							-10 -5 0 Favours control	5 10 Favours nutrition supp

Chin Med J (Engl). 2015

Adjuvant Efficacy of Nutrition Support During Pulmonary Tuberculosis Treating Course: Systematic Review and Meta-analysis Zhuang-Li Si ¹ Ling-Ling Kang ² Xu-Bo Shen ¹ and Yuanhigh-energy and protein dietary was superior to dietary advice only or general diet group

Zhuang-Li Si,¹ Ling-Ling Kang,² Xu-Bo Shen,¹ and Yuan-Zhong Zhou¹

Body mass index changed during follow-up

	Nutriti	C	Control			Mean Difference	Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV. Random, 95% CI	IV. Random, 95% CI
10.5.1 Use of any nutritio	n interve	ntion n	nethod	at 1 mo	nth				
Ma guiyan 2009	19.1	2.8	80	18	1.5	80	13.7%	1.10 [0.40, 1.80]	
Wang chuanmei 2011	23.1	4.3	42	18.9	4.2	40	4.4%	4.20 [2.36, 6.04]	
Xu yingling 2008	19.7	4.8	200	18.7	3.7	198	11.7%	1.00 [0.16, 1.84]	
Subtotal (95% CI)			322			318	29.8%	1.80 [0.48, 3.12]	
Heterogeneity: Tau ² = 1.04	; Chi ² = 1	0.35, df	= 2 (P	= 0.006	; 12 = 8	31%			
Test for overall effect: Z = 2	2.66 (P =	(800.0							
10.5.2 Use of any nutritio	n interve	ntion m	nethod	at 2 mo	nths				
Adrian R Martineau 2011	21.29	2.72	62	21.18	2.75	64	10.4%	0.11 [-0.85, 1.07]	
Trevino A Pakasi 2010	17.7	2	66	17.5	2.4	86	13.6%	0.20 [-0.50, 0.90]	
Subtotal (95% CI)			128			150	24.0%	0.17 [-0.40, 0.73]	-
Heterogeneity: Tau ^a = 0.00	; Chi? = 0	.02, df =	= 1 (P =	0.88); F	= 0%	-15,525		2020 - 1523 - 1920 - 1937 I.	1000
Test for overall effect: Z =									
10.5.3 Use of any nutritio	n interve	ntion n	tethod	at 3 mo	nths				
Nawal Salahuddin 2013	18.67	0.16	132	18.26	0.12	127	21.3%	0.41 [0.38, 0.44]	
Tan shouyong 2005	18.9	2.9	26	18.7	2.7	26	5.8%	0.20 [-1.32, 1.72]	
Subtotal (95% CI)	0.07033	신망	158	145947	0.0000	153	27.1%	0.41 [0.38, 0.44]	1
Heterogeneity: Tau ² = 0.00	; Chi ² = 0	.07. df =	= 1 (P =	0.79); 1	= 0%				
Test for overall effect: Z = 2					0.000.00				
10.5.4 Use of any nutritio	n interve	ntion m	nethod	at 6 mo	nths				
Tan shouyong 2005	19.1	2.8	26	18.9	2.7	26	6.0%	0.20 [-1.30, 1.70]	
Trevino A Pakasi 2010	18.3	2.02	66	18.4	2.62	86	13.1%	-0.10 [-0.84, 0.64]	
Subtotal (95% CI)			92			112	19.1%	-0.04 [-0.70, 0.62]	•
Heterogeneity: Tau ^a = 0.00	; Chi ² = 0	12, df	= 1 (P =	0.72); F	= 0%	531,129			5.25
Test for overall effect: Z =									
Total (95% CI)			700			733	100.0%	0.59 [0.16, 1.02]	+
Heterogeneity: Tau ^z = 0.23	; Chi ² = 2	4.66, df	= 8 (P	= 0.002	: IF = 6	38%			
Test for overall effect: Z =									-2 -1 0 1 2
Test for subaroup difference			ff = 3 /F	= 0.08	12 = 5	5.3%			Favours control Favours nutrition supp

high-energy and protein dietary vs dietary advice only or general diet group

Reported effects of nutritional support in patients with active TB

- Improved weight gain. Weight gains 1.6–2 times higher in group given adequate diet
- Decreased mortality in HIV negative patients was seen in two randomised controlled trials in the group given macronutrient supplement (RR =0.18)
- Decreased rate of unfavourable outcome. Patients who received nutritional support had a 50% reduced risk of unsuccessful treatment outcome compared to those who did not receive nutritional support
- Shorter time to sputum conversion: A shorter time to sputum conversion(3 months vs. 4 months)
- Increased muscle strength, Improved adherence to therapy and reduced rates of default in programmatic setting in Africa, India

Energy requirements

- Varies with their age, gender, their activity levels as in persons without active TB
- The additional requirements in view of the active TB disease
- The energy requirements for recovery of nutritional deficit

Energy requirements

- For energy for a sedentary adult is estimated to be 37 kcal/kg/day (man 39 kcal/kg/day and woman 35 kcal/kg/day). This calculation assumes that the body weight is in the normal range
- An additional energy requirement of 10% has been recommended in the case of patients with active TB
- Finally we have to consider the energy requirements for recovery of nutritional deficit. This will vary between patients depending on the severity of wasting and undernutrition.

Example of calculation of minimum acceptable or desirable body weight at the end of treatment

- A young woman with pulmonary TB has a weight of 38 kg and a height of 152 cm. or 1.52m. What should be her minimum acceptable body weight or her desirable body weight at the end of treatment?
- BMI = weight in kg/(height in m)2= 38 /(1.52)2.
- Her current BMI is therefore 38/2.31 = 16.45 kg/m2
- The weight corresponding to the desirable BMI of 21 kg/m2 = 21 x 2.31 = 48.5 kg.
- The weight corresponding to the BMI of 18.5 kg/m2=18.5 x 2.31 = 42.7 kg.
- This patient should therefore gain at least 4.7 kg from her current weight of 38 kg to achieve the minimum acceptable BMI of 18.5 kg/m2, and around 10.5 kg to achieve the desirable BMI of 21 kg/m2

Example of calculation of minimum acceptable or desirable body weight at the end of treatment

- To achieve a weight gain of 1 kg, an excess of 7500 calories of intake over expenditure is required.
- To achieve a weight gain of 5-10 kg in the first 3-6 months: 312 -625 kCal/day, or 7-15 kCal/kg /day
- In the initial phase, patients with severe undernutrition should be allowed to eat as much as they desire

Carbohydrate requirements

• 55-75% of total energy intake

 Carbohydrates are major sources of energy and patients can consume them during meals as well in snacks between meals to increase their energy intake

Protein requirements

- 1.2-1.5 g/kg ideal body weight per day
- Proteins should comprise around 10-15% of the total energy intake
- A daily protein intake of 51 -64 grams per day, would be required if we target the weight corresponding to the BMI of 18.5 kg/m2. If we consider the desirable weight as 48.5 kg corresponding to the BMI of 21 kg/m2, then the protein requirement would be in the range of 58-73 gms per day

Fat requirements

- 15-30% of total daily energy intake
- Fats are present in oils, nuts, milk and milk products, meat
- In patients with reduced intakes like patients with TB, the addition of oil, ghee and nuts to the diet can help achieve the goals of energy intake

Micronutrients

- The recommended daily allowances of vitamins, minerals
- We recommend that provision of 1 RDA of micronutrients as a supplement in view of the micronutrient deficiencies present in TB patients
- We recommend screening of TB patients for the presence of anemia, which is very common. Iron and folic acid tablets can be added to the micronutrient supplement after 2 weeks of starting Anti-TB therapy

Nutritional requirements in pregnant and lactating women with TB

- Pregnant and lactating women have additional requirements of energy, proteins, folic acid, calcium and iron, in addition to the enhanced requirements related to active disease and nutritional recovery.
- Pregnant women need an additional 300 cal, 15 g protein, 400 micrograms of folic acid, 1000 mg of calcium and 38 mg of iron per day.
- Lactating women require about 400-550 extra calories per day, 18-25 g additional protein, additional amounts of vitamin A.

Comorbidities

- HIV
- Diabetes mellitus
- Smoking
- Alcohol or substance abuse
- Which have their own nutritional implications, and these should be fully considered during nutrition screening, assessment and counselling.

Content of counselling

- Understanding the impact of TB on nutritional status and importance of nutritional recovery
- Providing intake of adequate energy, protein "Food first"
- Concept of healthy balanced diet
- What should be avoided
- Advice on increasing energy intake of diet by using locally available nutrient-rich food

Content of counselling

- Clarifying myths and misconceptions including expenses on costly fruits, costly tonics, commercial food supplements, and IV fluid therapy
- Food hygiene and cooking practices
- Understanding role of physical activity in strengthening muscles and improving appetite
- When to refer for admission and care.

What should be avoided

- Alcohol in any form is dangerous for the patient as it increases the risk of drug toxicity, and the patient should be supported in his attempt to quit alcohol.
- Carbonated drinks
- Excess of tea and coffee, or their intake with food
- Tobacco and tobacco products
- Excess of spices and salt

Identifying people who need referral or hospitalization

- A bed ridden patient who can't stand
- Patients with no appetite
- Those with recurrent vomiting or jaundice
- Breathless or drowsy patient

Clinical history	Dietary assessment	Socioeconomic status	Family history	
 History of unintended weight loss: >10% weight loss in 6 months or more than 5% of loss of in 1 month indicates severe weight loss History of alcohol intake History of abdominal pain/nausea and vomiting/diarrhoea History of diabetes 	 Vegetarian/non-vegetarian Appetite and intake of food Ability to cook and/or Ability to cook and/or availability of nutritious food at home Anyfood preferences (assess in terms of acceptability of supplements) 	 Income: regular income Number of family members Availability of a care giver in family Any eligibility for a social assistance scheme* 	 Number of people in the family living together Family history of TB or death due to TB. Diabetes 	

Phases of management of severe malnutrition

	Initial phase		Rehabilitation	Follow up
	Day 1-2	Day 3-7	Weeks 2-6	Weeks 7-26
 Hypoglycemia 				
2. Hypothermia	\rightarrow			
Fluid imbalance				
 Electrolyte imbalance 				
Treat infection				
 Correct micronutrient deficiencies 	Withou	it iron	with iron	
 Cautious feeding 				
 Increase feeding to recover lost weight 				

Dehydration

Component	Concentration
Glucose	125 mmol/L
Sodium	45
Potassium	40
Chloride	70
Citrate	7
Magnesium	3
Zinc	0.3
Copper	0.045

Potassium and Magnesium

• Potassium

- 3-4 mmol/kg/day
- Deficit can affect cardiac function, gastric emptying, and muscle strength

• Magnesium

- 0.4-0.6 mmol/kg/day
- Magnesium is needed to allow potassium to be retained within cells

Composition of F-75 and F-100

Ingredient	F-75*	F-100 [§]
Dried skimmed milk	25g	80g
OR Fresh Cow milk	300 ml	880 ml
Sugar	70 g	50 g (use 75 g if using cow's milk)
Cereal flour	35 g	-
Vegetable oil	27 g (17 g if using cow's milk)	60 g
Mineral mix**	20 ml	20 ml
Vitamin mix (of water soluble and fat soluble vitamins)	140mg	140mg
Water to make	1000 ml	1000 ml

Indications for NG feeding

- In patients in the initial phase of treatment due to severe anorexia, stomatitis glossitis or frequent vomiting
- Patients with severe dysphagia or odynophagia due to any cause
- Patients with tuberculous meningitis with an obtunded sensorium
- Critically ill patients in shock

Correct micronutrient deficiencies

- Micronutrient deficiencies are common and should be corrected
- Vitamin A: Vitamin A should not be routinely administered if the patient is pregnant or the patient has oedema
- Vitamin B: Higher doses may be required initially in light of increased thiamine requirement
- Iron: Iron supplementation is withheld during the initial phase associated with reduced iron binding capacity, iron may reduce resistance to infection, and may have adverse effects. Once appetite returns, and the acute complications have been dealt with the patient can be given an iron supplement containing 60 mg elemental iron.

Rehabilitation phase

- 2nd to 6th week
- Return of the appetite, and aims at intensive recovery of lost weight and lean body mass
- The formula feed recommended during the rehabilitation phase is the F-100 feed at a rate of 1.7 ml/kg/hour
- The target protein intake is 1.2-1.5 g/Kg/Ideal body weight/day
- Iron supplements may be introduced if indicated

Follow-up phase

- May last up to 6 months
- A less than 5% weight gain in 2 months
- A 10% weight gain in 3 months would be optimal

Micronutrients and TB

- less is known about micronutrient status and the TB disease process
- Vitamins A, C, E, B6 and folic acid and minerals zinc, copper, selenium, and iron all have key roles in metabolic pathways, cellular function, and immune competence
- Deficiency of single or multiple nutrients can reduce an individual's resistance to any infection
- In the era before drug management of active TB, administering cod liver oil (rich in vitamins A and D) was a common therapy to improve host defense
- Reduced micronutrient intake, and especially intake of vitamin A and antioxidant vitamins and minerals such as pro-vitamin A carotenoids, vitamins E and C, zinc, and selenium, has been associated with an impaired immune response

Micronutrients and TB

Vitamin A, which is usually assessed using serum retinol, also plays important roles in lymphocyte proliferation, generation of antibody responses, and maintenance of mucosal surfaces and epithelial function

Vitamin E protects cell membranes against lipid peroxidation and oxidative stress by scavenging free radicals and by stabilizing cell membranes

Zinc is essential for DNA synthesis and cell differentiation. Zinc deficiency is associated with recurrent infections, decreased phagocytosis, decreased B and T lymphocyte production, and depressed macrophage activity

Selenium is an essential part of antioxidative enzymes, such as glutathione peroxidase, which protects cells from oxidative damage

Micronutrients and TB

Blood micronutrient status is difficult to assess in the presence of infection because biochemical indicators of several micronutrients are affected by the immune system's acute phase response

Serum ferritin and copper are "positive" acute phase reactants that increase when the immune system responds to an infection, while albumin, retinol, and zinc are "negative" reactants

Measurement of "positive" acute phase reactants, such as serum ferritin and copper, may underestimate nutrient deficiency, while measurement of negative responders, such as serum albumin, retinol, and zinc, may lead to an overestimation of underlying deficiencies.

The micronutrients which have received the most attention are the following

- Vitamin A, which is involved in both T- and B-lymphocyte function, macrophage activity and the generation of antibody responses
- Vitamin D, which is involved in the function of macrophages, a key component of the immune response to tuberculosis
- Vitamin E, which has anti-oxidant properties and may protect against T-lympocyte failure due to oxidative stress
- Zinc, which is necessary for adequate functioning of many aspects of human immunity
- Selenium; which is essential for both cell-mediated and humoral immunity

B6

- Isoniazid (INH) inhibits the phosphorylation of pyridoxine, which results in increased excretion of vitamin B6
- Current treatment guidelines recommend that patients on INH with burning feet symptoms take supplemental pyridoxine

Vitamin D

The role of vitamin D in resistance to active TB has been known for more than 100 years, as vitamin D-rich cod liver oil and exposure to sunlight were once part of regular therapy for TB

Vitamin D is required for macrophage activation, which is essential for keeping TB in the latent phase

More recently, the role of vitamin D in the TB disease process re-emerged with the increased incidence of active TB in the winter months among individuals from the Indian subcontinent after moving to the United Kingdom

Vitamin A

- Vitamin A deficiency strongly predicted risk of incident TB disease among household contacts of TB patients.
- Vitamin A supplementation among individuals at high risk of TB may provide an effective means of preventing TB disease

Vitamin D supplementation had no beneficial effect on anti-TB treatment

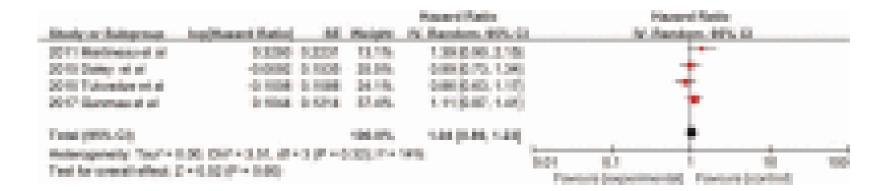
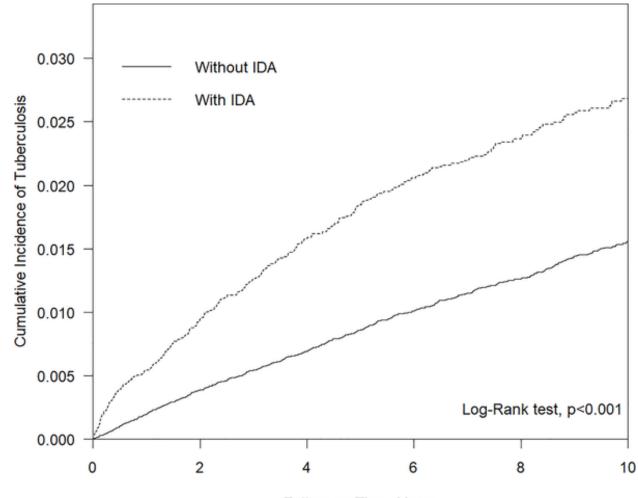


Fig 1. Cumulative incidence of TB in the IDA cohort and comparison group.



Follow-up Time, Years

Chu KA, Hsu CH, Lin MC, Chu YH, Hung YM, et al. (2019) Association of iron deficiency anemia with tuberculosis in Taiwan: A nationwide population-based study. PLOS ONE 14(8): e0221908. https://doi.org/10.1371/journal.pone.0221908 https://journals.plos.org/plosone/article?id=10.1371/journal.pone.022

LOS ONE

Anemia

• Anemia due to deficiency of micronutrients like iron and folates is very common in patients with TB

	Normal	Mild anemia	Moderate	Severe
	Hb		anemia	anemia
Men	≥13 g/dl	10 – 12.9	7 – 9.9 g/dl	< 7 g/dl
		g/dl		
Non-pregnant	≥12 g/dl	10 – 11.9	7 – 9.9 g/dl	< 7 g/dl
women		g/dl		
Pregnant women	≥11 g/dl	10 – 10.9	7 – 9.9 g/dl	< 7 g/dl
		g/dl		

Anemia

Age group	Normal Hb	Mild anemia	Moderate	Severe
			anemia	anemia
Children 5-11	≥11.5	11 – 11.4	8 – 10.9	< 8
years				
Children 12-14	≥12	11 – 11.9	8 – 10.9	< 8
years				
Boys >15 years	≥13	10 – 12.9	7 – 9.9	< 7
Girls >15 years	≥12	10 – 11.9	7 – 9.9	< 7

Hb= hemoglobin in gm/dL

Experience and considerations for incorporating nutrition into TB programs

- Accessing and successfully completing TB treatment is complex
- Multi-drug resistant TB is a serious challenge and growing concern
- Nutritional support could be beneficial to disease management
- Nutritional assessment to determine nutritional status and necessary referrals or intervention
- Nutrition education and counseling on symptom-management and improved dietary intake during and after TB treatment
- Targeted micronutrient supplementation (e.g., vitamin B6)

Experience and considerations for incorporating nutrition into TB programs

- The World Food Programme (WFP), the food aid arm of the United Nations
- One goal of the WFP is to improve nutrition, quality of life, and self-help of individuals and communities
- Their food assistance programs aim to enhance patient adherence to treatment, while helping patients in food insecure households meet their nutrient needs during treatment
- Food assistance increases health care center attendance thereby increasing case detection

Future Research

- 1. The ideal nutritional supplementation for the prevention and management of infectious diseases
- 2. Better understanding of interactions between immune signaling pathways and resistance to diseases
- 3. Advanced nutriogenomics studies for predisposition of the infectious diseases—in terms of transcriptomics, proteomics, and metabolomics with respect to dietary signals
- 4. To study the role of diet and lifestyle and how it affects the health
- 5. Role of nutrition among elderly and pediatric patient population to boost immunity
- 6. Effect of lipids over inflammation and infection, especially in TB and emergence of drug resistance
- 7. Association of impaired immune response and poor dietary intake
- 8. Association of TB infection and disease with Hidden hunger (micronutrient deficiency)

Thanks



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