

# Let's Talk TB

A Series on Tuberculosis, A Disease That Affects Over 2 Million Indians Every Year

## Nutritional Care and Support of Patients With Tuberculosis in India: A Primer for General Physicians

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### Abstract

*Nutritional care is considered fundamental to clinical practice and recognised to be an integral part of TB care, by the WHO and the Revised National Tuberculosis Control Programme (RNTCP). Undernutrition is a comorbidity which is widely prevalent, severe, and persistent even after cure in Indian patients, in the absence of nutritional support. This increases their risk of mortality, drug-induced hepatotoxicity, malabsorption of key drugs like rifampicin, performance status, and relapse even after successful treatment. Providers need to assess weight, height, edema, estimate BMI & measure haemoglobin. BMI < 14 kg/m<sup>2</sup>, edema, severe anaemia, inability to stand, are red-flag features which mandate referral for initial inpatient care. Patients should be counselled on an appropriate balanced diet with 3 meals and at least 2 snacks. The RNTCP has evolved food assistance packages consisting of cereals, groundnuts or pulses, milk powder or oil for provision of around 1000 calories and up to 50 gram proteins to patients during treatment, suggests provision of 1 recommended daily allowance of micronutrients and an enhanced quantum of food rations through the public distribution system to TB affected households.*

assessment and management are integral components of TB treatment and care.” – *Guideline: Nutritional care and support for patients with tuberculosis*. Geneva: World Health Organisation; 2013.

### SOME SCENARIOS OFTEN ENCOUNTERED IN INDIA

Shankar, a manual labourer, diagnosed as extensive smear-positive disease with no other co-morbidity, dies of the disease in the first month of therapy. He weighed just 34 kg with a height of 160 cm. Laxmi, another undernourished patient develops jaundice during the first weeks of therapy. Hamid who completed treatment successfully as a new case, but weighed 48 kg at the end of regular treatment, developed recurrence of disease after 6 months of stopping it.

It is important to realise that effective chemotherapy is a *necessary prerequisite* but *may not be sufficient* to eliminate the serious adverse outcomes of Mortality, Drug toxicity and Relapse in TB patients. For example, TB mortality in India remains unacceptably high with an estimated 480,000 deaths annually,<sup>1</sup> adverse effects of medicines was a leading cause of interruption of therapy in India,<sup>2</sup> while the rates of relapse are more than 10% in India, which is twice that considered acceptable (must be <5%).<sup>3,4</sup>

“All doctors should recognize that proper nutritional care is fundamental to good clinical practice.” – *Nutrition and patients: A doctor's responsibility*. Report of a Working Party. London: Royal Society of Physicians; 2002.

“Because of the clear bidirectional causal link between undernutrition and active TB, nutrition screening,

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The adverse outcomes in these patients illustrate the interaction between undernutrition and tuberculosis. Undernutrition impairs cell mediated immunity (similar to HIV) which provides protection against TB, and due to its high prevalence in the population, is the major driver of the TB epidemic in India. It contributes to 55% (or more than 1 million cases) of new cases every year.<sup>5</sup> Tuberculosis can itself lead to or worsen pre-existing undernutrition due to its effect on appetite, energy expenditure, and pro-teins catabolism.

The new END TB strategy emphasises integrated patient-centred care, which includes management of co-morbidities, as well as action on risk factors.<sup>6</sup> Undernutrition is a co-morbidity as well as a risk factor for adverse outcomes, which is often neglected.<sup>7</sup> Internationally, the perspective has changed as reflected in the recommendation from a WHO guideline quoted above.<sup>8</sup> The Revised National Tuberculosis Control Programme (RNTCP) has endorsed this changed perspective and released policy guidance on nutritional care and support suitable for the Indian context.<sup>9</sup> This chapter discusses the situation analysis of undernutrition in TB patients, its implications for outcomes in patients, and outlines a nutritional care pathway consisting of assessment, counselling, management and follow up. For more information, the healthcare providers can refer to the RNTCP Guidance Document and the relevant WHO documents.<sup>9-11</sup>

## WHAT DO WE KNOW ABOUT THE NUTRITIONAL STATUS OF INDIAN PATIENTS WITH TUBERCULOSIS, AT DIAGNOSIS AND AFTER TREATMENT?

Undernutrition is highly prevalent, of a serious nature and persists even after successful treatment in patients with TB in India. In a large

**Table 1 – Effect of undernutrition on different outcomes in patients with tuberculosis**

Outcome	Effect of undernutrition	Comment
<b>Mortality</b>	Increased risk of death irrespective of age, HIV status or drug-susceptibility status. <sup>23</sup>	BMI approaching 12 kg/m <sup>2</sup> can itself be fatal. <sup>24</sup> Weight less than 50 kg strong predictor of poor outcome in X-DR TB. <sup>25</sup>
<b>Morbidity</b>	Increased severity of disease.	Severe disease increases risk of death, and long-term sequelae
<b>Response to treatment</b>	<ul style="list-style-type: none"> <li>Effect on drug absorption</li> <li>Effect on drug metabolism</li> </ul>	<ul style="list-style-type: none"> <li>Sub-therapeutic level of Rifampicin documented<sup>26</sup></li> <li>Drug resistance and treatment failure</li> <li>Increased risk of drug induced hepatotoxicity,<sup>27,28</sup> and other adverse effects<sup>29</sup></li> <li>Drug toxicity may lead to interruptions of therapy or default</li> </ul>
<b>Relapse</b>	Low BMI and poor weight gain increase the risk of relapse <sup>30</sup>	Poor weight gain in Indian TB patients might be a contributor to higher relapse rates
<b>Performance status</b>	Poor weight gain means poor recovery of lean body mass	Impairment of muscle function could delay return to work and impair work capacity
<b>TB disease in household contacts</b>	Increased risk of disease in undernourished contacts <sup>22</sup> (Grave implications in contacts of patients with MDR-TB/X-DR TB)	Food security is worsened by loss of wages due to TB. Nutritional assessment and support of contacts of MDR-TB especially crucial
<b>Clinical presentation of TB disease</b>	Presentation may be atypical in severely undernourished children or adults	Lower lobe involvement <sup>31</sup> Presentation as an acute pneumonia. <sup>32</sup> A negative tuberculin skin test in undernourished children.

cohort study in rural patients with pulmonary tuberculosis, half of adult men had a weight below 42 kg, while half of adult women had a weight of less than 34 kg.<sup>12</sup> The reference weights recommended for healthy Indian men and women of 60 kg and 55 kg respectively.<sup>13</sup> In terms of body mass index (BMI calculated as weight in kg/(height in metre squared) half of the adult men had a BMI less than 16.0 kg/m<sup>2</sup>, while half of the adult women had a BMI of less than 15 kg/m<sup>2</sup>, and BMIs even below 13 were encountered.<sup>12</sup> Nearly three-quarters had anaemia and more

than half of the cohort had evidence of chronic undernutrition with stunting.<sup>12</sup> Nationally, the weight data is similar with half of men weighing less than 43 kg and women weighing less than 38 kg.<sup>14</sup> Micronutrient deficiency is also common in patients with active TB with iron and folate, vitamin A, zinc, vitamin D deficiencies.<sup>15-17</sup> Only one third of the men and a quarter of the women in the rural cohort, had BMIs in the normal range after cure.<sup>12</sup> Half of rural patients with active TB gained less than 3.9 kg,<sup>18</sup> which is similar to patients under the RNTCP, about 3.2 kg.<sup>19</sup> These are clearly suboptimal,

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**Table 2 – Tools for nutritional assessment- ABCD**

Tool	Basic assessment	Additional assessment and comments
<b>Anthropometry</b>	<ul style="list-style-type: none"><li>- Weight, height in all patients</li><li>- BMI for age/sex in 5-18 years age</li><li>- BMI in adults</li><li>- Weight for age z-scores in 0-5 years</li></ul>	Mid upper arm circumference In pregnant women, those with oedema, and those unable to stand
<b>Biochemical and laboratory assessment</b>	<ul style="list-style-type: none"><li>- Haemoglobin in all cases</li><li>- Peripheral smear in case of anaemia</li></ul>	Serum electrolytes required in severe undernutrition.
<b>Clinical assessment</b>	<ul style="list-style-type: none"><li>- Pallor</li><li>- Loss of buccal pad of fat</li><li>- Oedema on feet and legs suggesting hypoproteinaemia</li><li>- Wasting of muscles</li></ul>	Flaky skin, sparse pluckable hair with depigmentation especially is seen in under-5. Bitot's spots and glossitis suggest vitamin deficiencies
<b>Dietary assessment</b>	<ul style="list-style-type: none"><li>- Appetite</li><li>- Intake over past few days</li><li>- Food preferences: vegetarian or non-vegetarian</li></ul>	Food availability and diversity at household level. Access to supplementary nutrition programmes

while an optimal diet provided in the famous Madras trial resulted in much higher weight gains.<sup>20</sup>

## WHAT ARE THE IMPLICATIONS OF UNDERNUTRITION IN PATIENTS WITH TB?

Undernutrition affects occurrence of TB, its severity, its outcome during and after treatment. It may also influence clinical presentation of disease.

### Link between undernutrition and occurrence, severity of TB

Undernutrition is not only a risk factor for tuberculosis, but also makes the disease severe, which in turn worsens the undernutrition. As stated in a WHO guideline *“without nutritional support, patients, especially those already suffering from baseline hunger, can become enmeshed in a vicious cycle of malnutrition and disease”*.<sup>18</sup> This can even result in

death. Food insecurity has a strong association with risk of TB in contacts and undernutrition in household contacts increases the risk of active TB in them.<sup>21,22</sup>

### Link between undernutrition and outcomes in TB

Undernutrition at diagnosis in a patient with active TB can increase the risk of unfavourable outcomes. These are listed in **Table 1**.

## WHAT ARE THE FOOD-DRUG INTERACTIONS WITH FIRST-LINE ANTI-TB DRUGS? SHOULD ISONIAZID ALSO BE TAKEN IN FASTING STATE?

Rifampicin is usually advised to be taken on an empty stomach for better bioavailability. It is advisable to give other medicines like isoniazid also in the fasting state.<sup>33</sup> Recent studies have shown that food decreased the peak concentrations of isoniazid

and rifampicin in the range of 20 to 40%.<sup>34,35</sup> This lowering of serum levels of first-line drugs with food can impact treatment outcomes,<sup>36</sup> and may be of particular importance in undernourished patients who may have lower levels of rifampicin.<sup>26</sup> Physician often advise anti-TB drugs after meals when patient have gastrointestinal side effects. In such a case, it is advisable to take them 2-3 hours after a meal.<sup>37</sup> Antacids or H<sub>2</sub> blockers do not affect drug absorption, and may also be tried.<sup>33</sup> Drugs like Isoniazid can cause pyridoxine deficiency which can lead to peripheral neuropathy. This effect can be prevented by giving pyridoxine 10 mg per day, and this is especially important in undernourished individuals.

## WHAT ARE THE STEPS IN THE NUTRITIONAL CARE PATHWAY?

The steps in the nutrition care pathway consist of nutritional assessment, nutritional counselling, and nutritional support and follow up. The physician should also take into account any other co-morbidities of the patient e.g., diabetes which have their own implications for nutritional counselling and therapy

### Nutritional assessment

The tools for nutritional assessment can be classified as ABCD Anthropometry, Biochemical assessment, Clinical Assessment, and Dietary assessment summarised in **Table 2**.

The RNTCP guidance document has suggested the following red-flag features related to nutritional status which indicate need for patient care as indicated in **Box 1**.<sup>9</sup>

**Nutritional assessment of contacts.** The WHO recommends nutritional screening and screening of contacts of TB patients followed by management of undernourished contacts as per the guidelines.<sup>8</sup> Recent changes in weight may be a symptom

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**Table 3 – BMI based cut-offs suggested for nutritional classification**

BMI (Kg/m <sup>2</sup> )	Classification
<14.0	Extremely underweight
<16.0	Grade III underweight
16.0 – 16.9	Grade II underweight
17.0 – 18.4	Grade I underweight
18.5 – 24.9*	Normal weight

\*A WHO expert consultation in 2004 proposed different cut-offs for overweight and obesity in Asians. The different cut-offs for obesity are not mentioned here as this is less likely to be encountered in TB cases

of disease in contacts, while chronic undernutrition in those without disease, (especially children) should be addressed to decrease their risk of developing active TB.

## Nutritional counseling

The WHO guidelines recommend as a principle that “an adequate diet, containing all essential macro- and micronutrients, is necessary for the well-being and health of all people, including those with TB infection or TB disease”.<sup>8</sup>

The requirements of an adequate diet for a patient with active TB in India are as follows:<sup>9</sup>

- Approximately 40 kcal/kg of ideal or desirable body weight;\*
- Proteins should be 1.2 -1.5 gm/ideal or desirable body weight;
- Fat requirements are similar to general population;
- Micronutrient requirement is similar to general population. One daily allowance in the form of a multivitamin supplement is recommended.

Patients of TB in India, especially the poor, may not be able to meet their requirement for a healthy balanced diet

\*A desirable body weight is one which corresponds to the BMI of 20-22 kg/m<sup>2</sup>. See<sup>9</sup> for details.

and may require nutritional support. In a study the mean calorie intake in patients with TB and HIV was in the range of 1545-2016 calories per day, and was similar to the HIV negative community controls.<sup>38</sup>

The practical points to be emphasised during nutritional counselling are as follows:

**Balanced diet.** One which has adequate proportion of foods from all the food groups:

- Cereals, millets and pulses
- Vegetables and fruits
- Milk and milk products, meat, eggs and fish
- Oils, fats, nuts and oil seeds

Ask about preferences—vegetarian vs. non-vegetarian. Vegetarians can get adequate protein of good quality by combining cereals with pulses, and by consuming milk and milk products.

**Emphasise cost-effective locally available options in the food groups.**

Local cereals including millets, local pulses, and local fruits may offer good nutrition at lower cost. Egg protein is better compared to even proteins from fish and meat, while eggs are also cheaper. Groundnuts are a good source of calories and proteins, and equivalent to dry fruits. They should be eaten preferably roasted and with skin removed.

**Emphasise frequent feedings 3 meals + at least 2 snacks for nutritional recovery.** Increase caloric value of meals by adding ghee (if available) or oil to rice or chapatti. Snacks may be fruits (e.g., bananas), groundnuts, chikki, laddu, roasted horse-gram.

**Address misconceptions.** Commercial supplements provide the same nutrients at higher cost. A 200 gm tin of protein supplement costing around Rs. 175 has 40 gm protein, which can also be obtained in 1200 ml milk or 6 eggs, or 200 gm pulses. Tonics are not useful nor are IV drips.

**Recommend hygiene.** Recommend food hygiene, hand washing and

## Box 1 – Red-flag features on nutritional assessment

1. BMI of 14.0-15.9 kg/m<sup>2</sup> with no appetite OR bilateral oedema OR inability to stand, OR
2. BMI of less than 14 kg/m<sup>2</sup>, OR
3. Haemoglobin of less than 7 gm/dl.

good cooking practices.

**Recommend referral.** Recommend referral for patients with red-flag features on nutritional assessment (**Box 1**).

Contacts, especially young children who are undernourished can be referred to appropriate nutritional assistance services like ICDS services, nutritional rehabilitation centres.

*The annexures in the RNTCP document contain dietary requirements, exchange lists, sample meal plans and model diets for patients with tuberculosis.<sup>9</sup>*

## Nutritional support

Patients with undernutrition can be managed on an individualised basis with calculation of their energy and protein requirements. A food assistance package has been proposed which can serve the needs of individual patients and TB programmes. This is based on the pattern of weights in India, and is intended for all patients with active TB (irrespective of HIV status, drug-susceptibility status).

The RNTCP guidance document has also suggested a food assistance package for all patients with active TB which consists of the following:<sup>9</sup>

1. A food assistance package for the patient of 5 kg cereal (rice, wheat, millet) along with 1.5 kg milk powder and 3 kg groundnuts (preferably roasted and skinned). The other accompanying options with the cereal are 3 kg groundnuts and 1 kg oil OR 3 kg pulses and 1 kg oil. This would ensure provision of around 1000 calorie and up to 52 g

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protein per day;

2. A multivitamin tablet containing one recommended daily allowance of all micronutrients;
3. In addition, the RNTCP guidance document recommends doubling the PDS ration for the family to address food insecurity and provides an additional 500 calories for family members and the patient.

This form of nutritional support would ensure that patients are able to meet their usual requirement of calories and proteins and the 312-625 calories/day, they require in addition to recover the lost weight.

**Inpatient nutritional care and support for patients with red-flag features.** A certain proportion of patients with tuberculosis in India like Shankar mentioned earlier, have red-flag features at diagnosis. Shankar's BMI for example was 13.28 kg/m<sup>2</sup>, indicating high risk of complications including early mortality. Such patients should be treated as inpatients for initial 1-2 weeks. The management of such patients is discussed in the RNTCP guidance document as well as a WHO manual.<sup>8,9</sup> Briefly, the patient requires stabilisation of fluid, electrolyte status, and initiation of feeding in gradually increasing amounts in the first week. No weight gain should be expected in this initial phase. Patients will require supplementation with potassium and magnesium, thiamine and B-complex vitamins orally.<sup>39</sup> A potentially lethal complication of nutritional support- the refeeding syndrome, can occur if the refeeding is not cautious. This syndrome can manifest as life-threatening cardiac arrhythmias, severe electrolyte disturbances, neurological complications and hyperglycaemia.<sup>39</sup> The risk factors for refeeding syndrome are- patients with BMI less than 16 kg/m<sup>2</sup>, those with low potassium, magnesium prior to refeeding, and those who consume alcohol.<sup>39</sup> In the second week, once the patient has stabilised, the appetite has

improved, and the patient begins to gain weight, he can be discharged.

## Nutritional monitoring during follow up

Nutritional indices appropriate to the age group like BMI and weight or weight for age should be monitored monthly or at least at 2, 4 and 6 months of follow-up. A weight gain of at least 5% of baseline in the first 2 months should be the target, and a BMI of 21 kg/m<sup>2</sup> would be optimal.

Poor weight gain or occurrence of weight loss should be investigated. The possible causes can be treatment failure, non-adherence to therapy, food insecurity and inadequate dietary intake, or drug-induced hepatotoxicity.

## NUTRITIONAL SUPPORT: A BRIEF REVIEW OF THE EVIDENCE IN PATIENTS WITH TUBERCULOSIS

The evidence surrounding nutritional support lacks firm conclusions primarily due to the limited numbers of studies done with macronutrient supplementation which had inadequate sample sizes, as well as inability to achieve recommended dietary intakes. There is also an ethical issue about conducting RCTs on undernourished patients without providing them nutritional support. There is robust data from other fields on the effect of nutritional support on mortality. For example, management of severe acute malnutrition in children can reduce case-fatality by 55%.<sup>40</sup>

The old and emerging evidence related to nutritional support is clinically and programmatically important. The benefits include 1.6-2 times higher weight gain,<sup>20</sup> shorter time to sputum conversion and sustained microbiological cure,<sup>41</sup> improvements in muscle strength,<sup>42</sup> improved pharmacokinetics of rifampicin,<sup>43</sup> promising reduction of TB related mortality [Risk ratio: 0.18(0.02,1.48)]

in preliminary studies from India,<sup>44,45</sup> 50% reduction in unfavorable outcomes and improved adherence in the supplemented group in a programmatic setting in India.<sup>46</sup> Adequate weight gain was associated with a two fold higher odds of treatment successes in MDR-TB patients.<sup>47</sup> Finally, at the Papworth village settlement for the TB affected, social interventions of which adequate nutrition was considered the most important, reduced six-fold the incidence of TB in contacts which included young children, even when the patients had no access to TB drugs, and the contacts who were uniformly infected by the age of five years, and had not been vaccinated.<sup>48</sup>

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# CIS CME—Questions

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## Questions

- 1** Which of the following is true of undernutrition and TB?
  - a. Undernutrition is a risk factor for TB
  - b. Tuberculosis can lead to undernutrition
  - c. Undernutrition worsens severity of tuberculosis
  - d. Undernutrition is associated with adverse outcomes in TB patients
  - e. All of the above
  
- 2** A patient with a height of 170 cm has a weight of 45 kg. His calculated BMI would indicate
  - a. Normal body weight
  - b. Mild undernutrition
  - c. Severe undernutrition
  - d. Moderate undernutrition
  
- 3** Which of the following drug/s should be given on an empty stomach for better bioavailability.
  - a. Isoniazid
  - b. Rifampicin
  - c. Ethambutol
  - d. Isoniazid as well as rifampicin
  
- 4** A labourer with TB has signs of hypoproteinaemia. What would be an appropriate dietary advice?
  - a. Take 4 teaspoons of a commercial supplement, which has 40 gm protein in 200 gms
  - b. Eat mutton, chicken (if he is non-vegetarian)
  - c. Eat additional quantity of pulses or eggs (if he is non-vegetarian)
  - d. Take 2 tsp of a tonic containing amino acids daily
  
- 5** Pyridoxine deficiency can occur due to treatment of which anti-TB drug?
  - a. Rifampicin
  - b. Isoniazid
  - c. Ethambutol
  - d. Pyrazinamide
  
- 6** The following are true for inpatient care of patient with red-flag features in the first week, except
  - a. Feed vigorously with the daily requirement of calories and protein
  - b. Give adequate quantities of potassium, magnesium
  - c. Correct dehydration
  - d. Give thiamine and B-complex vitamins during this phase

*Answers on the next page*

## Answers

- 1** The correct answer is (e).
- 2** The correct answer is (c). BMI is calculated as weight in kg/(height in metre)<sup>2</sup>. The BMI in this patient would be  $45/(1.7)^2 = 15.57 \text{ kg/m}^2$ . This is less than  $16.0 \text{ kg/m}^2$  and indicates severe undernutrition.
- 3** The correct answer is (d). The bioavailability and peak serum concentrations of both isoniazid and rifampicin is affected by food.
- 4** The correct answer is (c): The commercial protein supplement may contain 40 gm protein in a 200-gm pack, but is costly and inappropriate, as are tonics with amino acids. Mutton and chicken are more expensive than eggs and the labourer is more likely to afford additional pulses or eggs, than eat chicken or mutton on a daily basis. The protein content per 100 gm, does not differ between eggs and chicken.
- 5** The correct answer is (b). Isoniazid interferes competitively with pyridoxine metabolism by inhibiting the formation of the active form of the vitamin, and hence often results in peripheral neuropathy. This is especially marked in malnutrition, pregnancy, lactation, HIV infection, diabetes and hypertension. This effect can be prevented by giving pyridoxine 10 mg per day.
- 6** The correct answer is (a). In a patient with very low BMI and who has probably been eating little for many days, vigorous feeding may result in refeeding syndrome which can be dangerous. The feeding should start at 50% of the dietary requirement or even lower in the first few days, along with the other measures mentioned.