Prevalence of undernutrition among children (6 months to 5 years) with tuberculosis and impact of nutritional counselling and tuberculosis treatment on the nutritional status: a cohort study from Pakistan

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Table of Contents

Abstract

Undernutrition and Tuberculosis (TB) are significant factors contributing to the mortality of children under 5 years old. Pakistan ranks 6th position globally in TB prevalence, with a high incidence of childhood TB cases compared to the worldwide average. The relationship between undernutrition and TB is reciprocal: undernutrition significantly raises the risk of TB development, while TB, in turn, exacerbates undernutrition. Effective management of undernutrition during TB treatment is crucial as it significantly impacts treatment outcomes. However, the inadequate Infant and Young Child Feeding (IYCF) practices in Low-Middle-Income countries further compound undernutrition when combined with TB. Hence, addressing both undernutrition through nutritional counselling to improve IYCF practices and TB treatment can substantially diminish morbidity and mortality rates among children.

This study aimed to explore the prevalence of undernutrition in children with TB and assess compliance with nutritional counselling for mothers to improve IYCF practices, observing changes in dietary patterns and nutritional status in children with TB. The data was collected from two major tertiary care hospitals in Lahore, Pakistan. Cross-sectional and prospective cohort study designs were used to achieve the objectives of this study.

The prevalence of undernutrition among children with TB was alarmingly high at 62.3%, accompanied by a significant mortality rate of 15%. IYCF practices were suboptimal at enrolment and 88% of mothers of children with TB showed good compliance to nutritional counselling with improvement in dietary practices. The prevalence of undernutrition decreased from 63% to 15% with nutrition counselling and TB treatment after 2 months of follow-up. The 12% of the children who did not adhere to nutritional counselling experienced static or worsened nutritional statuses compared to those who followed the advice.

These findings hold critical implications for the implementation of nutrition counselling programs. Nutrition counselling should be the part of TB treatment program as it can be an effective way to improve the nutritional status of children with TB and the feeding practices of the community.

List of Abbreviations

MAM – Moderate Acute Malnutrition

SAM – Severe Acute Malnutrition

TB – Tuberculosis

MTB – Mycobacterium Tuberculosis

BMI – Body Mass Index

WHZ – Weight for height z-scores

WAZ – Weight for age z-scores

HAZ – Height for age z-scores

SD – Standard Deviation

IQR- Interquartile range

RUTF – Ready to use therapeutic food

MNP – Multiple Micronutrient powder

WHO – World Health Organization

BCG – Bacillus Calmette-Guerin vaccine

WASH – Water sanitation and hygiene

IYCF – Infant and Young children feeding

TBM – Tuberculous meningitis

List of Tables

List of Figures

1. Introduction

1.1 Background

Childhood Tuberculosis (TB) is a major public health problem. According to the World Health Organization (WHO) Global TB Report 2023, there estimated 11 million new TB cases globally with 1.3 million deaths in the adult population (2). Of these, 1.3 million reported TB cases were among children aged 0–14 years, accounting for 12% of the estimated total TB cases. However, the actual notification of newly diagnosed cases was only 70%, with even lower percentages for specific age brackets: 49% for children aged 0–14 years and a concerning 42% for those under 5 years old. Adding to the gravity of the situation, TB-related deaths among children globally present alarming statistics. In 2022, an estimated 16% and 18% of deaths attributed to HIV-negative TB and HIV-positive TB, respectively, occurred in children. These rates surpass their proportional share of TB cases. Among HIV-negative 139,000 deaths were reported among children aged <5 years, with an additional 44,000 in older children and young adolescents aged 5–14 years. This signifies that Childhood TB stands out as a significant health challenge, particularly for children under 5 years of age, and calls for the urgent need for enhanced strategies to improve the diagnosis and management of children affected by TB.

Pakistan ranks fifth among the highest TB burden countries globally with a prevalence of 340 cases of TB per 100,000 population per year (3). It is estimated to have 510,000 newly diagnosed TB cases every year (4). Out of all TB cases in Pakistan, 14% of them are children which is approx. accounts for over 71000 newly diagnosed cases in Pakistan (2). The proportion of children with TB is higher than the global proportion of TB (14% versus 12%). The mortality rate due to TB is 20 per 100,000 population annually, resulting in 48,100 deaths in 2022, equivalent to one TB-related death every 11 minutes. Aligned with global efforts to combat infectious diseases, the Sustainable Development Goals (SDG) target 3.3 specifically addresses TB (5). The WHO's End TB Strategy, initiated in 2014, sets ambitious targets, including an 80% reduction in new cases by 2030, a 90% drop in TB-related mortality by 2023, and the complete elimination of catastrophic costs for TB-affected families (6). The National TB Control Program (NTP) in Pakistan launched the National Strategic Plan (NSP) for TB control, envisioning a TB-free Pakistan with zero deaths, diseases, and poverty related to TB by 2035. However, despite these efforts, Pakistan faces challenges in achieving SDG targets, experiencing only a 4.5% reduction in TB incidence against a 20% target and a 1.5% reduction in TB deaths against a 35% target from 2015 to 2022 (7).

1.1.1 Determinants of TB and Undernutrition

The situation of TB in Pakistan is complicated in the face of having a high and persistent burden of undernutrition and low socioeconomic indicators which increases the risk of getting TB. According to the National Nutrition Survey of Pakistan, 40% of children under five are stunted (low height for age), 17.7% are wasted (low weight for height), and 28.9% are underweight (low weight for age), 53.7% are anaemic and 5.7% are severely anaemic (8). One in eight adolescent girls is underweight whereas one in five adolescent boys is underweight whereas 14.4% of women of reproductive age are underweight and 37.8% are overweight (8).

Nearly half of women of reproductive age are illiterate, whereas 15.5% and 14.5% have completed higher and secondary education respectively (8). Pakistan is a lower middle-income country and 37% of the population has some grade of food insecurity, overcrowding, and low socioeconomic index (8). Lack of education and food insecurity further predispose to undernutrition and TB. Furthermore, all this acts both ways, that is, can be the result or can lead to food insecurity and poverty (9, 10). Undernutrition and food insecurity have become more prevalent in the pandemic of coronavirus disease (COVID-19) and its economic devastation worldwide (11). Therefore, it is necessary to determine the biological and socioeconomic factors that contribute to TB and undernutrition and its outcomes to understand and help in planning an integrated approach to manage children with TB (12-14).

Pakistan faces several significant challenges in achieving SDGs related to TB, especially in children. These challenges include poverty and limited healthcare infrastructure, low water and sanitation levels, low immunization coverage and high rate of undernutrition in children aged under 5 years, limited public health awareness and education, and challenges in TB case detection and reporting. Poverty restricts people in Pakistan from seeking timely medical care including TB, which leads to late diagnosis and increased transmission of the disease (15). Since the start of the COVID-19 pandemic, limited healthcare infrastructure has become a point of concern, shortage of healthcare workers and inadequate diagnostic facilities have been exposed (16). There were some similar symptoms between coronavirus and TB bacilli, which led to the initiation of COVID-19 treatment without confirming TB infection (17). Crowded houses, poor water and sanitation, unhygienic living conditions, low immunization, and undernutrition weaken children's immune systems making them more susceptible to TB infection (18) and these factors can be found common in Pakistan. The presence of social

stigma of TB is very high among all communities irrespective of education level, leading to underreporting of TB cases and increasing the burden of TB (19). Underreporting of TB cases and challenges in case detection hinder the effectiveness of TB control programs and delay in achieving SDGs related to TB (20). To control TB infection and achieve the SDGs related to TB, Pakistan needs an integrated approach that not only focuses on the treatment of TB but also addresses the factors that contribute to an increase in the incidence and poor prognosis from TB.

1.1.2 Undernutrition as the highest risk factor for TB

Undernutrition has been reported to be the highest risk factor for getting TB in the world and also in Pakistan. Of the global proportion of TB cases in 2022, 2.2 million new TB cases were attributable to undernutrition (21). It was also the highest risk factor attributable to TB in Pakistan. People who are undernourished are more likely to develop active TB, and they are also more likely to have a more severe case of TB (22).

Pakistan has a high prevalence of undernutrition in children under 5 years of age. The prevalence of wasting among young children is 17.7% which is higher than the internationally agreed emergency thresholds of 15%, 40.2% of children are stunted and 28.9% of children are underweight (23). Also, the National coverage for full immunization of children 12 to 23 months old children is only 54% (24). The undernourished population is at high risk of getting TB infection when they come in contact with the case of TB (9). Furthermore, in the undernourished population, the response to Bacillus Calmette Guerin (BCG) vaccination and Tuberculin skin test is also altered (9, 25) Higher incidence of TB in the country with higher incidence of undernutrition and low vaccination makes the younger population susceptible to TB.

Recently, a correlation between nutritional status and TB among children was studied in Indonesia which indicated a very strong correlation between TB and nutritional status among children, and the prevalence of undernutrition in children with TB was found to be over 60% (26). Unfortunately, such studies are not available from Pakistan.

1.2 Tuberculosis (TB)

TB is a lung disease that is caused by a bacterium known as Mycobacterium tuberculosis (MTB). TB is universally considered to be a lung disease (27). When a person who is infected with TB coughs or sneezes, they are releasing bacteria into the air, which facilitates the spread

of the disease. Although TB most commonly affects the lungs (also known as pulmonary TB), it can also affect other parts of the body (also known as extrapulmonary TB). Chest x-rays, the tuberculin skin test, the interferon-gamma release assay (IGRA), and the Gene-Xpert MTB/RIF are some of the diagnostic tools that can be utilized to diagnose TB. TB is endemic in low & low-middle-income countries. Low-income countries account for more than 95% of cases and deaths by TB (27). About two-third of total TB cases are found in eight countries including India, China, Pakistan, Indonesia, The Philippines, Nigeria, South Africa, and Bangladesh (28). Undernutrition is also a common problem in these countries except China. Almost 98% of undernourished children are in developing countries where TB is endemic (29).

1.3 Undernutrition & its forms

Undernutrition signifies an insufficient amount of nutrient intake to satisfy the individual's demand to retain good health (30). Undernutrition can be sub-categorized as wasting, stunting, and underweight (31).

I. Wasting: It can also be referred to as low weight-for-height. It indicates severe weight loss because of insufficient food according to the body's need or if the individual has any infectious disease i.e., diarrhea. It is also called acute undernutrition or acute malnutrition and can be treated. Wasting can make the individual prone to infectious disease and vice versa (32). Wasting can be identified by measuring an individual's weight and height. If the weight of children according to their height is lower than the normal weight according to the WHO growth standards, then the child is wasted (33). Wasting can be moderate or severe. If the weight-for-height according to WHO's weight-height z-score (WHZ) is between <-2 and -3 standard deviation (SD), it is said to be moderate acute malnutrition (MAM) and if WHZ is <-3 standard deviation it is said to be severe acute malnutrition (SAM).

II. Stunting: It can also be referred to as low height-for-age. It is a chronic form of undernutrition caused by poor feeding practices during early life, modest maternal health, low socio-economic status, etc. Stunted children cannot reach their potential physical and cognitive development, which impacts the overall quality of life of the child (34, 35). Stunting can be assessed by measuring children's length or height (length for children less than 2 years of age and height for children of 2 years or older). Compare the height with acceptable standard values for normal children provided in WHO's growth standards, if the height is -2SD less than the standard value, the child is considered to be stunted (36).

III. Underweight: It is referred to as low weight-for-age. According to the WHO recommendation, an individual is said to be underweight when its body mass index (BMI) is below 18.5 (37). The underweight child can be stunted, wasted, or both.

1.4 Risk factors for undernutrition with TB

Undernutrition is a risk factor for TB, but TB is a risk factor to further worsen nutritional status irrespective of the nutritional status at the time of diagnosis. This is because of a variety of factors related to the disease process, reduced diet due to lack of awareness resulting in inadequate infant and young child feeding practices (IYCF) or sociocultural practices, repeated infections in the child because of inadequate vaccination or unsafe water and sanitation practices, socioeconomic factors, poor maternal health, climate factors, inadequate health system (38-40). Below is a discussion on how these factors contribute to undernutrition in children with TB.

1.4.1 Factors related to the disease process

Children with TB are particularly vulnerable to undernutrition due to a combination of factors. These challenges significantly impact their nutritional status and overall well-being:

1. **Reduced Appetite:** Children with TB often experience a diminished appetite, leading to decreased food intake and inadequate nutrient consumption (40).

2. **Gastrointestinal Symptoms:** TB can cause symptoms such as vomiting and diarrhoea, which impede the absorption of essential nutrients from the diet (41).

3. **Increased Catabolism:** The breakdown of muscle tissue for energy (catabolism) is heightened in individuals with TB, contributing to muscle wasting and nutritional depletion (40).

4. **Metabolic Demand:** The body's increased metabolic demands during TB infection can lead to a higher requirement for nutrients, which may not be met through regular dietary intake (40).

5. **Inflammation and Malabsorption:** TB-induced inflammation can affect the absorption of nutrients in the gastrointestinal tract, leading to malabsorption issues (42).

6. **Respiratory Effort:** The increased respiratory effort in children with TB can elevate energy expenditure, further exacerbating the risk of undernutrition (43).

7. **Disease-Related Stress:** The stress associated with TB can impact the nutritional status of children, influencing their overall well-being (40).

1.4.2 Poor IYCF practices, inadequate diet and cultural taboos

The primary sources of nutrition during early childhood consist of breastfeeding and complementary feeding. Scientific evidence has demonstrated that breastfeeding is the most ideal form of nourishment for new-borns (44). After the age of 6 months, an infant's energy and nutrient requirements begin to surpass the quantity supplied by breast milk; therefore, complementary foods become essential to fulfil those requirements. (45) **There are poor IYCF practices in Pakistan**, only 46% of new-born receive early breastfeeding (within the first hour of birth), only 48% of infants get exclusive breastfeeding up to 6 months of age, 68% of infants get continued breastfeeding till 1 year and 56% children get continued breastfeeding till 2 years of age (46, 47). Only 36% of children get age-appropriate complementary feeding. The minimum diversity of food defined as consumption of all food groups: breast milk, dairy products, carbohydrates group, pulses group, flesh foods, fruit and vegetables which is necessary for normal growth and development was only 14% and a minimum meal frequency was only 18% in young children from Pakistan (47). UNICEF reported that complementary feeding practices are independent of economic status, these practices are suboptimal even among wealthy people (46). In low-middle-income countries, very few children get safe and nutritionally adequate complementary feeding, mostly, children either get it too early, or too late, or too little, or too much, or not nutritionally adequate (48). The factors associated with improper IYCF practices include a lack of knowledge about the nutritional value and importance of each food group and inadequate child care (49). Inappropriate feeding practices eventually lead to inadequate dietary intake which is the immediate cause of undernutrition which then lead to weakening of immune system in younger children and make the children prone to infections like TB. Insufficient adherence to WHO guidelines on IYCF practices was also found in low-middle-income countries (50-53)**.** Children with TB often face cultural taboos and mother of those children avoid breastfeeding those children. Adhering to food taboos and limiting the consumption of a balanced diet are also factors that lead to the development of undernutrition in children with under 5 years of age (54).

1.4.3 Repeated infections and ill health of children

Inadequate vaccination:

Children under 5 years old are susceptible to a range of common infectious diseases, including acute respiratory infections, TB, diarrhoea, measles, mumps, rubella, chickenpox, diphtheria, and tetanus. Incomplete or lack of vaccination increases their vulnerability to these childhood illnesses (55). The interaction between undernutrition and infectious diseases like TB creates a detrimental cycle, with each condition exacerbating the other, hindering the achievement of optimal nutritional status. Infectious diseases stimulate the immune system, elevating metabolism and energy requirements for immune health and tissue repair. However, the heightened dietary needs, when coupled with insufficient food intake, can exacerbate nutrient depletion, contributing to undernutrition (56).

Unsafe water and sanitation: Contaminated water significantly heighten the risk of infections and nutrient loss, intensifying the complexities associated with undernutrition. When communities lack access to clean, safe drinking water, there is a heightened susceptibility to ingesting contaminants. Children with TB with weekend immune system are more susceptible to diseases like diarrhoea and gastrointestinal disorders if consuming unsafe water. These illnesses, in turn, contribute to undernutrition by causing nutrient loss through symptoms like vomiting, diarrhoea, and diminished appetite (57, 58).

1.4.4 Socioeconomic factors

Low socioeconomic status

Individuals with TB often struggle to access or afford nutritious food due to their low socioeconomic status and food insecurity. The prevalence of TB is notably higher among those in lower socioeconomic strata (18, 59). Families dealing with childhood TB may encounter significant financial challenges, including the costs associated with diagnosis, treatment, and management (59). Parents or caregivers may need to take time off from work to care for an ill child, resulting in lost income and potential economic difficulties.

Poor maternal nutrition and health

Undernourished mothers are prone to TB infection which is closest source of infection transmission to young children. Maternal health can highly affect the health of the children.

Undernourished mothers with TB have far-reaching consequences on breastfeeding practices and infant care, perpetuating a cycle of undernutrition. Particularly crucial during the initial months of life, breastfeeding serves as a vital source of nutrition and immunological components for infants. When a woman is undernourished, her breast milk supply may be insufficient or lacking in essential nutrients, posing challenges to the optimal nourishment of the baby. Children born underweight and facing nutritional difficulties early in life are more prone to enduring growth stunting, micronutrient deficiencies, infectious diseases, and developmental delays. These early setbacks can exert lasting impacts on the child's health, cognitive development, and overall potential (60, 61).

1.4.5 Environmental factors

Environmental factors, such as climate-related challenges, can impact agriculture and food production, affecting food availability and human health (62). Pollution of air and water make the individuals highly susceptible to TB (63, 64). Exposure to household air pollution from biomass fuels (e.g., wood, dung) or poorly designed cooking stoves releases harmful pollutants like particulate matter and carbon monoxide, making individuals cough and increase the chances of spreading the TB infection, which can then lead to undernutrition (65).

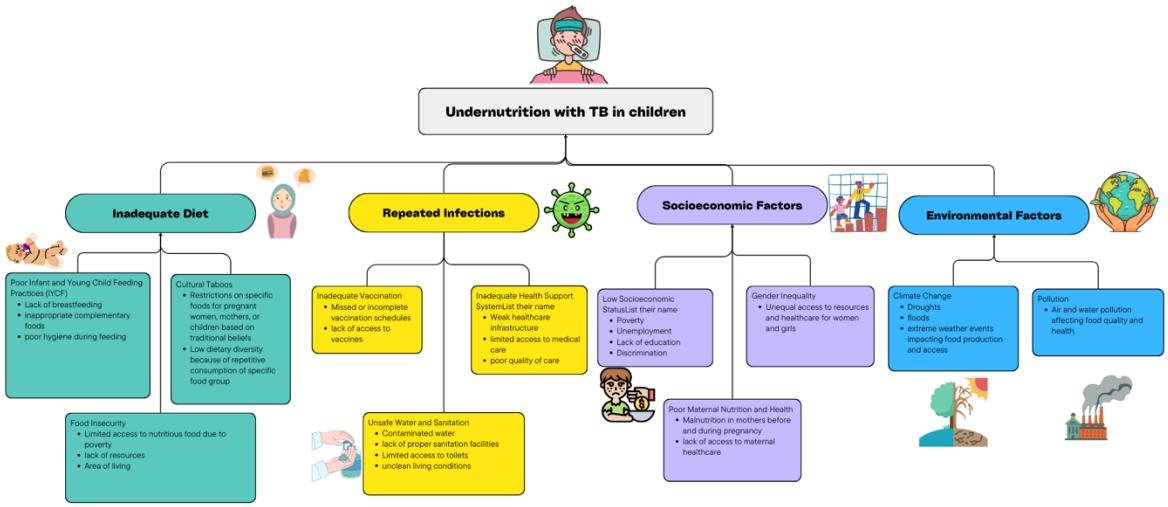


Figure 1: Risk factors for undernutrition with TB in children

1.5 Impact of undernutrition and TB on health of the child

Childhood TB coupled with undernutrition can have both short-term and long-term devastating effects on a child's health.

I. Short term effects

The intricate relationship between TB and undernutrition significantly influences the course and severity of TB infections. Undernutrition compromises the immune system's ability to effectively respond against MTB infection, leading to delayed pathogen clearance from the host's system (40). This delay is attributed to the impaired cell-mediated immunity from undernutrition, hindering the host's capacity to control and eliminate TB (40, 66, 67). The compromised nutritional condition also hinders the body's capacity to heal, restore injured tissues, and react to treatments. This leads to more prolonged hospitalizations and high healthcare costs for the patient and the health system (68, 69).

Undernutrition significantly influences the response to **anti-TB treatment. The p**atients may experience increased sensitivity to the **side effects of TB medications**, making it harder for them to adhere to prescribed medication regimens. The **absorption of vital drugs** such as Rifampicin and Isoniazid may be reduced in undernourished patients and affect the efficacy of drugs (70, 71). The decrease of fat-free mass in undernourished patients with TB may affect the response to anti-TB treatment (ATT) and may result in toxicity of drugs such as ethambutol and streptomycin (72). Concomitant administration of feeding and ATT may reduce the efficacy of ATT (73). Another study by van Lettow et al. found that undernutrition was associated with an increased risk of TB treatment failure and relapse.

Furthermore, undernourished individuals with TB face an **increased risk of mortality** because of the add-on effect of all the factors mentioned above. Undernutrition intensifies the severity of diseases, increases the frequency of infections, diminishes appetite and nutrient absorption, and elevates the body's energy requirements. This escalation in risk contributes to a higher likelihood of child mortality (74). For example, a study by Zachariah et al. demonstrated that undernutrition was a significant predictor of mortality among TB patients in a resource-limited setting. A study from Malawi reported that patients with moderate to severe undernutrition died in the first four weeks of treatment (10.9%) as compared to those who had mild or no undernutrition (6.5%) (75).

Severe undernutrition at diagnosis of TB and lack of increase in BMI during TB treatment is associated with 4 and 5 fold increase risk of mortality respectively (76, 77).

Not only is weight at the time of diagnosis of TB important, but weight gain during ATT also has significant value. Undernutrition increases the risk of relapse in cases of treated TB as their compromised immune systems may be insufficient to eradicate latent TB germs after the

completion of therapy**.** Some researchers reported that weight less than or equal to 90% of ideal body weight at the time of diagnosis or weight gain less than 5% after the initial two months of treatment was associated with a 2.4-fold increase in relapse (78). In a study from Brazil for a 1 kg increase in weight, the chance of treatment failure decreased by 12% (79). Patients with weight gain less than or equal to 5% at completion of treatment were associated with twice the chance of treatment failure or relapse of TB (76).

II. Long term effect of undernutrition coupled with TB

The effect of undernutrition in childhood has long-term effects on children. It can result in stunting, impacting physical development and stature. Malnutrition during critical developmental stages can lead to cognitive deficits, affecting learning abilities and intellectual potential (80, 81). The dual burden of TB and undernutrition may increase the risk of chronic health conditions in adulthood, including respiratory issues, cardiovascular diseases, and diabetes (80).

1.6 Vicious cycle of TB and undernutrition

To sum it up, TB and undernutrition have a bi-directional relationship; undernutrition is a leading risk factor for TB (82) and on the other hand, TB can also increase the risk of becoming undernourished (83). Figure 2 represents the vicious cycle of TB and undernutrition. It is a cyclical process in which TB and undernutrition feed on each other, making it difficult to break the cycle unless the multiple factors are addressed.

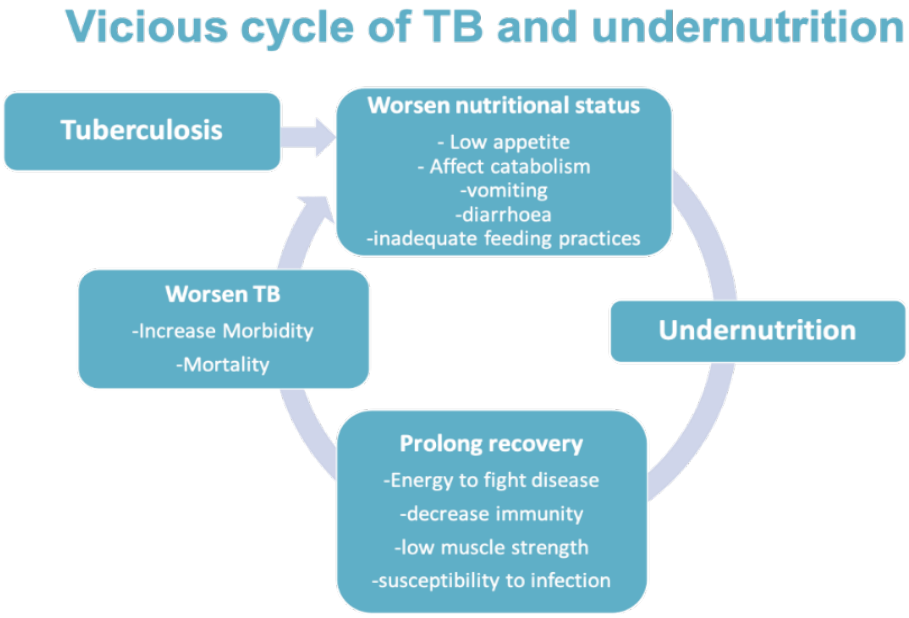


Figure 2 Continuous vicious cycle of undernutrition and TB

1.7 Strategies to prevent and combat TB and undernutrition

Undernutrition in TB has multifaceted etiology and addressing them requires a multisectoral approach at multiple levels of the health system and the government (84). In this thesis, the factors that affect the nutritional status of children with TB at the individual level directly or indirectly will be addressed. As we can't make major changes in the government, we can take short steps to improve the education of the mothers to make a behavior change toward the health of the family and the community. The factors that can be addressed at the individual level are improper dietary intake, IYCF practices, water, sanitation, and hygiene (WASH) practices and immunization. Counselling mothers on all these aspects is a crucial step to improve these factors (85). Health education leading to improvement in awareness may lead to a change in behaviors and the resultant outcome.

1) **Nutrition education on IYCF practices:**

The nutritional status of children can be significantly improved through the correct implementation of IYCF practices through nutrition education programs for mothers. Nutrition education is a major step in promising lifelong healthy eating habits which should be implemented during the early stage of life (86, 87). Young children do not choose what to eat and what not to eat, their parents decide and prepare food for them, and educating them will improve the dietary habits and eating behavior of young children (87, 88). Through nutrition education, mothers will gain a better understanding of how to select appropriate and safe food ingredients, as well as how to provide their children with nutritious food, which will help to prevent and improve nutritional disorders in children (85). Mothers who possess sufficient nutritional knowledge and adhere to proper hygiene practices contribute positively to the dietary diversity and nutritional status of their children. Providing nutrition education to mothers would contribute to improved IYCF and dietary practices and improved nutritional status for their children (89, 90). The timely introduction of healthy and diverse complementary feeding leads to better health outcomes throughout the entire course of life (49). Education on complementary feeding alone can improve the wasting rate by 11% and it has a significant impact on the WHZ score of children under 2 years of age in settings where food insecurity is prevalent (44). Educating mothers about IYCF practices is a crucial step in improving feeding practices. Greater knowledge leads to better feeding practices (91).

2) **Counselling on Water, sanitation, and hygiene practices:**

Water, sanitation, and hygiene are three distinct but connected categories that are collectively referred to by the acronym WASH. There is not enough evidence to prove WASH conditions

directly contribute to improving undernutrition in children (92, 93) but improving WASH practices can improve diarrhoea and other infectious diseases which indirectly improve undernutrition, and availability and accessibility of clean water, sanitation, and hygiene promotion provides important health and nutritional benefits (58, 94, 95)

Teaching mothers to prevent contaminating water sources, and sanitation entails the establishment of facilities and procedures for the safe disposal of human waste (57, 58). Menstrual hygiene, handwashing, and general cleanliness are all part of hygiene, which focuses on maintaining personal and environmental cleanliness to stop the transmission of illness.

3) **Counselling on the importance and schedule of immunization:**

Promoting and adhering to routine immunization protocol reduces the occurrence of infectious diseases like TB, Hepatitis, pneumonia, and diarrhoea (96). By preventing these diseases, immunization prevents the occurrence of undernutrition because of poor appetite, reduced food intake, and impaired nutrient absorption caused by these infectious diseases (30).

SOLUTION: Practices to treat undernutrition among children in Pakistan

In Pakistan, there are multiple international non-governmental organizations (INGOs) and local non-governmental organizations (NGOs) that supply nutritional supplements such as therapeutic food (i.e., Ready-to-use therapeutic food RUTF, Acha mum, Wawa mum) and micronutrient powders (MNP) to prevent and treat wasting. Ready-to-use therapeutic food (RUTF) has been given to children with SAM and multiple micronutrient powder (MNP) is given to children with MAM and this same practice has been continuous since 2010. These practices are considered the best for rapid improvement but there is very little focus on change in dietary habits, which can be the cause of unsustainable behaviour and an increasing number of cases of wasting every passing year. The WHO recommends nutrition counselling, nutritional supplements, and micronutrient powder in their recommendations to treat undernutrition, but in places like Pakistan, these recommendations are never carried out. It is a proven fact that undernutrition can be addressed by improving breastfeeding and dietary practices along with consumption of safe water, improving sanitary and hygiene practices, treating comorbid conditions (i.e., specifically TB and Oedema), and timely immunization, which eventually improves TB treatment outcome among undernourished children.

1.8 Process of Nutritional Rehabilitation

The process of restoring a person's health and nutritional condition through suitable nutritional therapies is known as nutritional rehabilitation. This can be accomplished in several ways, such as dietary adjustments, nutritional supplements, and medical procedures.

Nutritional rehabilitation of children under 5 years of age with undernutrition follows the World Health Organization (WHO) protocol, which typically involves a comprehensive approach known as the Integrated Management of Childhood Illness (IMCI). The key components of nutritional rehabilitation include:

1.8.1 Assessment: Children are assessed for the degree and type of undernutrition using anthropometric measurements such as weight-for-height (wasting), height-for-age (stunting), and weight-for-age (underweight).

1.8.2 Classification: Based on the assessment, children are classified into different categories of undernutrition, such as moderate acute malnutrition (MAM) or severe acute malnutrition (SAM). If WHZ score equals to or less than -3SD, or mid-upper arm circumference (MUAC) less than 115mm, or presence of bi-lateral pitting oedema, then the condition of the children is considered as SAM, and if WHZ score is between -3SD and -2SD, or MUAC is between 125mm to 115mm, then the condition of the children is called as MAM.

1.8.3 Treatment Plans:

Moderate Acute Malnutrition (MAM): Children with MAM are often managed at the community level through interventions like supplementary feeding, nutritional counselling, and monitoring of growth.

Severe Acute Malnutrition (SAM): Children with SAM require more intensive care, and treatment may involve therapeutic feeding with ready-to-use therapeutic foods (RUTF), medical treatment for associated illnesses, and close monitoring of weight gain and recovery.

1.8.4 Ready-to-Use Therapeutic Foods (RUTF): RUTF is a specialized, energy-dense, and nutrient-rich food designed for the nutritional rehabilitation of children with SAM. It does not require cooking, making it suitable for use in various settings.

1.8.5 Medical Care: Alongside nutritional interventions, medical care is provided to address any underlying health issues contributing to malnutrition. This may involve the treatment of infections, deworming, and vitamin and mineral supplementation.

1.8.6 Monitoring and Follow-up: Regular monitoring of the child's progress is crucial. This includes tracking weight gain, assessing appetite, and addressing any emerging health concerns. Follow-up visits help ensure sustained recovery and prevent relapse.

1.8.7 Family Involvement: Family engagement and education are integral to the success of nutritional rehabilitation programs. Families and caregivers are educated on proper feeding practices, hygiene, and preventive healthcare.

1.8.8 Integrated Approach: The WHO protocol emphasizes an integrated approach that combines nutritional rehabilitation with broader health interventions to address the multifaceted nature of malnutrition in children.

1.9 Rationale of the study

There is no previous study in Pakistan that estimates the burden of undernutrition among children aged 6 months to 5 years of age with TB. No study has been done on nutritional counselling in children with TB and behavior change towards healthy eating habits to improve nutrition status in undernourished children with TB.

IYCF practices in Pakistan are not up to the mark, food diversity is very low, and unhealthy cooking practices are very common, these factors lead to undernutrition in children. Nutritional rehabilitation followed by Nutrition counselling and proper IYCF practices along with water, sanitation, and hygiene (WASH) practices tends to have a long-term effect on undernutrition and health. It will benefit the child's family and the community as health messages spread quickly.

2. Objectives & Hypothesis

2.1 Main Objective

To study the prevalence of undernutrition among children aged 6 months to 5 years with TB and the impact of nutritional counselling of mothers and TB treatment on the nutritional status of children recruited prospectively from two tertiary care hospitals in Pakistan from December 2023 till July 2023.

2.1.1 Specific Objectives

1. To measure the prevalence of undernutrition
2. To study the compliance with the nutritional counselling provided to the mothers of children and change in dietary patterns.
3. To study the impact of nutritional counselling and TB treatment on nutritional status.

2.2 Research Question

Does the provision of nutritional counselling along with TB treatment improve nutritional status among children 6 months to 5 years of age with TB?

2.3 Hypothesis

Nutrition counselling of undernourished children along with TB treatment will improve the nutritional status of children aged 6 months to 5 years.

3. Methodology

This study is a part of the project named "Improving diagnosis and management of childhood TB in low-recourse, high TB burden setting: A study from Pakistan."

3.1 Study Design

A combination of cross-sectional and cohort studies was used in this study. To further monitor changes in the enrolled participants, we followed the registered patients for 2 months (until the intensive phase of TB treatment).

3.2 Setting

The data was collected from 2 tertiary care hospitals in the public and private sector (Gulab Devi Chest Hospital & Children Hospital) in Lahore, Pakistan. These both are tertiary care hospitals and specialized in TB care. Children with Presumptive TB are often referred either to Children Hospital Lahore or Gulab Devi Chest Hospital, Lahore for consultation and treatment from all the different parts of Lahore and surrounding areas. These hospitals are equipped with advanced laboratories for the timely diagnosis of TB and both hospitals follow standardized anti-TB treatment.

The sample size was calculated using the WHO sample size calculator. A similar study revealed the prevalence of undernutrition in children with TB was 60%. Assuming 95% CI, a 10 % margin of error, we needed to enroll 93 undernourished children 6 months to 5 years of age

diagnosed with TB. However, because of time constraints and limited resources, only 51 children were enrolled in this study.

The inclusion criteria for this study were, that the children should be living in Lahore or nearby areas and aged between 6 months to 5 years. The children should be newly diagnosed with TB and should not have any history of relapse. Children must be willing to give anthropometric measurements at the time of enrollment and follow-up. Children with previous history of TB, children with multi-drug resistant TB, and human immunodeficiency virus (HIV) positive children were not included in this study.

3.2.1 Enrollment process

The patients with symptoms and signs suggestive of TB and were diagnosed with TB by the hospital physicians were enrolled in the study, if the child and/or parents gave consent to take part in the study. They were also willing to come for timely follow-up.

We strengthened the management of children with TB by providing nutrition counselling materials to the children and their parents, did anthropometric measurements, and provided nutrition counsellors/dietitians at both working sites for proper diagnosis of undernutrition and age-appropriate nutrition counselling.
All the children with TB aged between 6 months to 5 years were assessed by measuring height, weight, and MUAC according to standard methods and WHO standard growth charts were used to classify nutritional status according to WHO guidelines. We did nutrition counselling of the children and parents of undernourished children for age-appropriate energy-dense homemade foods and also strengthened their cooking skills by providing them with healthy cooking recipes. All the enrolled children were given nutrition counselling and Information education & communication (IEC) material along with normal TB treatment protocol and multivitamins. IEC material included key messages posters and counselling cards for age-appropriate diet, good dietary practices, dietary diversity, IYCF practices, water sanitation, and hygiene (WASH) practices and immunization, different cooking techniques, and some verbal messages.

Children were followed-up after monitored on a weekly or fortnightly basis, depending on the severity of their malnutrition and TB. During these follow-up visits, the children's nutritional status, compliance with treatment, and their response to nutritional counselling were assessed using a pre-designed questionnaire. On every follow-up, study participants received nutritional

counselling and IEC material. Conclusive follow-up for this study was done after the completion of the intensive phase of TB treatment (2 months after the initiation of anti-TB treatment (ATT)).

3.2.1.1 Diagnosis of TB

There were two pathways for enrolment of children with TB; 1) All children with symptoms and signs suggestive of TB, who were present at the Pulmonology clinic, Children Hospital Lahore and Pediatric Outpatient Department (OPD), Gulab Devi Hospital, Lahore were screened for enrolment according to WHO guidelines of management of Childhood TB 2022 and those scoring greater than 10 according to the algorithm B of the WHO guidelines (see appendix A) were enrolled in the study. 2) Children diagnosed to have TB by the hospital physicians anywhere in both the hospitals, either other OPDs or inpatients who come to the TB counter for registration and getting ATT were enrolled in the study and assessed according to the TB score and guidelines. TB was classified for site and severity of the disease according to WHO 2022 guidelines (97).

3.2.1.2 Diagnosis of Undernutrition and Nutritional Assessment

After confirmation of TB, anthropometric measurements: height, weight, Mid upper arm circumference measurements were done according to the methods described below:

3.2.1.2a Weight Measurement

The weight of the children was measured using a Digital Infant Scale for infants and those children who can't stand by themselves without any support, and a digital weight measuring scale for children who can stand themselves without any support. Appendices B and C explain the steps followed to record the measurements.

3.2.1.2b Length/Height Measurement

The length was measured using an infantometer for children less than 24 months of age and for those who can't stand straight, and height was measured using a stadiometer for children more than 24 months of age. Figures 3 and 4 show the proper way of using an infantometer and stadiometer respectively. Appendices D and E explain the steps followed to record the measurements.

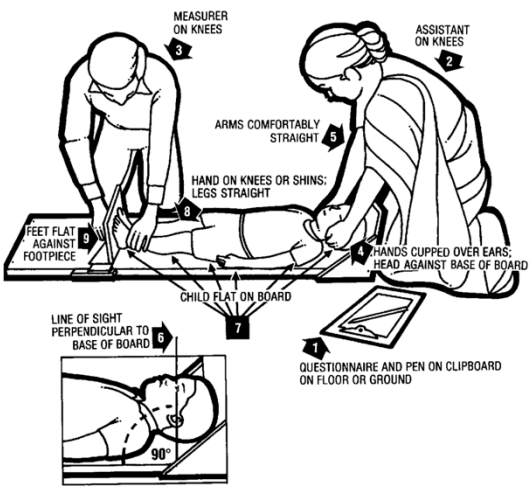


Figure 3 Steps followed using infantometer (1)

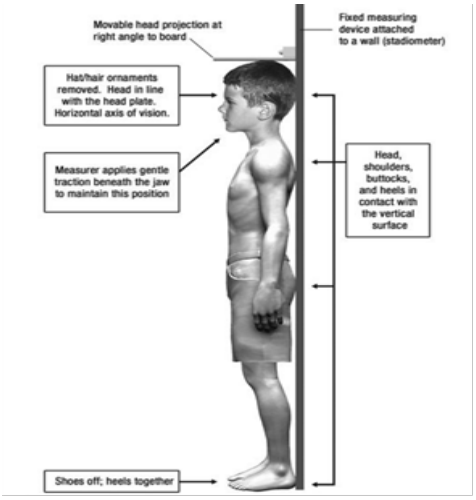


Figure 4 Steps followed using a stadiometer (98)

3.2.1.2c: Weight for length z-score (WLZ) / weight for height z-score (WHZ)

World Health Organization (WHO) growth charts for children aged under 2 years and children aged under 5 years (see appendix F, G, H, and I) were used to plot and assess the child's WLZ scores and WHZ scores after recording children's weight and height. The highlighted lines served as a guide to understanding the degree of severity of acute malnutrition. The children were classified as having moderate malnutrition (MAM) if the point where their weight and height interact fell between the orange and red lines, and as having severe malnutrition (SAM) if the point dropped below the red line. The child was considered as normal if the point where weight and height interact fell above orange line.

3.2.1.2d Mid-upper arm circumference (MUAC):

Mid-upper arm circumference tape (MUAC Tape) was used to measure the MUAC of the children during enrollment to diagnose the severity of acute malnutrition. (figure 5)

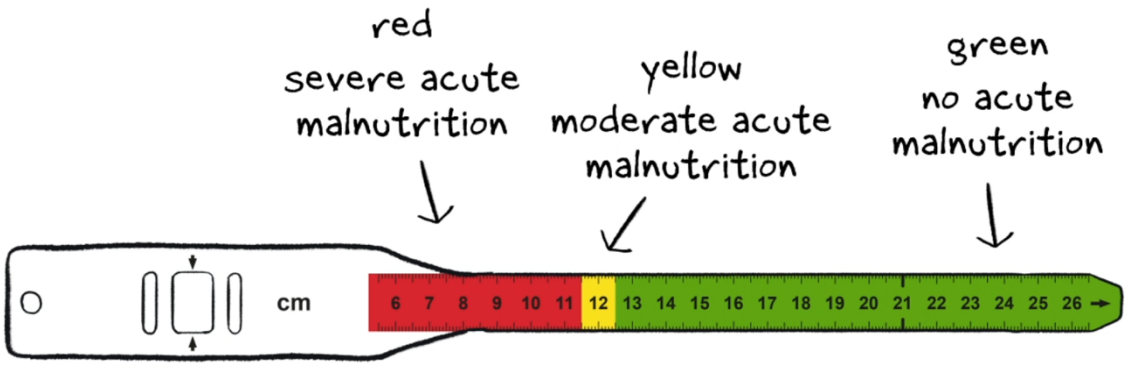


Figure 5 Mid-upper arm circumference (MUAC) tape

Steps mentioned in Appendix J were followed to properly use MUAC tape. The reading on the MUAC tape was interpreted in a way that if the measurement on the MUAC tape was between less than 125mm and 115mm, or if the window on the tape showed the color yellow, then the child was deemed to be a MAM. On the other hand, if the measurement on the MUAC tape was less than 115mm, or if the window on the tape showed the color red, then the child was regarded to be a SAM. If a child's measures were above 125 millimeters, it was regarded to be healthy and not suffering from acute malnutrition.

3.2.1.2e Bilateral pitting oedema (Nutritional oedema)

Nutritional oedema was diagnosed by putting thumb pressure on both feet together for a few seconds. The child was determined to be a case of bi-lateral pitting oedema if the pit appeared in both patient's feet after the application of pressure for a few seconds and the subsequent removal of the thumbs as shown in Figure 6.

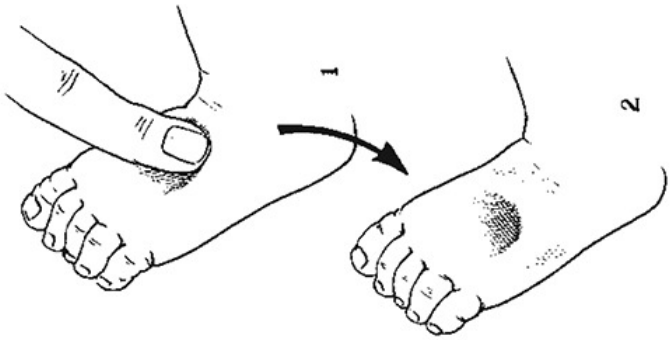


Figure 6: Diagnosis of bilateral pitting oedema using thumb pressure.

There were three ways used to identify the nutritional status of children. (99)

1. Weight and height were then plotted onto the WHO's growth standard charts according to the age and gender of the patient and then we identified the children as Normal, moderately acute malnourished (MAM), or severely acute malnourished (SAM). If the plotted point on the WHO growth standard chart fell between +1SD to -2SD, then the child was considered as a Normally nourished child. If the plotted point fell between -2SD and -3SD, then the child was considered as moderately undernourished child (Child with MAM), and if the plotted point fell below -3SD, then the child was considered as severely undernourished child (child with SAM).

2. We used standard MUAC tape to measure the MUAC of the child for the diagnosis of undernutrition.

3. Presence of bi-lateral pitting oedema.

Measurement	Tool used
Weight	**Digital Weighing scale** for children greater than 2 years of age **Digital infant scale** for children who can't stand
Length / Height	**Infantometer** to measure recumbent length. Stadiometer to measure height
Mid-upper Arm Circumference (MUAC)	**MUAC Tape**
Bilateral pitting oedema	**Thumb pressure**

We regarded a child to be undernourished when it was identified as undernourished by any of the aforementioned methods.

3.2.1.3 History of food intake and feeding practices

After a thorough diagnosis of malnutrition, a history of feeding practices and food intake was collected. For IYCF practices, the caretaker was asked about the early initiation of breastfeeding, exclusive breastfeeding, and continued breastfeeding along with complementary feeding using our pre-designed standard questionnaire based on WHO recommendations. Food history was taken using 24-hour recall, food recall of the previous week. The number and quantity of meals taken over the previous 24 hours and previous week for age-appropriate feeding practices was estimated according to WHO recommendations. The food consumption score was formulated during this study which was used to measure the number of food groups consumed in the last 24 hours and/or during the last week to estimate the dietary diversity among enrolled children.

3.4.1.4 History of socioeconomic factors and Immunization status

After taking dietary history, details on socioeconomic factors such as parent/guardian's occupation, household income, level of education of both parents, family type, and living conditions including the area of house, number of rooms in the house, and number of people living together in the house was taken from the parents of the study participants along with the vaccination status of the study participants including BCG vaccination.

3.2.2 Nutrition counselling

After the enrollment process, we counselled the patients and their caretakers regarding Infant and young child feeding (IYCF) practices including exclusive breastfeeding and complementary feeding along with continuous breastfeeding till 2 years of age, healthy eating and balanced diet, water sanitation and hygiene (WASH) practices and age-appropriate immunization. I designed and created some age-appropriate Information, Education, and Communication (IEC) materials so that my intended messages are better understood. We handed over those IEC materials to the caretaker of the children so they could recall the counselling provided. Verbally delivered counselling messages and provided IEC material were designed according to WHO's guidelines. IEC materials were designed in the locally spoken and understandable language i.e., Urdu with some pictorial representation of messages.

Figure 7 represents a leaflet that explains the primary messages pertaining to exclusive breastfeeding for six months and the appropriate amount of milk to be provided. This image also defines the age-specific practice of complementary feeding. This leaflet provides an explanation of the specific dietary composition and recommended portion sizes for children within the age ranges of 6 to 9 months, 9 to 12 months, and 12 to 24 months. It also illustrates the need to provide appropriate care for children, including routine immunization and regular check-ups for the well-being and proper growth of the child.

Figure 7: Counselling messages for children aged 6 to 24 months including exclusive breastfeeding, complementary feeding & WASH.

Figure 8 also represents a leaflet that explains the recommendation to sustain nursing until the age of two, while also highlighting the significance of giving milk to children up to the age of two. It provides information on the administration of multivitamins to children and the need to adhere to the prescribed medication regimen for the treatment of TB until completion of the treatment course. The figure further demonstrates the requisite standard of nutrition that must be supplied to children, including the incorporation of all essential food categories within their dietary intake. This leaflet incorporates essential hygiene and sanitation practices, such as frequent handwashing, thorough dish cleaning, daily bathing, as well as safe storage of food in a hygienic environment.

Figure 8 Counselling messages for children aged up to 2 years including good eating practices, food groups, and safe hygiene and sanitation.

The leaflet in Figure 9 elucidates the significance of maintaining a nutritious diet from the ages of 3 to 10, including the promotion of optimal development, the enhancement of antibody production, and the facilitation of positive academic advancement. Additionally, it explains the quality and quantity of dietary intake, as well as different food groups that need to be consumed daily.

اہم پیغامات

بچوں کی نشوونما کے لیے 3 سے 10 سال کی عمر بہت اہم ہے۔ یہ غذائیت کی کیفیت کو بہتر بنانے اور انفیکشن اور بیماریوں سے لڑنے کے لیے جسم کے مدافعتی نظام کو بڑھانے کا ایک مناسب وقت ہے۔

- اس عمر میں بچوں میں ذائقہ کی تیز رفتاری، بہتر ہاضمہ اور جذب کرنے کی صلاحیت، بہتر انزائمز اور ہارمونل رطوبت، ہم آہنگی اور خاندانی کھانوں کو ہضم کرنے، جذب کرنے اور استعمال کرنے کی صلاحیت پیدا ہوتی ہے۔
- وہ بچے جو غذائیت سے بھرپور کھانا کھاتے ہیں ان کی اسکول کی کارکردگی بہتر ہوتی ہے۔
- مختلف قسم کے غذائیت سے بھرپور غذائیں متعارف کروانا جن میں دودھ اور دودھ کی مصنوعات، گوشت اور گوشت کی مصنوعات، سبزیاں اور پھل، اناج اور دالیں شامل ہیں اور کھانے کی تعدد میں اضافہ بچوں کو نہ صرف اپنی روزمرہ کی غذائی ضروریات کو پورا کرنے کے قابل بنائے گا بلکہ غذائیت کے ذخیروں کو بھی بھر سکے گا۔

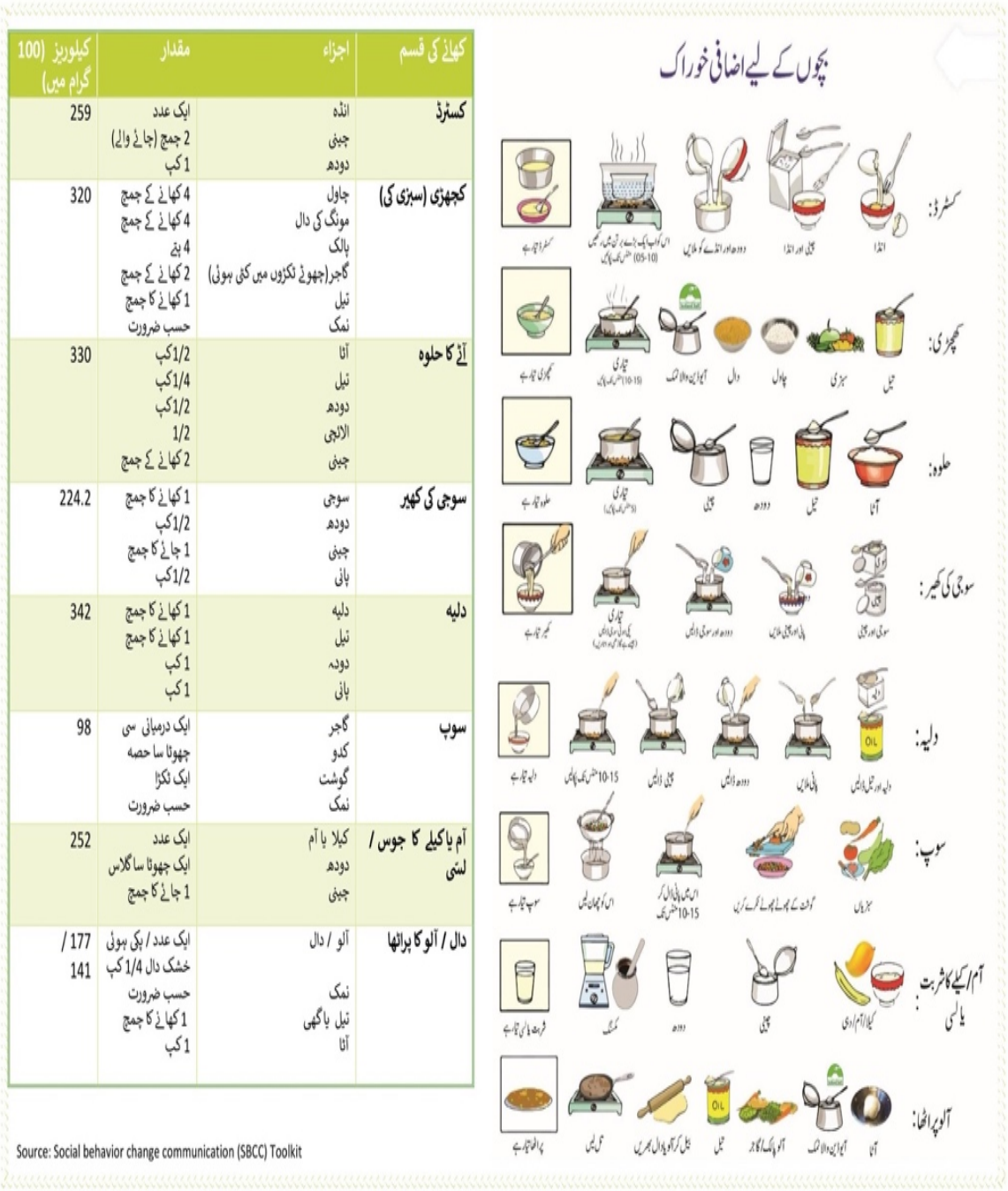
3 سے 10 سال کی عمر کے بچوں کے لیے خوراک اور سرونگ کا سائز

کھانے کے گروپ	فی دن سرونگز کی تعداد	سرونگ سائز اور تفصیل
دودھ اور دودھ کی مصنوعات	2 سے 3	1 سرونگ = 1 کپ دودھ یا 1 کپ دہی یا پنیر کا 1 ٹکڑا یا 1 کپ کھویا یا فیرنی یا دیگر دودھ پر مبنی مصنوعات جو 1 کپ دودھ سے فراہم کردہ غذائی اجزاء کے برابر ہیں۔ 1 کپ پورا دودھ 160 کیلوریز فراہم کرتا ہے۔
اناج اور اناج کی مصنوعات	3 سے 5	1 سرونگ = 1 چپاتی* یا بریڈ کے 2 سلائس (ٹوسٹ) یا 2/3 کپ پکے ہوئے چاول یا 1 کپ اناج جو روٹی کے 2 سلائس سے فراہم کردہ غذائی اجزاء کے برابر ہے۔ چپاتی کا ایک سرونگ یا روٹی کے 2 سلائس 160 کیلوری فراہم کرتا ہے۔ **نشاستہ دار سبزیاں:** 1 آلو (100 گرام) یا مکئی (1/2 کپ)، مٹر (1/2 کپ) کدو (1 کپ)، میٹھا آلو (1/2 کپ) 80 کیلوریز فراہم کرتا ہے۔
سبزیاں	2 سے 3	1 سرونگ = ½ کپ پکی ہوئی غیر نشاستہ دار سبزیاں یا ½ کپ سبزیوں کا رس/سوپ یا 1 کپ تازہ سبزیاں/سلاد۔ سبزیوں کی ایک سرونگ 25 کیلوریز فراہم کرتا ہے۔
پھل	2 سے 3	1 سرونگ = 1 چھوٹے سائز کا کیلا یا 1 سیب یا 1 آڑو یا 2-3 بیر یا 3-4 خوبانی۔ ہر سرونگ 60 کیلوریز فراہم کرے گی۔
گوشت، دالیں اور انڈے	3 سے 4	1 سرونگ گوشت (28 گرام، 1 اونس دبلا گوشت = 1-2 چھوٹے گوشت کے ٹکڑے یا مچھلی کے 1-2 ٹکڑے یا 1 انڈا، یا ½ کپ پکی ہوئی دالیں۔ درمیانی چربی کے ساتھ گوشت کی ایک سرونگ 75 کیلوریز فراہم کرے گی۔ زیادہ چکنائی والے گوشت کی ایک سرونگ 100 کیلوریز فراہم کرے گی۔

3 سے 10 سال کی عمر کے بچوں کے لیے غذائیت سے متعلق مشاورت

Figure 9: Counselling messages for children aged 3 to 10 years regarding healthy eating practices.

Figure 10 represents the brochure which presents a variety of locally sourced nutritious food dishes intended for consumption by young children, along with detailed instructions on their preparation. It demonstrates the use of certain cooking techniques and the incorporation of supplementary ingredients in order to enhance the nutritional value of locally sourced meals, particularly for the benefit of young children.



کھانے کی قسم	اجزاء	مقدار	کیلوریز (100 گرام میں)
کسٹرڈ	انڈہ چینی دودھ	ایک عدد 2 چمچ (چائے والے) 1 کپ	259
کچھڑی (سبزی کی)	چاول مونگ کی دال پالک گاجر(چھوٹے ٹکڑوں میں کٹی ہوئی) تیل نمک	4 کھانے کے چمچ 4 کھانے کے چمچ 4 پتے 2 کھانے کے چمچ 1 کھانے کا چمچ حسب ضرورت	320
آٹے کا حلوہ	آٹا تیل دودھ الائچی چینی	1/2کپ 1/4کپ 1/2کپ 1/2 2 کھانے کے چمچ	330
سوجی کی کھیر	سوجی دودھ چینی پانی	1 کھانے کا چمچ 1/2کپ 1 جائے کا چمچ 1/2کپ	224.2
دلیہ	دلیہ تیل دودھ پانی	1 کھانے کا چمچ 1 کھانے کا چمچ 1 کپ 1 کپ	342
سوپ	گاجر کدو گوشت نمک	ایک درمیانی سی چھوٹا سا حصہ ایک ٹکڑا حسب ضرورت	98
آم یا کیلے کا جوس / لسی	کیلا یا آم دودھ چینی	ایک عدد ایک چھوٹا سا گلاس 1 جائے کا چمچ	252
دال / آلو کا پراٹھا	آلو / دال نمک تیل یا گھی آٹا	ایک عدد / پکی ہوئی خشک دال 1/4 کپ حسب ضرورت 1 کھانے کا چمچ 1 کپ	177 / 141

Source: Social behavior change communication (SBCC) Toolkit

Figure 10 Pakistani local healthy food recipes for young children

Figure 11 represents a brochure that illustrates the implementation of the "My Plate" idea in Pakistan, specifically focusing on locally available food options for school-going children. It illustrates the essential food groups necessary for optimal growth and highlights the advantages of including each food group in the dietary patterns of school-aged children.

Figure 11 Concept for My Plate for School-going Children in Pakistan containing local recipes.

3.2.3 Follow-up of the Enrolled patients

All the patients who were enrolled as study participants were scheduled for follow-up appointments either one week or two weeks following enrolment, depending on the severity of their illnesses and undernutrition. All the assessment steps that were mentioned in point 3.4.1.2

were followed again to determine the nutritional status at that point in time. A questionnaire consisting of subjective inquiries with quantifiable conclusions was used to assess the degree of adherence. (see Appendix K for the overview of a questionnaire). This method was utilized instead of qualitative data collection due to its simplicity and time efficiency.

4. Ethics

The project "Improving diagnosis and management of childhood TB in low-recourse, high TB burden setting: A study from Pakistan." was approved by the Regional Ethical Committee (REK) in Norway and Institutional Review Boards of Children Hospital, Lahore and Gulab Devi Chest Hospital, Lahore in Pakistan. All the participants gave written consent before any data collection. (see Appendix L, M, N)

5. Results

During the period spanning from December 2022 to July 2023, a total of 51 children between the ages of 6 months and five years were diagnosed with TB and enrolled in the study. Out of 51 enrolled children, 26 children were followed-up by the research staff. The flowchart below (figure 12) shows the number of children enrolled at both study hospitals.

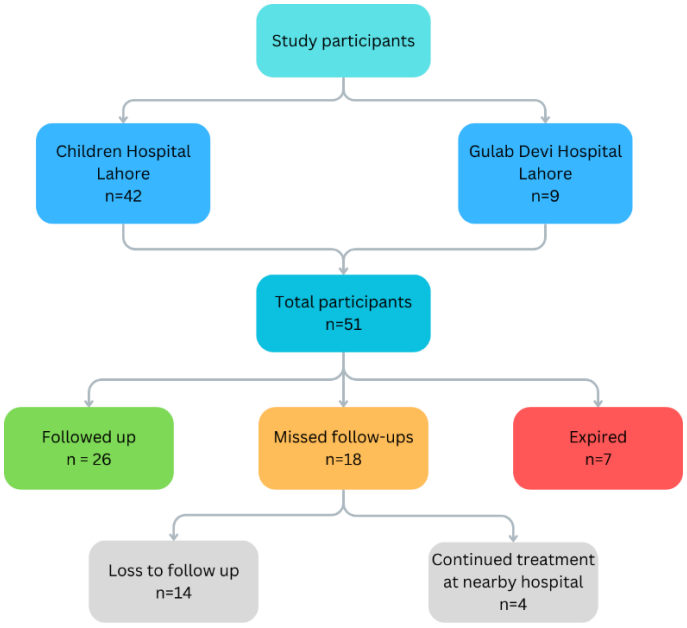


Figure 12 Flowchart of study participants (children with TB aged six months to 5 years)

5.1 Sociodemographic characteristics of the study participants

Table 1 shows the sociodemographic characteristics of the study participants. Fifty-one children were enrolled in the study and categorized into two age groups based on differences

in feeding recommendations. The first group comprised infants aged 6 to 24 months, while the second group comprised children aged 25 to 60. The two groups had 17 (33%) and 34 (67%) children, respectively. The proportion of male children (63%) was higher than female children (37%). Most children (88%) resided in households where both parents were present. The proportion of extended family type was 55% compared to the nuclear family type i.e., 45%. The majority of parents with enrolled children (69%) possessed their own house, with a significant proportion (61%) residing in "pakka" houses (houses made up of modern material like cement, brick, steel etc.). Approximately two-thirds (67%) of households had a kitchen, while a substantial number (88%) had a proper sewage system.

Additionally, nearly half (49%) of households utilized a filtration plant as their primary water source. The majority of parents of children were engaged in employment at small private vendors (61%). At the same time, a significant portion worked as laborer or in occupations like rickshaw driving, donkey cart driving, or other forms of self-employment (33%). Approximately 27% of the patient's guardians were employed on income below the minimum wage threshold of 20,000 Pakistani Rupee. Approximately 53% of fathers and 49% of mothers within the surveyed population lacked formal education, while fewer than 10% of parents had a college or university level of education.

Table 1 Socio-demographic characteristics of the study participants (children with TB aged between 6 months to 5 years)

	Age groups in months		
Characteristics	**6 – 24** **n (%)** **17 (33.3%)**	**25 – 60** **n (%)** **34 (66.7%)**	**Total** **n (%)** **51 (100%)**
Gender			
Male	9 (52.9%)	23 (67.6%)	32 (62.7%)
Female	8 (47.1%)	11 (32.4%)	19 (37.3%)
Family arrangement			
Lives with both parents	14 (82.4%)	31 (91.2%)	45 (88.2%)
Lives with one parent	2 (11.8%)	2 (5.9%)	4 (7.8%)
Lives with relatives	1 (5.9%)	1 (2.9%)	2 (3.9%)
Parental marital status			
Living together	14 (82.4%)	32 (94.1%)	46 (90.2%)
Father expired	1 (5.9%)	0 (0.0%)	1 (2.0%)
Mother expired	1 (5.9%)	0 (0.0%)	1 (2.0%)
Both parents expired	0 (0.0%)	1 (2.9%)	1 (2.0%)
Parents separated	1 (5.9%)	1 (2.9%)	2 (3.9%)
Family type			
Nuclear	4 (23.5%)	19 (55.9%)	23 (45.1%)

Extended	13 (76.5%)	15 (44.1%)	28 (54.9%)
Ownership of the house			
Own house	12 (70.6%)	23 (67.6%)	35 (68.6%)
Lives in a family house	4 (23.5%)	1 (2.9%)	5 (9.8%)
Rented house	1 (5.9%)	10 (29.4%)	11 (21.6%)
Guardian occupation			
Government employee	1 (5.9%)	2 (5.9%)	3 (5.9%)
Employed in a private company	11 (64.7%)	20 (58.8%)	31 (60.8%)
Self-employed	5 (29.4%)	12 (35.3%)	17 (33.3%)
Household income			
PKR[1] 20,000 or less	5 (29.4%)	9 (26.5%)	14 (27.5%)
More than PKR* 20,000	12 (70.6%)	25 (73.5%)	37 (72.5%)
Father education			
No formal education	10 (58.8%)	17 (50.0%)	27 (52.9%)
Up to primary education	1 (5.9%)	4 (11.8%)	5 (9.8%)
Up to secondary education	6 (35.3%)	11 (32.4%)	17 (33.3%)
College/University level education	0 (0.0%)	2 (5.9%)	2 (3.9%)
Mother education			
No formal education	10 (58.8%)	15 (44.1%)	25 (49.0%)
Up to primary education	2 (11.8%)	6 (17.6%)	8 (15.7%)
Up to secondary education	3 (17.6%)	10 (29.4%)	13 (25.5%)
College/University level education	2 (11.8%)	3 (8.8%)	5 (9.8%)
Type of house			
Pakka house[2]	10 (58.8%)	21 (61.8%)	31 (60.8%)
Kacha house[3]	3 (17.6%)	3 (8.8%)	6 (11.8%)
Mix of Pakka and Kacha house	4 (23.5%)	10 (29.4%)	14 (27.5%)
Source of water supply			
Groundwater	4 (23.5%)	8 (23.5%)	12 (23.5%)
Filtration Plant	8 (47.1%)	17 (50.0%)	25 (49.0%)
Hand pump	4 (23.5%)	5 (14.7%)	9 (17.6%)
Tube well	0 (0.0%)	1 (2.9%)	1 (2.0%)
Tank water	1 (5.9%)	3 (8.8%)	4 (7.8%)
Toilet facility in-house			
Sewer system installed	15 (88.2%)	30 (88.2%)	45 (88.2%)
Flush to open drains	1 (5.9%)	3 (8.8%)	4 (7.8%)
No facility/bush/field	0 (0.0%)	1 (2.9%)	1 (2.0%)
Open pit	1 (5.9%)	0 (0.0%)	1 (2.0%)
Kitchen in house			
No	4 (23.5%)	13 (38.2%)	17 (33.3%)
Yes	13 (76.5%)	21 (61.8%)	34 (66.7%)

[1] PKR = Pakistani rupee

[2] Pakka house = house constructed with modern materials i.e., bricks, concrete, cement, steel

[3] Kacha house = houses made from basic and natural materials i.e., mud, bamboo, grass

5.2 Clinical features of study participants

Table 2 shows the clinical features of the 51 enrolled children (6 to 50 months of age). Pulmonary TB was found in 47%, and extrapulmonary TB in 53% children. The majority of the participants (94%) had severe TB according to WHO criteria. A substantial majority of children (80%) were vaccinated with BCG. 45% of the enrolled children were severely undernourished, around 18% were moderately undernourished and remaining 37% had no form of undernutrition.

Table 2 Clinical features of the study participants (children with TB aged between 6 months to 5 years)

	Age groups in months		
Clinical features	**6 – 24** **n (%)** **17 (33.3%)**	**25 – 60** **n (%)** **34 (66.7%)**	**Total** **n (%)** **51 (100%)**
Type of TB			
Pulmonary TB	8 (47.1%)	16 (47.1%)	24 (47.1%)
Extra-pulmonary TB	9 (52.9%)	18 (52.9%)	27 (52.9%)
Severity of TB			
Non-severe	1 (5.9%)	2 (5.9%)	3 (5.9%)
Severe	16 (94.1%)	32 (94.1%)	48 (94.1%)
BCG[1] vaccination status			
Not vaccinated	5 (29.4%)	5 (14.7%)	10 (19.6%)
Vaccinated	12 (70.6%)	29 (85.3%)	41 (80.4%)
Nutritional status			
Normal	4 (23.5%)	15 (44.1%)	19 (37.3%)
Moderate Acute Malnutrition (MAM)	2 (11.8%)	7 (20.6%)	9 (17.6%)
Severe Acute Malnutrition (SAM)	11 (64.7%)	12 (35.3%)	23(45.1%)

5.3 Anthropometric measurements of the study participants

Histograms in figure 13 displayed the data distribution. Shapiro-Wilk normality test was performed to confirm the normality. A p-value of more than 0.05 (p-value = 0.42 for weight and 0.71 for MUAC) confirms that the data is not skewed and can be considered to have a normal distribution.

[1] BCG = Bacillus Calmette-Guerin

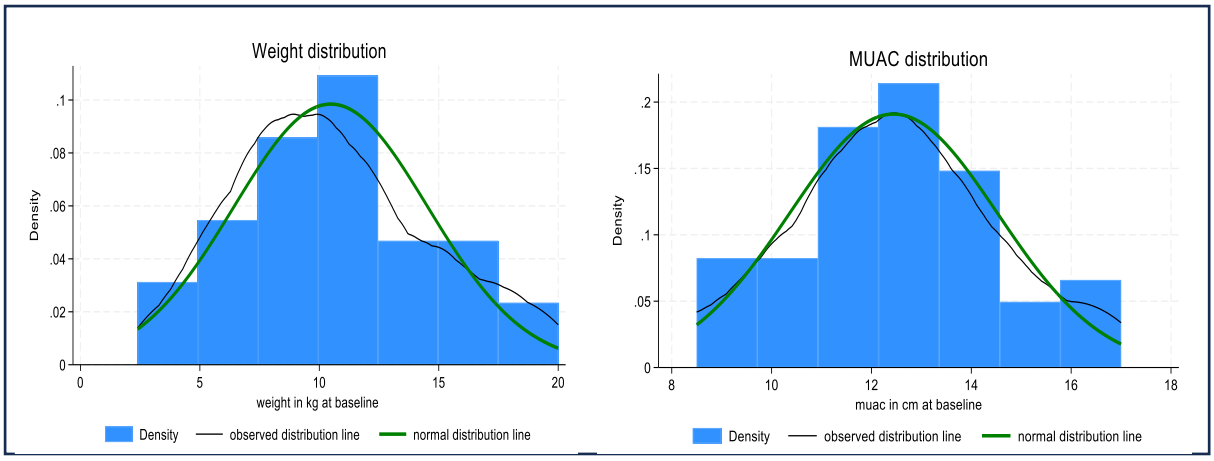


Figure 13 Weight and MUAC distribution among children with TB aged 6 months to 5 years at the time of enrollment

Table 3 presents the statistical measures of central tendency (mean), dispersion (standard deviation), as well as the range (minimum and maximum) for the variables of weight, height, and MUAC for the children under 5 in the two age categories.

Table 3 Anthropometric measurements of children with TB aged 6 months to 5 years at the time of enrollment.

Variables	**Mean**	**Standard deviation**	**Minimum**	**Maximum**
Age 6-24 months				
Height (cm)	69.2	9.1	53	89
Weight (kg)	6.9	2.1	2.4	10
MUAC (cm)	11.0	1.75	8.5	14
Age 25-60 months				
Height (cm)	91.7	17.1	58	114
Weight (kg)	12.3	3.6	4.8	20
MUAC (cm)	13.0	1.9	8.5	17

Table 4 represents the nutritional status of children based on the HAZ, WAZ, and WHZ scores obtained after the plotting of anthropometric measurements on WHO standard growth charts.

Table 4 z-scores of children with TB aged 6 months to 5 years at the time of enrolment.

Z-scores	-3 SD (severe undernutrition) n (%)	-2 SD (moderate undernutrition) n (%)	-1 SD (at risk of undernutrition) n (%)	0-3 SD (normal) n (%)
Height for age z-score (HAZ)	15 (29.4%)	8 (15.7%)	12 (23.5%)	16 (31.4%)
Weight for age z-score (WAZ)	19 (37.2%)	10 (19.6%)	7 (13.7%)	15 (29.4%)
Weight for height z-score (WHZ)	14 (27.4%)	8 (15.7%)	9 (17.7%)	20 (39.2%)

5.4 Nutritional status of the study participants

The nutritional status of participants was assessed according to WHO criteria using weight for length/height z-scores and/or MUAC and/or bilateral pitting oedema. Among the 51 enrolled participants, only 19 (37%) exhibited a normal nutritional status. Conversely, 9 (18%) participants were identified as moderately acutely malnourished, while 23 (45%) participants were classified as severely acutely malnourished, contributing to the prevalence of undernutrition observed i.e., 63%. (figure 14)

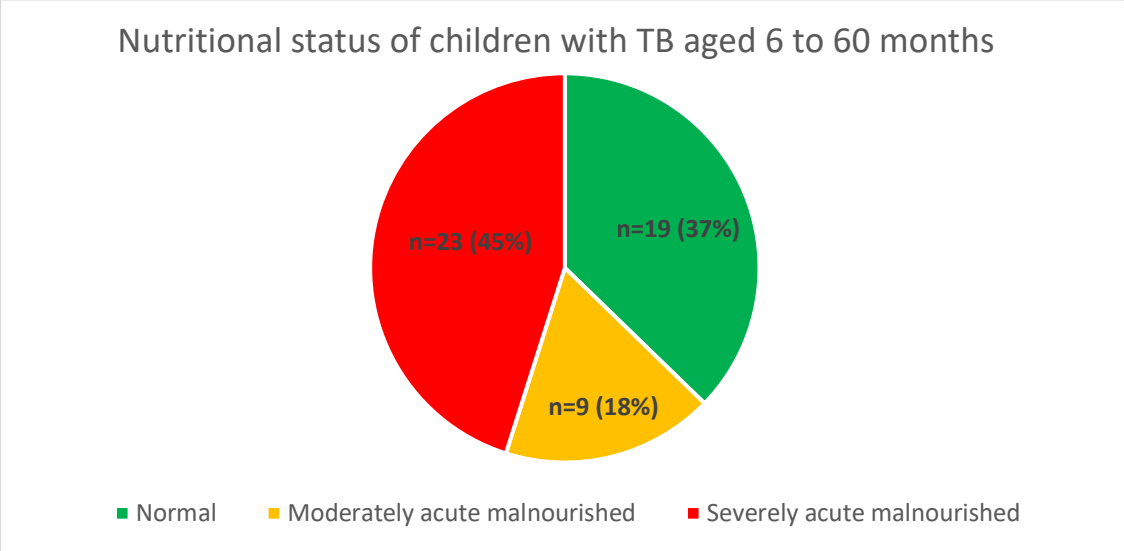


Figure 14: Nutritional status of children with TB aged 6 months to 5 years.

5.5 Factors associated with undernutrition among children with TB aged 6 months to 5 years

Table 4 presents the association of various factors that affect nutritional status. Children with moderate and severe acute malnutrition are grouped as undernourished.

Table 5 Factors associated with undernutrition defined according to WHO criteria

Variable	Sub-grouping	Undernourished n (%)	Normal n (%)	Odds ratio	95% Confidence Interval
Age	6 to 24 months	13 (76.5%)	4 (23.5%)	2.57	0.68 - 9.5
	25 to 60 months	19 (55.9%)	15 (44.1%)	1	
Gender	Male	21 (65.6%)	11 (34.4%)	1.39	0.43 - 4.46
	Female	11 (57.9%)	8 (42.1%)	1	
Severity of TB	Non-Severe TB	0 (0.0%)	3 (100.0%)	1	
	Severe TB	32 (66.7%)	16 (33.3%)	1	
Type of TB	Pulmonary TB	16 (66.7%)	8 (33.3%)	1.37	0.43 - 4.31
	Extrapulmonary TB	16 (59.3%)	11 (40.7%)	1	
Food consumption score	3 or less	24 (75.0%)	8 (25.0%)	4.8	1.21- 18.97
	4 or more	5 (38.5%)	8 (61.5%)	1	
Adequate number of meals	No	23 (63.9%)	13 (36.1%)	0.88	0.18- 4.14
	Yes	6 (66.7%)	3 (33.3%)	1	
Adequate quantity of food	No	27 (67.5%)	13 (32.5%)	3.11	0.46 - 20.98
	Yes	2 (40.0%)	3 (60.0%)	1	
Household income	PKR 20,000 or less	11 (78.6%)	3 (21.4%)	2.8	0.67 - 11.7
	More than PKR 20,000	21 (56.8%)	16 (43.2%)	1	
Father education	No formal education	18 (66.7%)	9 (33.3%)	1.42	0.46- 4.46
	Formally educated	14 (58.3%)	10 (41.7%)	1	
Mother education	No formal education	17 (68.0%)	8 (32.0%)	1.56	0.49- 4.89
	Formally educated	15 (57.7%)	11 (42.3%)	1	

The above data shows that the only statistically significant variable is the food consumption score, representing dietary diversity. The chances of getting undernourished among children consuming three or fewer groups are 4.8-fold higher than those consuming four or more food groups.

5.6 Mortality

The mortality rate was around 19% in this cohort. Among children who expired under treatment 85% had extrapulmonary TB. See Table 6 for a comparison of the overview of clinical features of expired patients as compared to alive.

Table 6 Clinical characteristics of the expired children aged six months to five years during the study period.

Variable	Sub-grouping	Status		p-value
		Alive[1]	Expired	
Number	n (%)	30 (81.1%)	7 (18.9%)	
Age	6 – 24 months	9 (30.0%)	2 (28.6%)	0.941
	25 – 60 months	21 (70.0%)	5 (71.4%)	
Type of TB	Pulmonary TB	17 (56.7%)	1 (14.3%)	0.043
	Extra-pulmonary TB	13 (43.3%)	6 (85.7%)	
Severity of TB	Non-severe TB	3 (10.0%)	0 (0.0%)	0.383
	Severe TB	27 (90.0%)	7 (100.0%)	
Vaccinated for TB (BCG)	No	5 (16.7%)	1 (14.3%)	0.878
	Yes	25 (83.3%)	6 (85.7%)	
Nutritional status	Normal	10 (33.3%)	3 (42.9%)	0.301
	MAM	8 (26.7%)	0 (0.0%)	
	SAM	12 (40.0%)	4 (57.1%)	

57% of the expired children had tuberculosis meningitis (TBM), 14% had disseminated TB, 14% had abdominal TB, and rest 14% had pulmonary TB.

5.7 Clinical features of the Loss to follow-up cases

The rate of loss to follow-up was 35% in this cohort. Table 7 compares the clinical features of cases who completed the follow-up with loss to follow-up cases. The P-value suggests that there was no significant difference between both groups relating to any variable.

Table 7 Clinical characteristics of the loss to follow-up of enrolled cases during the study period.

Variable	Sub-grouping	Status		p-value
		Cases with successful follow-up	Loss to follow-up cases	
Number	n (%)	26 (65.0%)	14 (35.0%)	
Age	6 – 24 months	8 (57.1%)	6 (42.9%)	0.445
	25 – 60 months	18 (69.2%)	8 (30.77%)	
Type of TB	Pulmonary TB	15 (71.4%)	6 (28.6%)	0.378
	Extra-pulmonary TB	11 (57.9%)	8 (42.1%)	
Severity of TB	Non-severe TB	3 (100.0%)	0 (0.0%)	0.186
	Severe TB	23 (62.2%)	14 (37.8%)	
Vaccinated for TB (BCG)	No	5 (55.6%)	4 (44.4%)	0.500
	Yes	21 (67.7%)	10 (32.3%)	
Nutritional status	Normal	9 (60.0%)	6 (40.0%)	0.328
	MAM	7 (87.5%)	1 (12.5%)	
	SAM	10 (58.8%)	7 (41.2%)	

[1] Alive = Cases which we were sure about their status, loss to follow-up cases were not included in this analysis

5.8 Nutrition counselling

Figure 15 illustrates the adherence to nutritional counselling. According to the pie chart, most participants' parents (88%) completely adhered to the recommendations and modified their food patterns in favor of a healthy and nutritious diet. Approximately 8% of participants' parents partially adhered to the guidance provided, maintaining their prescribed food regimen for almost five days each week. However, 4% of participants' parents did not change their dietary habits and adhered to conventional nutritional practices.

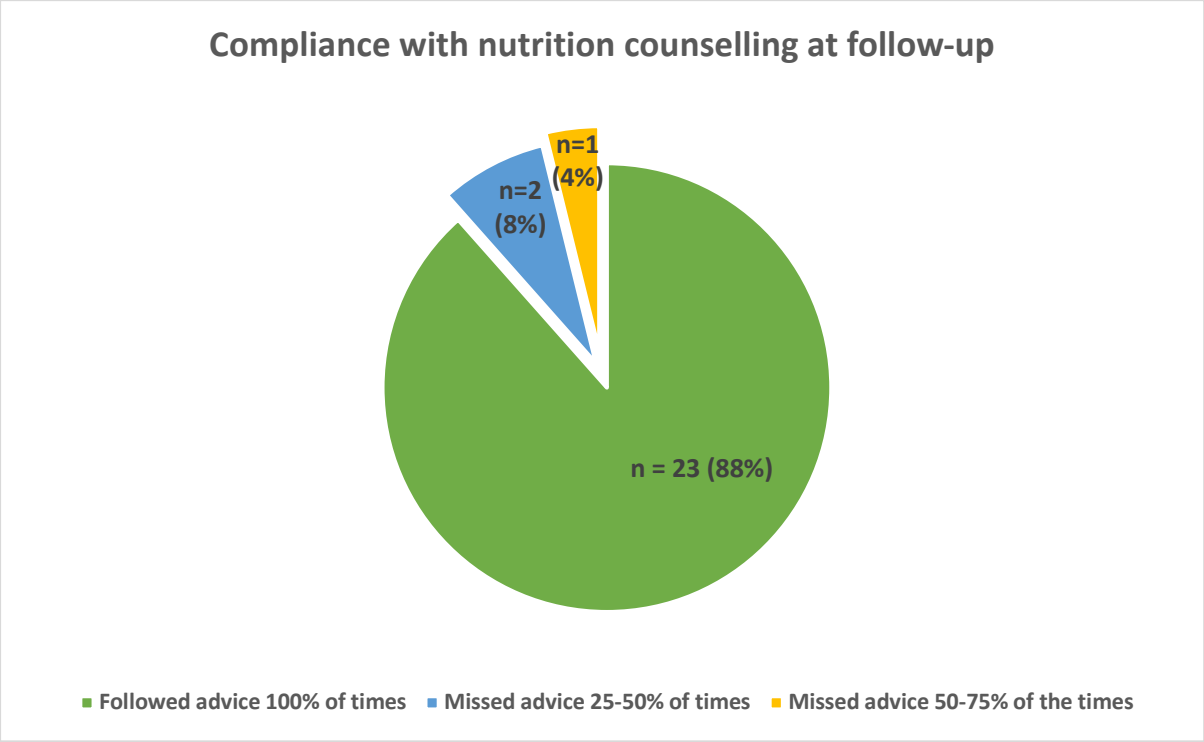


Figure 15 Compliance on nutritional counselling and change in dietary behavior by child's parents on behalf of their children aged six months to five years.

Multiple factors influenced compliance with food intake, including time limitation, support from the family, affordability, child behavior, and assumptions about the food. Figures 16 and 17 represent the reasons behind compliance with nutrition counselling and the frequency and percentage of individuals with poor compliance.

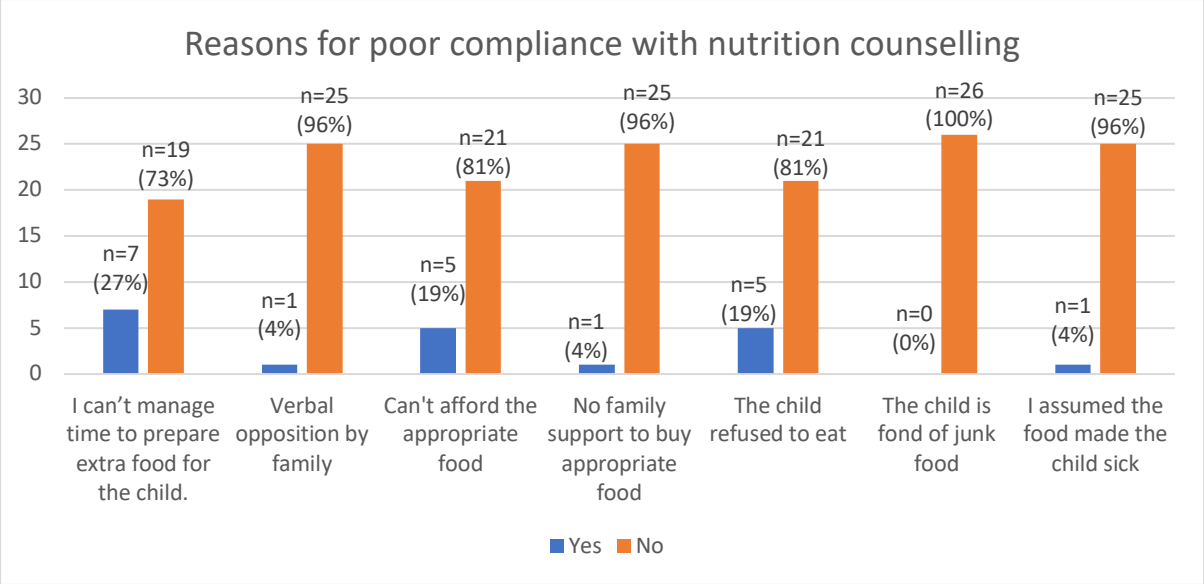


Figure 16 Reasons for poor compliance with nutrition counselling among children with TB aged six months to five years.

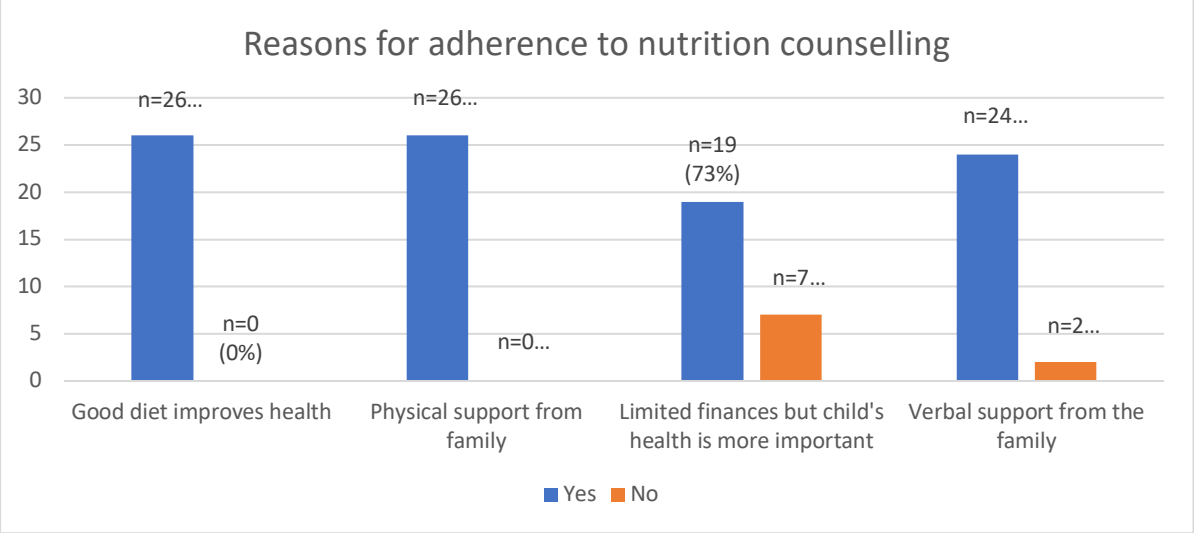


Figure 17 Reasons for compliance with nutrition counselling & changing dietary habits among children with TB aged six months to five years.

As the above data shows, after counselling, all participants' parents agree that a good diet helps improve health. People have less finances, but they somehow arrange good diets to enhance their children's health.

Association between compliance with nutrition counselling and nutritional status at 2 months

Three cases (12% of the total cases at follow-up) did not adhere to the counselling provided. Figure 18 shows the trends of change in weight, MUAC, and WHZ score after 2 months of TB treatment among cases with good and poor compliance with nutrition counselling.

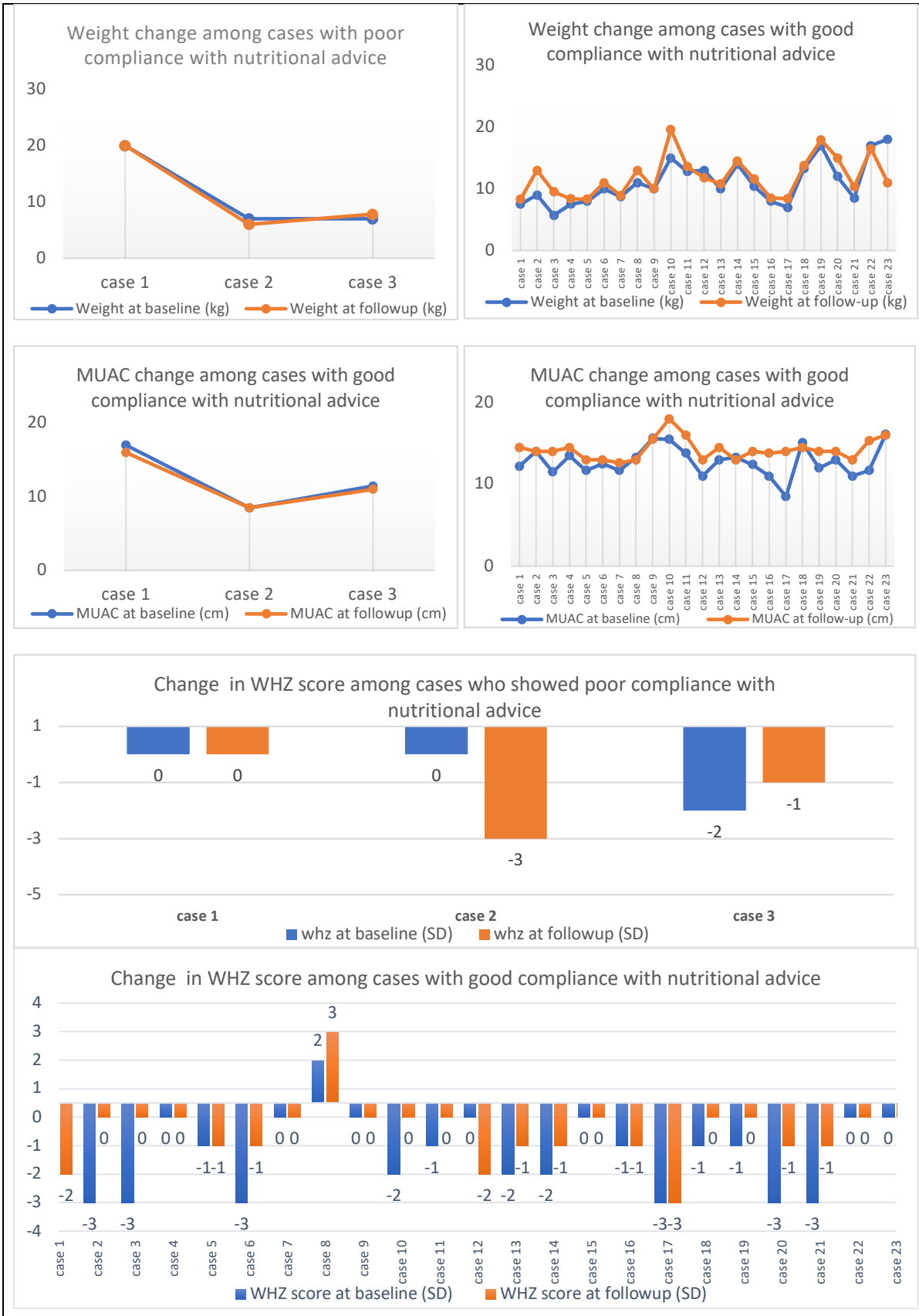


Figure 18 Change in weight, MUAC, and weight for height z-score (WHZ) among children with TB who did not follow the nutritional advice compared to those who followed nutritional advice.

The plots represent that the weight, MUAC, and WHZ scores remained stable or decreased among participants with poor compliance and mostly positive trends among those who followed the nutritional counselling.

5.9 Change in eating habits

At baseline, approximately 77% of children consumed 3 or less food groups, and only 23% consumed four or more food groups. With the support of counselling, the percentage of consuming 4 or more food groups improved to 65% (figure 19). A p-value of 0.018 confirmed the significance of the difference between the two groups.

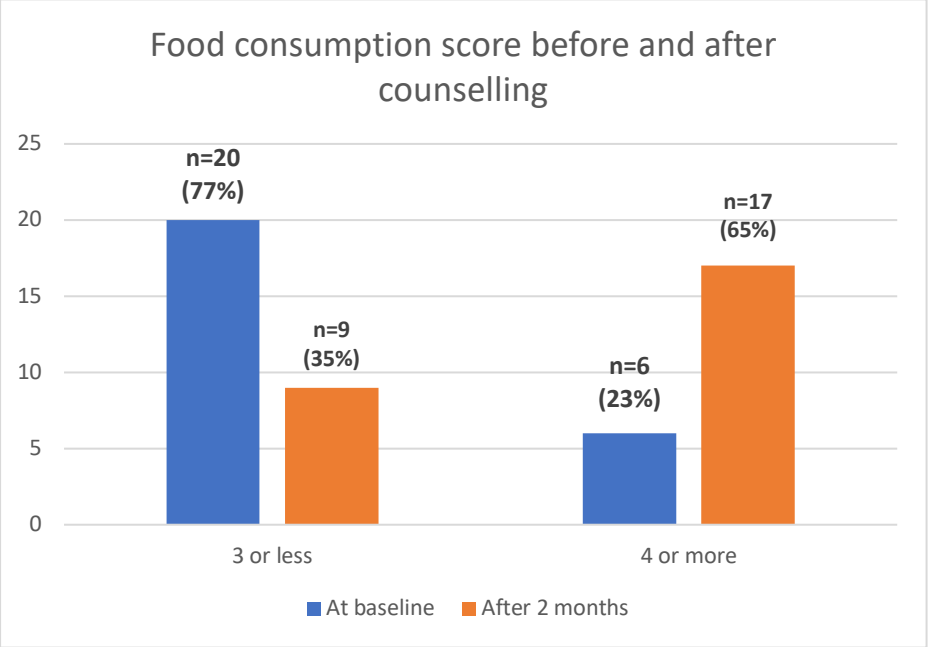


Figure 19 Food consumption score at baseline & after counselling among children with TB aged six months to five years.

Figure 20 illustrates that the quantity of food and number of meals consumed by children was low at the time of enrollment. Over 80% of children were not consuming an adequate number of meals, and around 92% of children were not consuming enough food per meal as per WHO recommendations. After counselling, the rate of an adequate number of meals eaten in a day for the last seven days increased to 61%, and 80% of children were consuming an adequate quantity of food per meal.

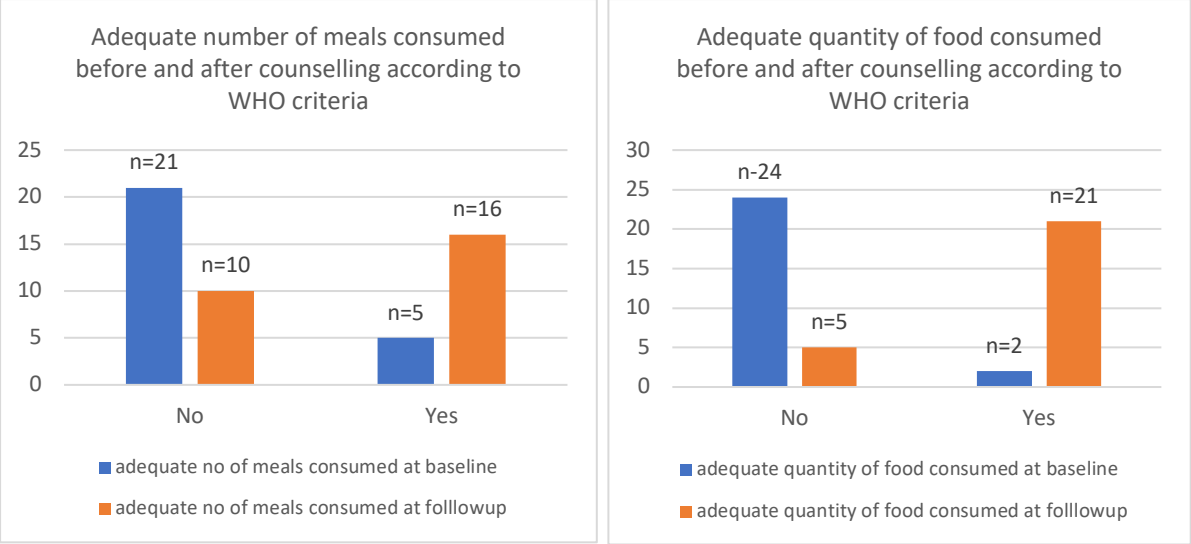


Figure 20 Adequate number of food and quantity of food consumed in last 7 days at the time of enrollment and at follow-up after counselling among children with TB aged six months to five years.

5.10 Effect of nutritional counselling on anthropometric measurements

To determine the efficacy of nutritional counselling, the baseline anthropometric measurements (weight, MUAC, weight for length/height z-scores) are compared to the anthropometric measurements at the two-month follow-up.

Impact of nutritional counselling and TB treatment on the nutritional status

Figure 21 illustrates the weight at baseline and weight after 2 months.

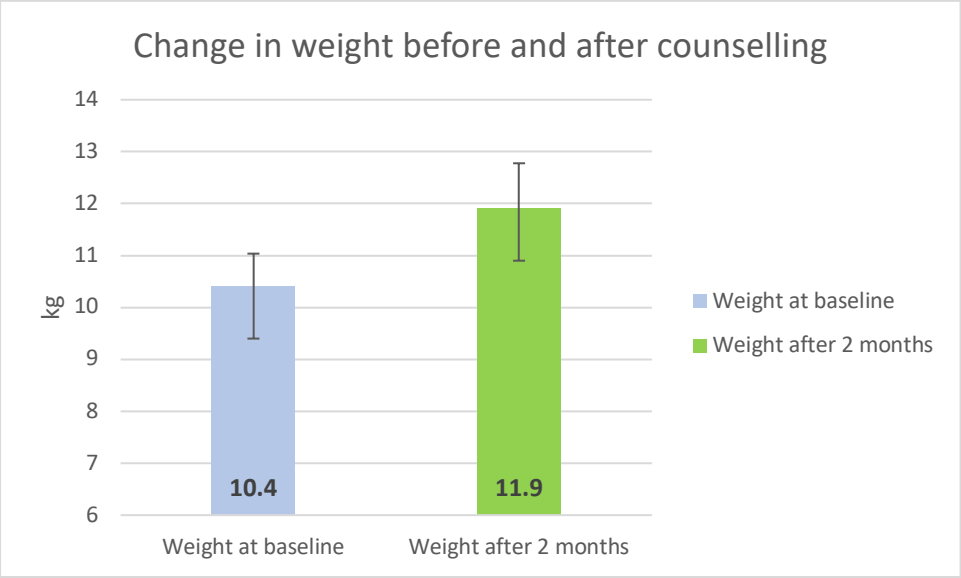


Figure 21 Weight comparison (Median, 25th and 75th percentile, minimum and maximum) before and after counselling

The data shows that the mean weight increased from 10.4 kg to 11.9 kg and a p-value of 0.007 obtained using a paired t-test proves the significance of weight gain.

MUAC comparison at baseline and at follow-up after 2 months

Figure 22 illustrates the MUAC at baseline and MUAC after 2 months.

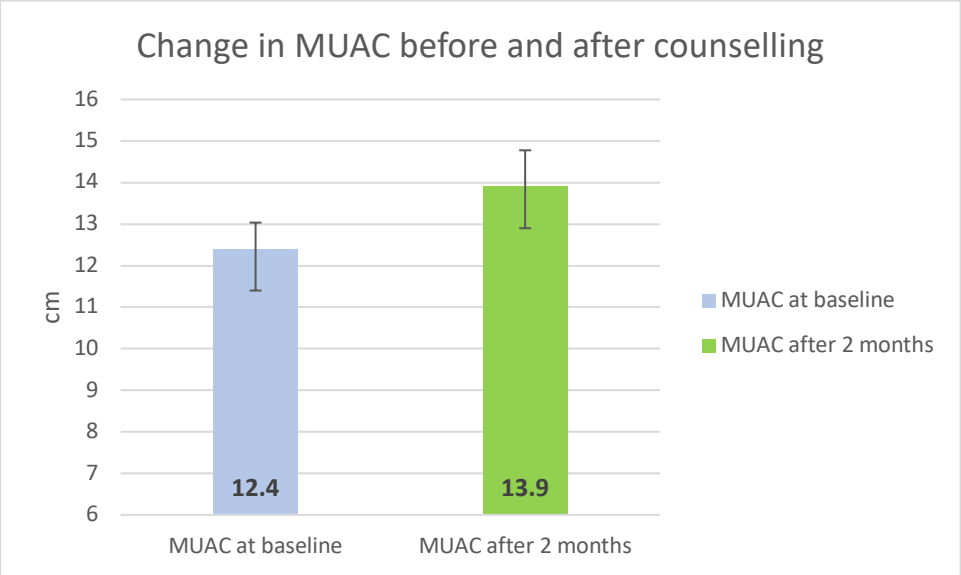


Figure 22 MUAC comparison (Median, 25th and 75th percentile, minimum and maximum) before and after counselling

The data shows that the mean MUAC of the enrolled children increased from 12.4 cm to 13.9 cm after 2 months. Considering the MUAC's normal distribution at enrollment, the paired t-test and p-value of 0.0003 proved that the difference in MUAC at follow-up after counselling is statistically significant.

Out of 26 children who were successfully followed up, 7 (27%) were moderately undernourished (MAM), 11 (42%) were severely undernourished (SAM) and only 8 (31%) had normal nutrition status. 87% of the eight individuals with normal nutritional status at baseline maintained their nutritional status, while 12.5% deteriorated to moderate undernutrition. All the participants who were moderately undernourished at the outset improved their nutritional status to normal by the time of follow-up. 73% of individuals severely undernourished at baseline improved to a normal state, 9% improved marginally and were classified as moderately undernourished, and 18% kept up their initial status. Figure 23 illustrates the transition of nutritional status before counselling to 2 months after counselling at follow-up.

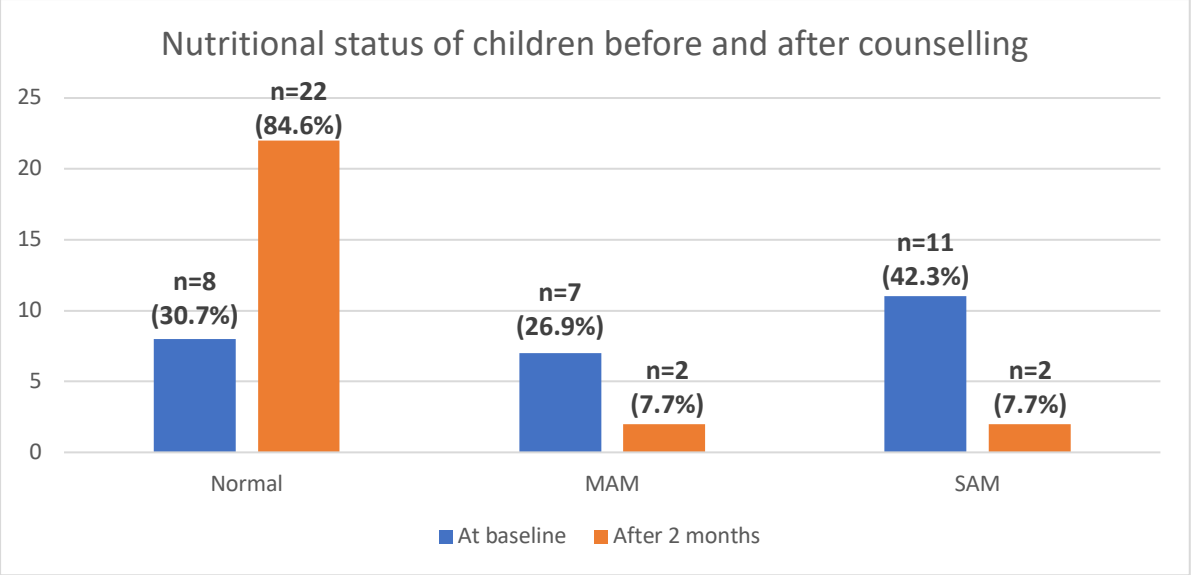


Figure 23 Nutritional status of children with TB aged 6 months to 5 years before and after counselling.

At follow-up, the proportion of individuals with normal nutritional status increased from 31% to 85%. In comparison, the proportion with moderate malnutrition decreased from 27% to 8%, and the proportion with severe malnutrition decreased from 42% to 8%. A p-value of 0.4 shows an insignificant improvement in nutritional status at follow-up.

The nutritional status of enrolled children improved from 63% undernutrition to 15% with the help of nutrition counselling and TB treatment.

5.11 Factors associated with improvement in weight and MUAC

The weight gain percentage was evident in children aged 6 months to 24 months, however, improvement in MUAC was better among children aged 25 to 60 months. Parental education influences the weight gain of the child after counselling. Table 7 and 8 illustrates the improvement in weight and MUAC respectively related to different associated factors in children with TB.

Table 8 Factors associated with the change in weight among children with TB aged six months to 5 years

Variable	**sub-groups**	**No improvement or decreased n (%) 6 (23.1%)**	**Improvement in weight n (%) 20 (76.9%)**	**P-value**
Age	Age 6 to 24 months	1 (14.3%)	6 (86.7%)	0.518
	Age 25 to 60 months	5 (26.3%)	14 (73.7%)	
Gender	Male	1 (6.7%)	14 (93.3%)	0.020
	Female	5 (45.4%)	6 (54.6%)	
Severity of TB	Non-Severe TB	0 (0.0%)	2 (100.0%)	0.420

	Severe TB	6 (25%)	18 (75.0%)	
Type of TB	Pulmonary TB	1 (9.1%)	10 (90.9%)	0.147
	Extrapulmonary TB	5 (33.3%)	10 (66.7%)	
Food consumption score	3 or less	3 (33.3%)	6 (66.7%)	0.366
	4 or more	3 (17.6%)	14 (82.4%)	
Adequate number of meals	No	2 (20.0%)	8 (80.0%)	0.768
	Yes	4 (25.0%)	12 (75.0%)	
Adequate quantity of food taken	No	1 (20.0%)	4 (80.0%)	0.856
	Yes	5 (23.8%)	16 (76.2%)	
Household income	PKR 20,000 or less	2 (22.2%)	7 (77.8%)	0.940
	More than 20,000 PKR	4 (23.5%)	13 (76.5%)	
Father's education	No formal education	4 (26.7%)	11 (73.3%)	0.612
	Formally educated	2 (18.2%)	9 (81.8%)	
Mother's education	No formal education	3 (21.4%)	11 (78.6%)	0.829
	Formally educated	3 (25.0%)	9 (75.0%)	

Table 9 Factors associated with the change in MUAC among children with TB aged six months to 5 years

Variable	**sub-groups**	**No improvement or reduction in MUAC n (%) 9 (34.6%)**	**improvement in MUAC n (%) 17 (65.4%)**	**P-value**
Age	Age 6 to 24 months	3 (42.9%)	4 (57.1%)	0.592
	Age 25 to 60 months	6 (31.6%)	13 (68.4%)	
Gender	Male	5 (33.3%)	10 (66.7%)	0.873
	Female	4 (36.4%)	7 (63.6%)	
Severity of TB	Non-Severe TB	1 (50%)	1 (50%)	0.634
	Severe TB	8 (33.3%)	16 (66.7%)	
Type of TB	Pulmonary TB	2 (18.2%)	9 (81.8%)	0.131
	Extrapulmonary TB	7 (46.7%)	8 (53.3%)	
Food consumption score	3 or less	6 (66.7%)	3 (33.3%)	0.012
	4 or more	3 (17.7%)	14 (82.3%)	
Adequate number of meals	No	4 (40%)	6 (60%)	0.648
	Yes	5 (31.2%)	11 (68.8%)	
Adequate quantity of food taken	No	2 (40%)	3 (60%)	0.778
	Yes	7 (33.3%)	14 (66.7%)	
Household income	PKR 20,000 or less	3 (33.3%)	6 (66.7%)	0.920
	More than 20,000 PKR	6 (35.3%)	11 (64.7%)	
Father's education	No formal education	6 (40%)	9 (60%)	0.500
	Formally educated	3 (27.3%)	8 (72.7%)	
Mother's education	No formal education	3 (21.4%)	11 (78.6%)	0.127
	Formally educated	6 (50%)	6 (50%)	

The Chi-square test was performed to check the significance of improvement, and no statistical significance was found other than gender. In table 8, a p-value of 0.03 for gender suggests that females tend to significantly improve weight better as compared to males. And in table 9, a p-value of 0.012 for food consumption score shows the significant MUAC gain in the group who consumed 4 or more food groups as compared to those who consumed 3 or less food groups.

6. Discussion

The prevalence of undernutrition among children aged six months to 5 years with TB was alarmingly high at 62.7%. Initially, feeding practices were below recommendations, but substantial improvement occurred after nutritional counselling, showcasing parental compliance. Over the two-month follow-up period, anthropometric measurements and nutritional status showed marked improvement. These findings underscore the significance of addressing undernutrition and improper feeding practices in children with TB through nutritional counselling, even in low socioeconomic and low education settings.

One notable observation from our study is the remarkably high prevalence of extra-pulmonary TB, accounting for 53% of cases, a figure surpassing the rates reported in other studies (typically falling within the range of 15 to 20%) (100). Within our cohort, consisting exclusively of children under the age of 5, a majority exhibited severe TB, emphasizing a distinctive vulnerability in this specific population. The elevated prevalence of extra-pulmonary TB and the severity of the disease can be attributed to the inherent susceptibility of young children to more severe manifestations of TB. This vulnerability stems from the immaturity of their immune systems, making them less capable of mounting a robust response against MTB. Consequently, the bacteria can proliferate within the body, contributing to the higher prevalence of severe TB cases (101). This vulnerability is further compounded by the coexistence of a high prevalence of undernutrition within our cohort, compromising the immune system even further.

Diagnosing TB in young children presents a challenge due to the manifestation of non-specific symptoms. Coupled with diagnostic delays, this significantly contributes to the severity of the disease (101). The cumulative impact of all these factors underscores the importance of giving special attention to the well-being of this vulnerable group.

The study revealed a high prevalence of undernutrition (62.7%) among children with TB, highlighting a significant public health concern. This finding is higher than that reported in other studies (47, 102). The elevated prevalence of undernutrition can be attributed to various interconnected factors. Pakistan has a high prevalence of undernutrition in children in the general population, which is further high in children with TB because of the factors associated with TB leading to further undernutrition, such as low appetite, poor absorption, increased nutrient requirements, etc. (40, 47). Moreover, broader issues like low income, low education, low socioeconomic status and a lack of awareness about nutritious diets in Pakistan compound the problem, as evidenced by these factors among the study's participants (40, 103). This highlights that special attention should be given to the nutritional status of this high-risk group in addition to ATT.

This study emphasises the important role of nutritional counselling for mothers of children with TB in the comprehensive management of the disease, evident in the overall increase of anthropometric parameters observed during follow-up. Notably, cases of MAM showed complete improvement, and some SAM cases showed complete recovery, while others demonstrated marginal improvement. This emphasizes that, while nutritional counselling effectively prevents further deterioration in MAM cases, SAM cases need more support beyond nutritional counselling alone. Nonetheless, nutritional counselling offers several advantages. Firstly, it enhances both the quantity and quality of food intake. Secondly, as TB medications can impact appetite, digestion, and nutrient absorption, nutritional counselling plays a crucial role in managing these medication-related side effects. Nutritional counselling mitigates the adverse effects on nutritional status by ensuring adequate nutrient intake. Collectively, these factors contribute to an overall improvement in the nutritional well-being of children undergoing TB treatment.

Another salient feature of the study is that nutritional counselling improved the diversity of food intake as evidenced by the food consumption score before and after the counselling. This is crucial for children with TB, as they often experience micronutrient deficiencies linked to a limited variety of food intake. Such deficiencies weaken the immune function, making it necessary to enhance the intake of diverse foods. This improvement in micronutrient intake contributes to better overall health and a more effective response to TB treatment, as highlighted by existing literature (40, 104, 105).

The significance of food diversity in combating undernutrition is further underscored by a key finding of the study. Children who consumed a restricted variety of food groups faced a fivefold risk of undernutrition. Food groups have different macronutrients and essential micronutrients required for growth and development. Consuming some food groups and leaving others will lead to a deficiency of essential nutrients needed for growth and development and results in undernutrition. It has also been reported by analysing 11 Demographic Health Surveys (106). Thus, nutritional counselling on diverse food and consuming diverse food groups is mandatory to prevent and treat undernutrition (106).

This study revealed interesting results regarding IYCF Practices. While these practices were insufficient upon enrolment, marked improvements occurred post-nutritional counselling at the assessment on follow-up. The study explored various factors impacting adherence to this counselling, uncovering noteworthy insights. Upon understanding the benefits, many mothers actively sought and embraced the support needed to adhere to dietary advice. Despite challenges faced by some from low-income households in accessing nutrient-rich foods, they made concerted efforts to compensate. Cultural beliefs initially conflicting with counselling recommendations were gradually embraced following proper guidance and family support. Most mothers effectively managed their time to provide extra food for their children. These findings suggest an initial lack of awareness regarding healthy diets among families of children with TB. However, it also highlights the potential for positive change through nutritional counselling integrated into routine care, as suggested by other researchers (107, 108). Tailoring counselling to suit cultural contexts, offering practical dietary suggestions and ongoing support, and ensuring access to nutritious foods can significantly improve compliance.

The mortality rate was 14% in the 65% of the enrolled children who were followed up. Our population of children with TB were children under 5 years of age and this is the age group of children with high mortality due to high rates of undernutrition and severe disease presentation. A significant difference was observed in the type of TB between the expired vs alive cases. Extra-pulmonary TB contributed to the major cause of mortality. This can be because of delay in diagnosis of TB, compared to the characteristic cough and sputum production seen in PTB, EPTB can manifest through diverse symptoms depending on the affected organ (e.g., meningitis, bone pain, joint swelling, abdominal pain) (109). Also, EPTB is more likely to disseminate to other organs through the bloodstream, leading to life-threatening complications

like miliary TB and meningitis. Disseminated TB has a significantly higher mortality rate compared to PTB (110).

The loss to follow-up was 35%. These children did not come for follow-up at the hospital, and the two phone numbers that they gave at enrolment to be contacted for follow-up were not responding. The reason for the loss to follow up could be that TB still carries a significant stigma in many communities. Families might avoid follow-up due to fear of discrimination, especially if they perceive TB as shameful or contagious. Some families might not fully understand the importance of follow-up appointments or the severity of TB, leading to non-compliance with medical advice.

In order to reduce the possibility of selection bias, a Chi-square test was used to compare the baseline clinical features between participants who attended follow-up sessions and those who lost to follow-up. The results indicated no statistically significant differences (p-value > 0.05) suggesting that, in terms of these measured variables, the two groups were comparable. This analysis offers reassurance that potential biases resulting from participant attrition may have been mitigated, thus enhancing the study's outcomes' robustness.

The study has some strengths and limitations. The strength of the study includes a prospective design that allowed the collection of data at the time of enrolment (before counselling) and also at each follow-up (after counselling), which allowed us to estimate the impact of counselling on children with TB. Secondly, the standardized assessment tools were used to evaluate nutritional status ensuring the accuracy and consistency of the collected data. These strengths enhance the internal validity of the study.

The limitation of the study includes the small sample size. This was due to challenges in the recruitment and retention of participants. This limited the statistical power of the study and may have affected the generalizability of the findings. The data was collected from two tertiary care hospitals, which may limit the generalizability of the findings to the broader population of children with TB. The healthcare settings and patient population in tertiary care hospitals may differ from those in primary care settings or community settings or those with different comorbid conditions and severity. The follow-up period of two months may be too short to fully assess the long-term impact of the counselling on child health outcomes. Furthermore, a 35% loss to follow-up has further reduced the statistical power of the study by reducing the study size at follow-up.

Recommendations:

Despite these limitations, the study offers important insights into the efficacy of nutritional counselling along with TB treatment in enhancing the nutritional status of children who are undernourished and have TB. Based on the findings, it is recommended that nutritional counselling be incorporated into the routine treatment of TB in children. Additional research with larger sample sizes, more extended follow-up periods, and a more diverse sample population is required to determine the long-term impact of nutritional counselling on children's health outcomes.

7. Conclusion

The study demonstrates that there is a high prevalence of undernutrition among children with TB. Nutritional counselling of mothers and children, in conjunction with TB treatment, improved the nutritional status and feeding practices of these children. These findings highlight how important it is to address nutritional needs as an integral part of TB treatment for children who are being treated.

The findings of this study have important implications for the development and implementation of nutrition counselling programs. The results suggest that nutrition counselling can be an effective way to improve dietary diversity.

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HEIGHT OF CHILDREN OVER 2.
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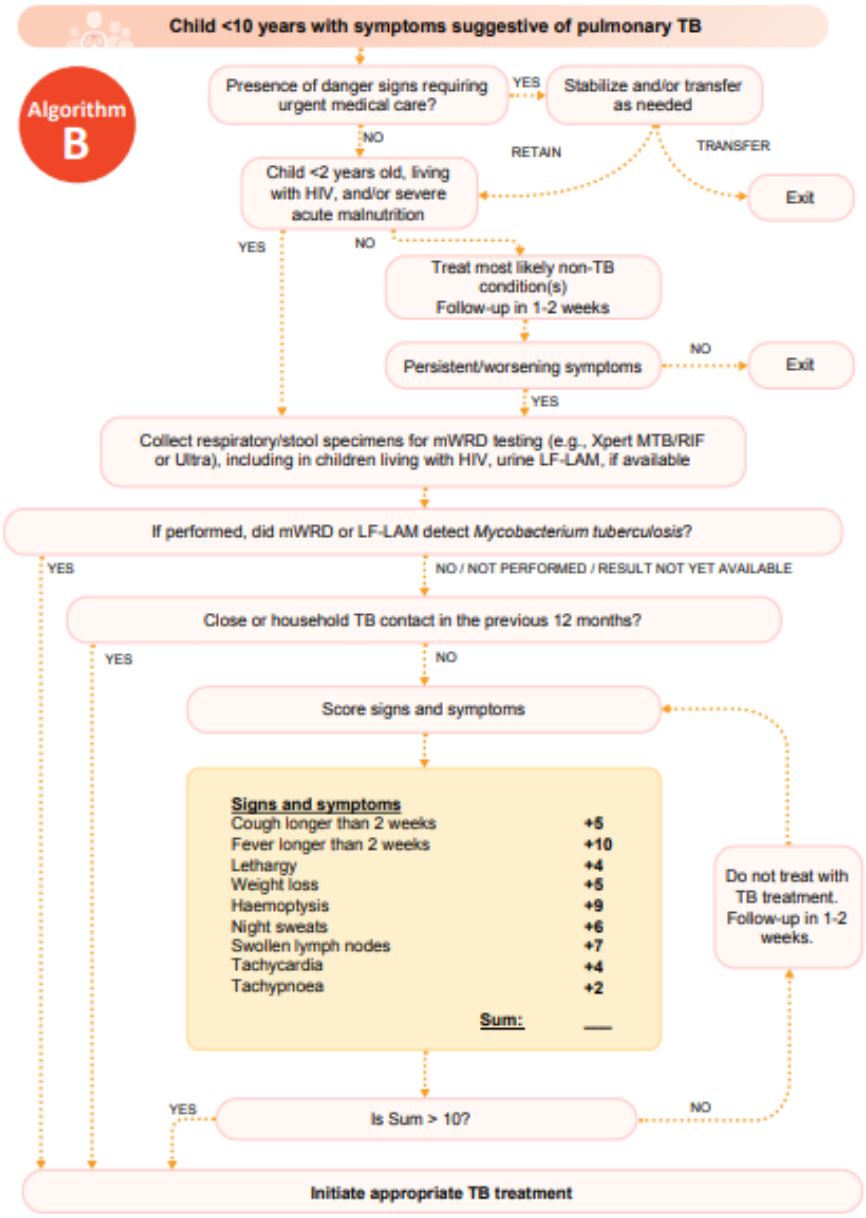
Appendices

Appendix A: Integrated treatment decision algorithms for Pulmonary TB in children – algorithm b



Appendix B – Steps to measure weight of the children aged 0 to 24 months using an infant weighing scale

Infant Scale: Measuring Weight

Birth to 24 Months of Age

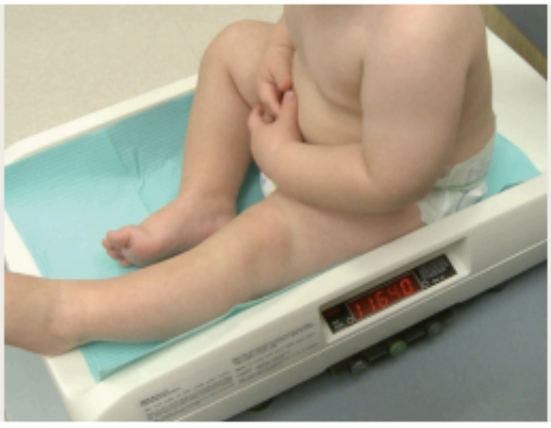
Public Health Setting

STEP 1: Preparation

- Weigh infants birth to 8 weeks nude
- Weigh infants 2 to 24 months in a clean, dry diaper
- Place a paper barrier on the scale
- With the paper barrier in place, "zero" the scale

STEP 2: Weighing

- Place the infant in the middle of the scale; do not leave infant unattended



STEP 3: Read and record the measurement

- Read the measurement to the nearest 0.001 kg or 0.01 kg increment and record

STEP 4: Checking calibration

- Check with calibration weight monthly and record

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Appendix C – Steps to measure weight of the children aged above 24 months using a digital weighing scale

Child/Adolescent Scale: Measuring Weight

2 to 19 Years of Age

STEP 1: Preparation

- Remove shoes, hats or bulky items like coats and sweaters
- Place a paper barrier on the scale
- With the paper barrier in place "zero" the scale

STEP 2: Weighing

- Ask the child to stand in the middle of the scale platform
- Weigh the child standing without assistance

STEP 3: Read and record the measurements

- Read the measurement to the nearest 0.1 kg increment and record

STEP 4: Checking calibration

- Schedule professional calibration yearly or more frequently if required

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Appendix D – Steps to measure height of the children aged 0 to 24 months using an infantometer

Infant Length Board: Measuring Length

Birth to 24 Months of Age

STEP 1: Preparation

- Measure infant wearing light clothing or diaper
- Remove shoes, hat and bulky clothing such as coats and sweaters
- Cover length board with a paper barrier

STEP 2: Child positioning is important!

- Place infant on their back in the centre of the length board
- Two people are needed to get an accurate measurement

Staff Role

- Align trunk and legs
- Extend both legs, toes pointed up
- Bring footboard firmly against the heels
- One hand on knees to maintain full extension

Parent Role

- Hold head against the headboard to compress the hair

Child Positioning

- Eyes looking straight up
- Chin not tucked or stretched too far back

STEP 3: Read and record the measurements

- Measure to the nearest 0.1 cm and record

STEP 4: Checking calibration

- Check with calibration rod monthly and record

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Appendix E – Steps to measure height of the children aged above 24 months using a stadiometer

Stadiometer: Measuring Height

2 to 19 Years of Age

STEP 1: Preparation

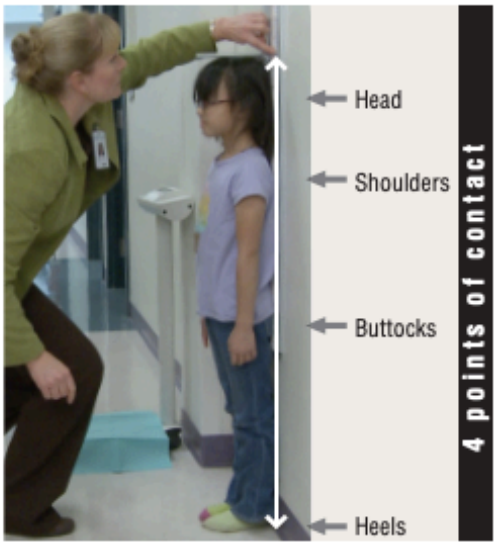
- Remove shoes, hats and bulky clothing such as coats and sweaters
- Undo hair styles and remove hair accessories that may interfere with measurement

STEP 2: Child positioning is important!

- Ask the child to stand against the stadiometer with heels together, legs straight, arms at sides and shoulders relaxed

Staff Role

- Bring the headpiece down to touch the crown of the head with enough pressure to compress the hair
- Measurer's eyes should be parallel with the headpiece to read the measurement



Child Positioning

- Head, shoulders, buttocks, and heels touching vertical surface
- Eyes should be looking straight ahead
- Chin not tucked or stretched too far back

STEP 3: Read and record the measurements

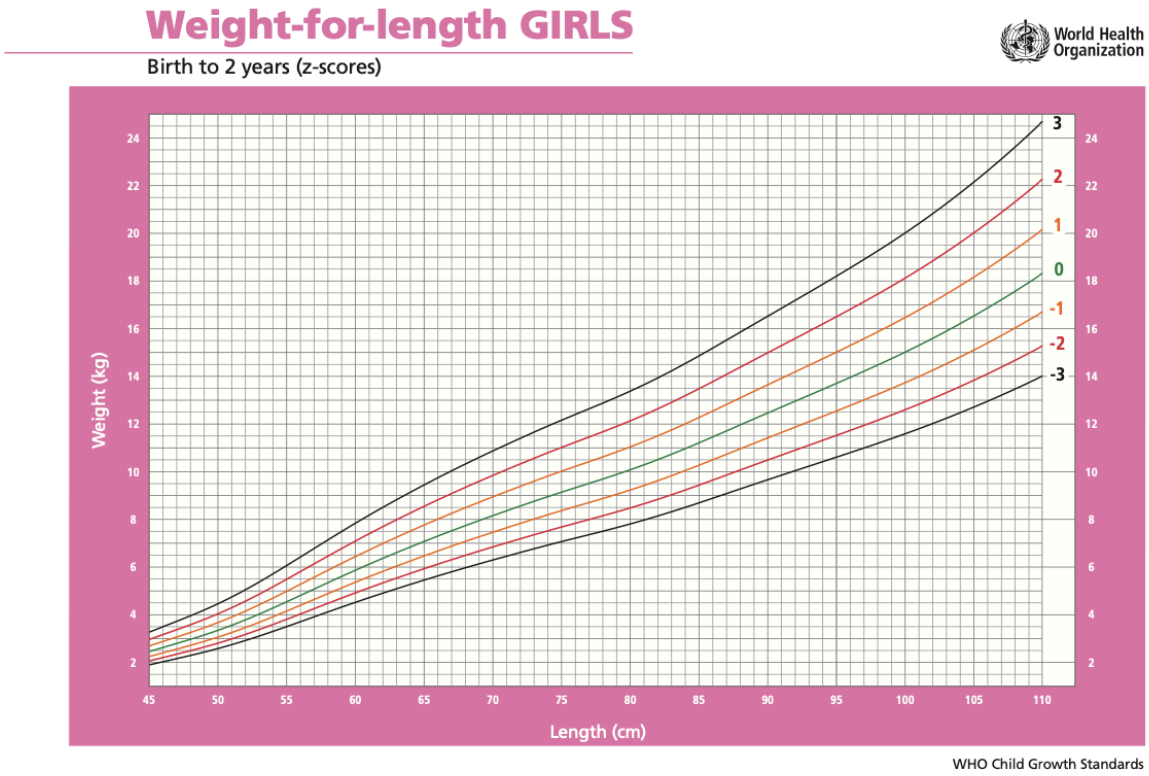
- Measure to the nearest 0.1 cm and record
- If the child cannot stand unassisted, measure recumbent length, **subtract 0.7 cm** to convert to height

STEP 4: Checking calibration

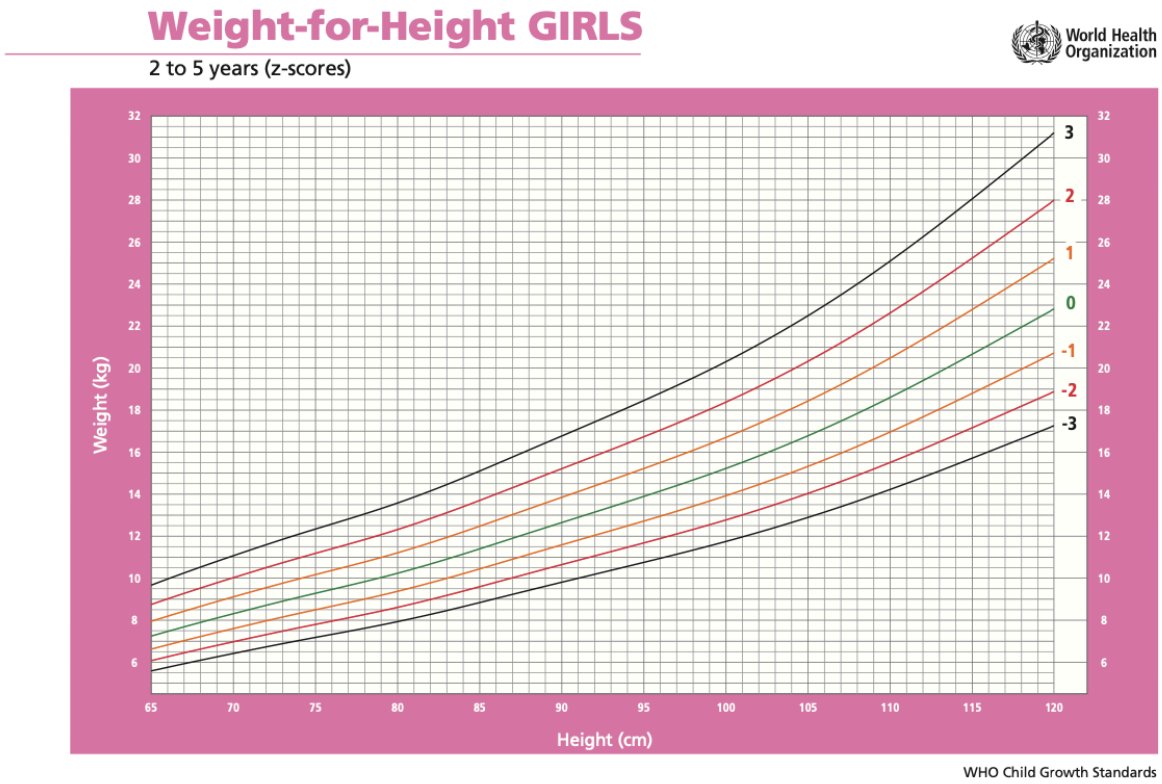
- Check with calibration rod monthly and record

www.albertahealthservices.ca Alberta Health Services

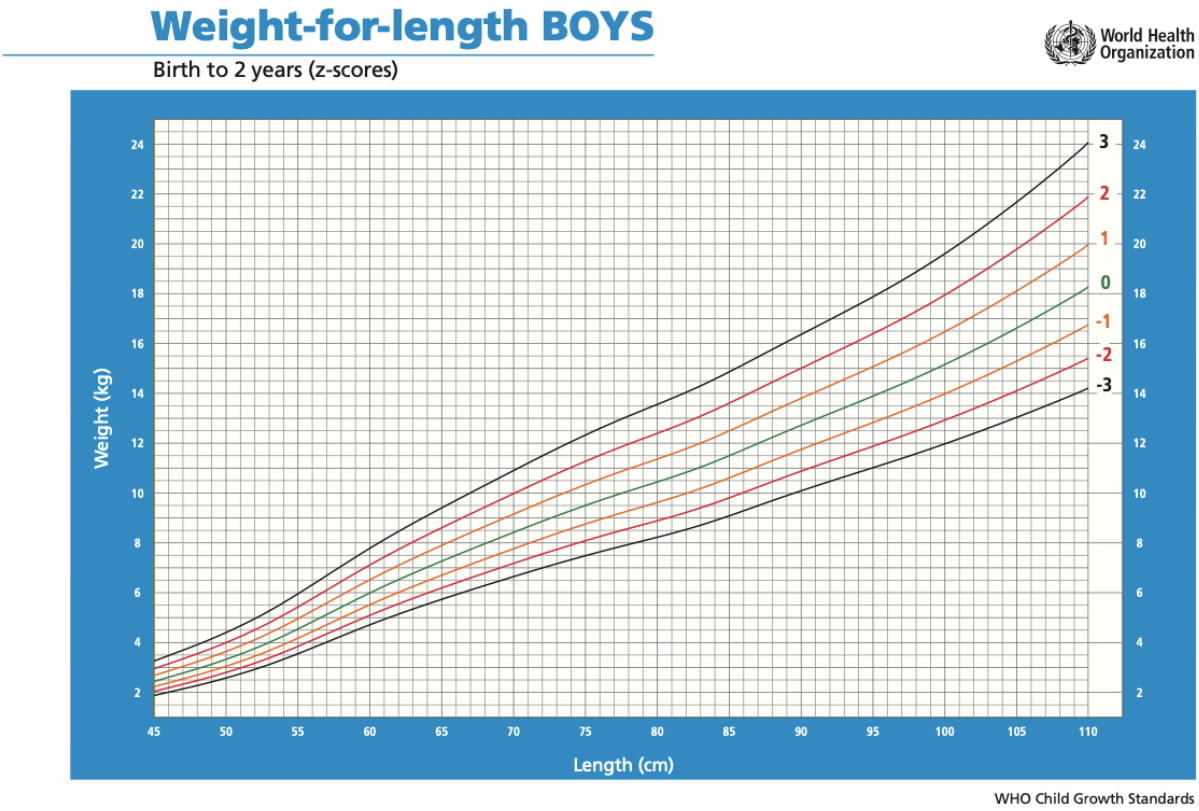
Appendix F - WHO growth standards - Weight for length z-score for girls aged 0 to 2 years.



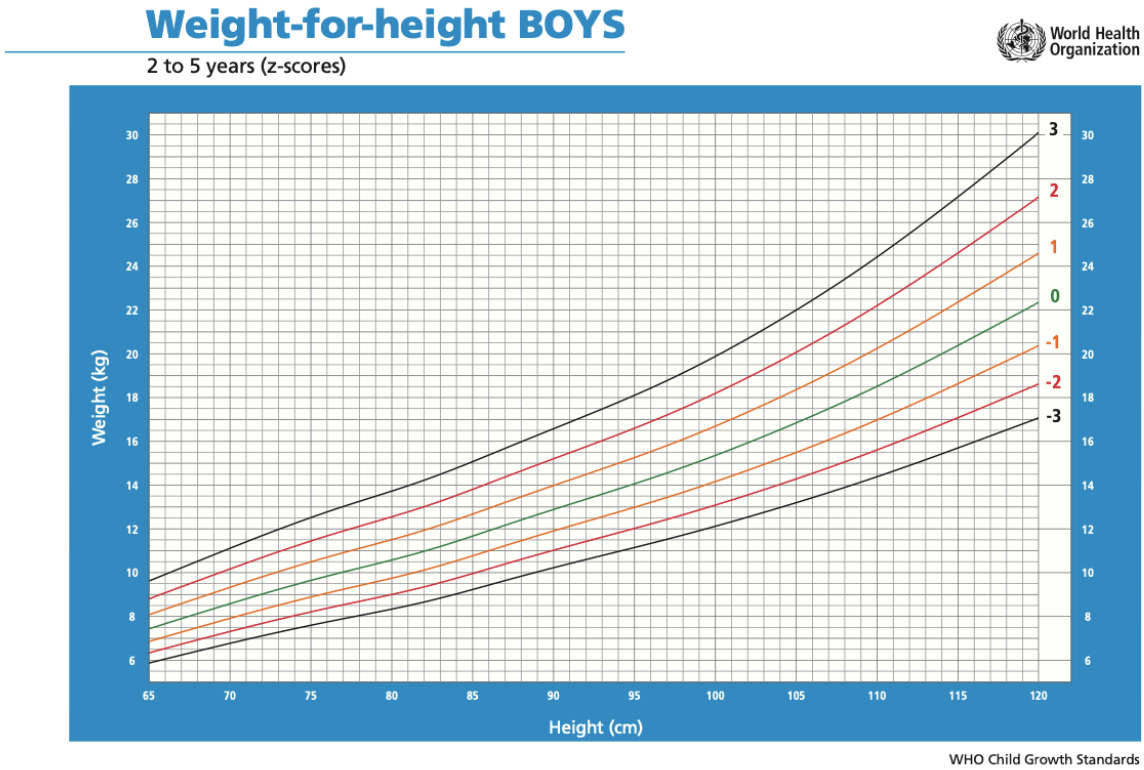
Appendix G - WHO growth standards - Weight for height z-score for girls aged 2 to 5 years.



Appendix H - WHO growth standards - Weight for height z-score for boys aged 0 to 2 years.



Appendix I - WHO growth standards - Weight for height z-score for boys aged 2 to 5 years.



Appendix J – Steps to measure MUAC of the children aged 6 months to 5 years using MUAC tape

unicef	**PRODUCT SPECIFICATION SHEET (for local and regional procurement)** **Child MUAC Tape**	Version no: 4 Material no: S0145620 Author: AK, AF Date: 12.05.2020

General Description:

Children's Mid Upper Arm Circumference (MUAC) measuring tape with cut-off point at 11.5 cm, pack of 50 tapes with text and pictorial instructions for use.

Technical Specifications:

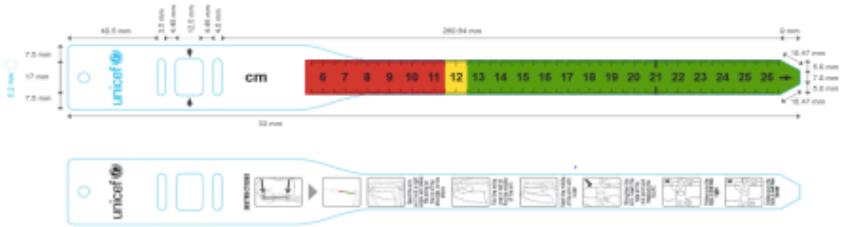
MUAC measuring tape is suitable for measuring child's Middle Upper Arm Circumference (MUAC)with range up to 26.5 cm.
Graduated with 1 mm precision with thicker line at 21.0 cm.
Accuracy: ± 1 mm of the maximum measurement (26.5 cm)

Front side:
Colour-coded as follows:
Red (Pantone code 1795 C): from 0 to 11.5 cm,
Yellow (Pantone code 107 C) from 11.5 to 12.5 cm,
Green (Pantone code 369 C) from 12.5 to 26.5 cm.
Optionally includes UNICEF logo in pantone Cyan Process R56 /G142 / B199 (at UNICEF's request)

Reverse side:
Includes instructions and diagrammatic drawings. The written instructions may be requested to be in Arabic, Spanish, French or English. The drawings represent 5 steps in taking the MUAC measurement either the 'string' method of measuring the mid-point, or the 'tape' method.

String method for finding the mid-point of the arm:

Drawing 3: Bend the arm so it is at a right angle, and place the string on the tip of the shoulder, to the elbow.
Drawing 4: Fold the string over in half to find the middle of the arm
Drawing 5: Mark the middle of the arm with a pen
Drawing 6: Straighten the arm, insert the tape at the mid-point and measure the MUAC
Drawing 7: Make sure the tape is not too tight
Drawing 8: Make sure the tape is not too loose



Appendix K – Follow-up questionnaire

IMPROVING DIAGNOSIS AND MANAGEMENT OF CHILDHOOD TB IN LOW-RESOURCE, HIGH-TB BURDEN SETTINGS: A STUDY FROM PAKISTAN; FOLLOW UP FORMS

DETAIL FOLLOW UP FORM TO BE FILLED AT 2 , 4 AND 6 MONTHS OF START OF ATT

8.0	Interviewer Name----------	8.1 Date of assessment----------
8.2	Respondent name----------	8.3. Relationship of the respondent----------
8.4	Phone number of the respondent---------	8.5 Hospital; Children hosp/GDH
8.6	Study Enrolment Number----------	8.7. Patient Name----------
8.8	Date of Birth	8.9 Age of the child
8.10	**Type of TB:** Pulmonary TB/Extrapulmonary TB	**8.11 Severity of TB:** Severe/Non-Severe
8.12	**PreviousNutritional status.** Normal/MAM/SAM	
8.13	**Previous NRS score:** No risk/mild/moderate/Severe	**8.14. Previous STRONG score**: No risk/moderate/Severe risk
8.15	Nutritional problem identified previously	1. To improve quantity of food 2. To improve quality of food 3. Both 1 and 2
8.16	Current number of follow up	----------
8.17	No of days after last visit	----------
8.18	Reason for follow up	1. Monthly TB follow up 2. Scheduled TB follow up for complications 3. Scheduled follow up for NRS 4. Monthly nutritional follow up
8.19	How is the condition of your child in your opinion?	1.Markedly improved 2. Somewhat improved 3. No improvement, 4. Worse than before
8.20	Which Regimen of ATT is the child on?	1. HRZE 2. HRZ 3. HR
8.21	Which month of ATT is the child on?	1/2/3/4/5/6
8.22	Did you give ATT to the child as advised?	1.Yes 100% 2, Missed sometimes (25-50%) 3.Missed majority of the times (50-75%) 4. Did not give ATT
8.23	Did you feel any side effects of giving ATT to the child?	1.Nausea, 2. Vomiting, 3. Diarrhoea, 4. Itching 5. Jaundice 6. Problems with vision
8.24	Did you have any problems with giving ATT to the child?	1. Child refuse to take ATT 2. Give the child ATT with great difficulty 3. Caretaker often forget to give ATT 4. Got short of supply of ATT 5. Other----------
8.25	Did you give diet to the child as advised?	1.Yes 100% 2. Missed sometimes (25-50%)

Appendix L – Ethical approval from REK, Norway

REK

REGIONALE KOMITEER FOR MEDISINSK OG HELSEFAGLIG FORSKNINGSETIKK

Region:	Saksbehandler:	Telefon:	Vår dato:	Vår referanse:
REK vest	Anna Stephansen	45008356	26.03.2023	532676

Tehmina Mustafa

Prosjektsøknad: Forbedring av tuberkulosediagnose og behandling hos barn i et lavressurs- høyendemisk område
Søknadsnummer: 532676
Forskningsansvarlig institusjon: Universitetet i Bergen
Samarbeidende forskningsansvarlige institusjoner: Helse Bergen HF - Haukeland universitetssykehus

Prosjektsøknad godkjennes

Søkers beskrivelse

Globally, an estimated 1.1 million new childhood tuberculosis (TB) cases occur annually. Recently, WHO issued new guidelines for diagnosis and treatment. The objective of this project is to 1) pilot the new guidelines, 2) improve the treatment outcomes by optimizing the management of undernutrition and anemia, 3) study the healthcare-seeking pathway, diagnostic delay, and its impact on the treatment outcomes and quality of life. Using a prospective cohort study design, 500 children diagnosed with TB will be enrolled at two tertiary care hospitals in Pakistan. Data will be collected by using pre-formed and standard questionnaires. A predeveloped simple clinical tool for monitoring response to treatment will be validated. Treatment outcomes will be compared among children; 1) with and without undernutrition, 2) with and without anemia, 3) receiving 4 and 6 months of treatment. Diagnostic delay and Quality of Life will be estimated. The project is expected to improve childhood TB care.

Søknaden ble behandlet av Regional komité for medisinsk og helsefaglig forskningsetikk REK vest i møtet 25.10.22 Vurderingen er gjort med hjemmel i helseforskningsloven § 10.

REKs vurdering

REK vest ba i møte om følgene tilbakemelding på to punkter:

- Lokale godkjenninger sendes REK vest.
- Organisering av den generelle biobanken og prøver som skal lagres i denne.

REK vest ber prosjektlederen om å ettersende DTA (data transfer agreement) så snart den er signert og har ikke flere merknader til verken organisering av biobanken eller informasjonsskrivene.

REK vest
Besøksadresse: Armauer Hansens Hus, nordre fløy, 2. etasje, Haukelandsveien 28, Bergen
E-post: rek-vest@uib.no
Web: https://rekportalen.no

Vedtak
Prosjektet godkjennes med hjemmel i helseforskningsloven § 10 samsvar med forelagt søknad.

Sluttmelding
Prosjektleder skal sende sluttmelding til REK på eget skjema via REK-portalen senest 6 måneder etter sluttdato 31.12.2028, jf. helseforskningsloven § 12. Dersom prosjektet ikke starter opp eller gjennomføres meldes dette også via skjemaet for sluttmelding.

Søknad om endring
Dersom man ønsker å foreta vesentlige endringer i formål, metode, tidsløp eller organisering må prosjektleder sende søknad om endring via portalen på eget skjema til REK, jf. helseforskningsloven § 11.

Klageadgang
Du kan klage på REKs vedtak, jf. forvaltningsloven § 28 flg. Klagen sendes på eget skjema via REK portalen. Klagefristen er tre uker fra du mottar dette brevet. Dersom REK opprettholder vedtaket, sender REK klagen videre til Den nasjonale forskningsetiske komité for medisin og helsefag (NEM) for endelig vurdering, jf. forskningsetikkloven § 10 og helseforskningsloven § 10.

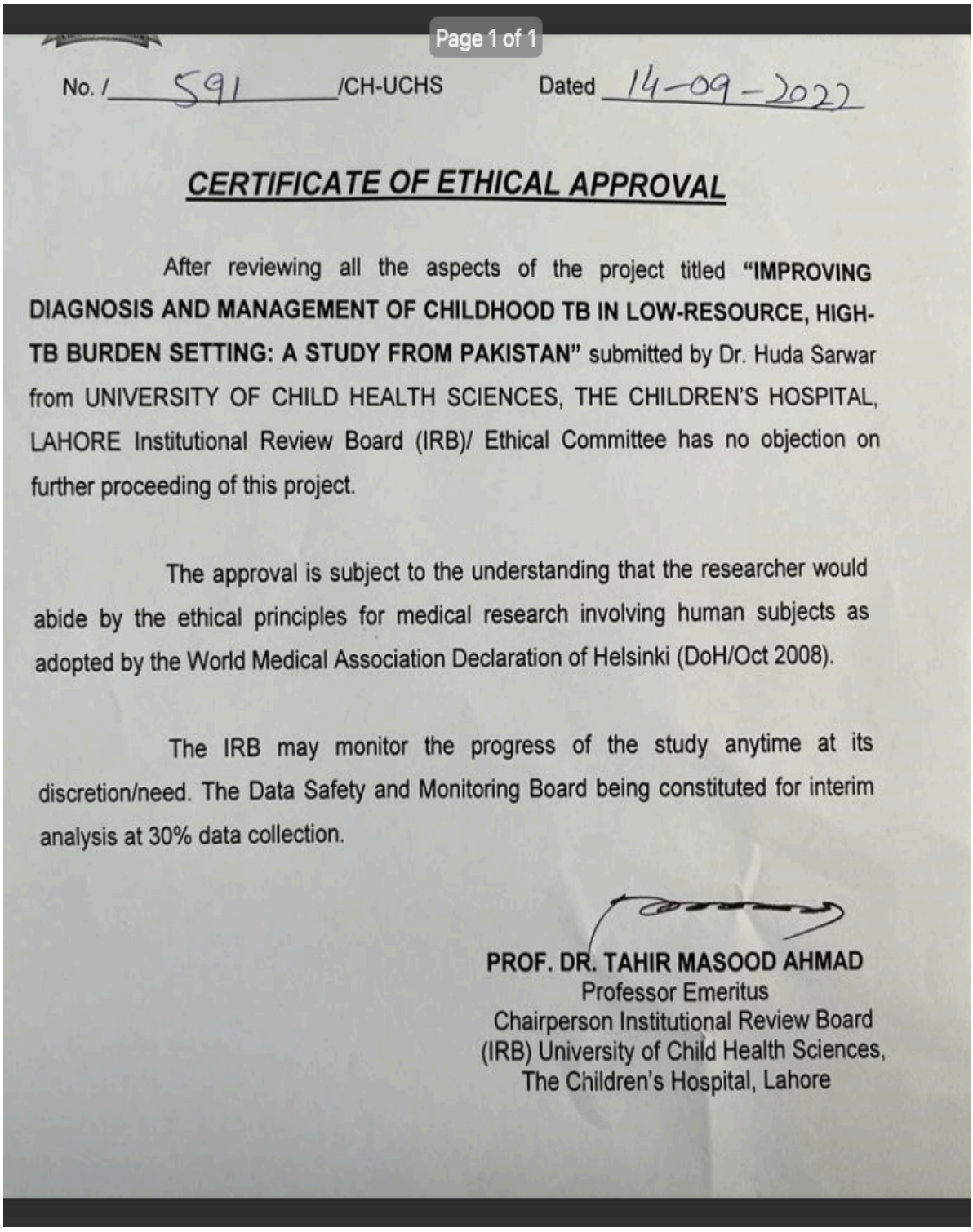
Vennlig hilsen,
Nina Langeland REK vest leder,
Professor, dr.med. UiB og

Anna Stephansen
Sekretariatsleder/kontorsjef
REK vest rek-vest@uib.no

Kopi til:

Universitetet i Bergen
Helse Bergen HF - Haukeland universitetssykehus

Appendix M: Ethical approval from Children Hospital Lahore



Page 1 of 1

No. / 591 /CH-UCHS Dated 14-09-2022

CERTIFICATE OF ETHICAL APPROVAL

After reviewing all the aspects of the project titled **"IMPROVING DIAGNOSIS AND MANAGEMENT OF CHILDHOOD TB IN LOW-RESOURCE, HIGH-TB BURDEN SETTING: A STUDY FROM PAKISTAN"** submitted by Dr. Huda Sarwar from UNIVERSITY OF CHILD HEALTH SCIENCES, THE CHILDREN'S HOSPITAL, LAHORE Institutional Review Board (IRB)/ Ethical Committee has no objection on further proceeding of this project.

The approval is subject to the understanding that the researcher would abide by the ethical principles for medical research involving human subjects as adopted by the World Medical Association Declaration of Helsinki (DoH/Oct 2008).

The IRB may monitor the progress of the study anytime at its discretion/need. The Data Safety and Monitoring Board being constituted for interim analysis at 30% data collection.

PROF. DR. TAHIR MASOOD AHMAD
Professor Emeritus
Chairperson Institutional Review Board
(IRB) University of Child Health Sciences,
The Children's Hospital, Lahore

Appendix N: Ethical approval from Gulab Devi Chest Hospital, Lahore

AL-ALEEM MEDICAL COLLEGE

(A Company set up under Section 42 of the Companies Act 2017)

GULAB DEVI CHEST HOSPITAL, FEROZEPUR ROAD LAHORE, PAKISTAN

INSTITUTIONAL REVIEW BOARD (IRB)

AAMC/IRB/EA 35 2022

18th August, 2022

Ethical Approval

***Research Title**: Improving diagnosis and management of Childhood TB in low-resource, high-TB burden settings: a study from Pakistan*

***Principle Author:** Dr. Huda Sarwar*

This ethical approval is issued subject to following conditions that

- The researcher will abide by the ethical principles of medical research involving human subject, as adopted by the word medical association declaration of Helsinki (DoH/ Oct 2008)
- It remains the principal investigator's responsibility to ensure that all necessary documents and consent forms related to the study are retained for maximum of two years for future reference.
- The IRB may monitor the progress of the study anytime at its discretion / need.

Prof. Dr. M. Zia-ul-Miraj Ahmad
MBBS, FRCS (Edinburgh), Dipl. Paed. Surg. (London)
DCH (Glasgow), D.U. (London), CRCP (DUHS), MME (UoL)
Director, Department of Medical Education, AAMC

Mr. Shehryar Ali
Chairperson
Institutional Review Board
Al-Aleem Medical College

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