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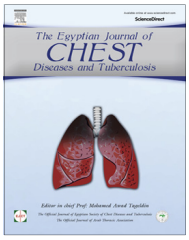

ORIGINAL ARTICLE

# Plasma vitamins and essential trace elements in newly diagnosed pulmonary tuberculosis patients and at different durations of anti-tuberculosis chemotherapy

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**Abstract** Tuberculosis (TB) is a public health challenge worldwide and advancement of latent TB to active disease and drug resistant TB is on the increase as a result of immune suppression induced by *Mycobacterium tuberculosis*. There are empirical evidences relating immune suppression and malnutrition. To improve the management strategy of TB patients, this study determined micronutrient concentrations in TB patients and established duration (months) post commencement of anti-tuberculosis (anti-TB) chemotherapy that is most important for micronutrient supplementation.

Plasma iron, zinc, copper, vitamins A, C, D and E were determined in twenty-four (24) active tuberculosis patients at diagnosis, 2 months, 4 months and 6 months post-commencement of anti-TB chemotherapy, as well as twenty (20) healthy controls. Plasma concentrations of the micronutrients iron, zinc, copper, vitamins A, C, D and E were significantly reduced in TB patients at diagnosis and throughout the period of treatment when compared to controls. Plasma zinc and copper levels were significantly increased at 4 months and 6 months of drug therapy when compared with levels at diagnosis whereas plasma iron was significantly reduced at 4 months of treatment compared with their levels at diagnosis. Vitamins A, C, D and E in TB patients were significantly reduced at 2 months and 4 months of treatment compared to diagnosis.

*Abbreviations*: TB, tuberculosis; Mtb, *Mycobacterium tuberculosis*; Anti-TB, anti-tuberculosis; ROI, reactive oxygen intermediate; RNI, reactive nitrogen intermediate

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This study concluded that there is micronutrient (Fe, Zn, Cu, Vit A, C, D and E) malnutrition in tuberculosis patients at diagnosis and throughout the duration (6 months) of chemotherapy. Supplementation with vitamins and zinc is advised within the first 4 months of commencing anti-tuberculosis chemotherapy.



## Introduction

Tuberculosis (TB) remains a major global health challenge with 8.7 million new cases and 1.4 million deaths annually [1]. Approximately one third of the world's population is latently infected with *Mycobacterium tuberculosis* (Mtb), the etiologic agent of TB. Latently Mtb infected immunocompetent individuals have a 10% lifetime chance of reactivation to active disease but higher chance (up to 90%) of reactivation to active TB in immuno-compromised individuals [2]. About 60% of all TB cases occur in Africa and South East Asia [2], and this has been associated with extreme poverty, malnutrition, poor hygiene and HIV infection which predisposes to immunosuppression [3].

Mtb establishes and expands infection within resident alveolar macrophages by subverting the natural killing mechanism of these cells. Generation of reactive oxygen intermediates (ROI) and reactive nitrogen intermediates (RNI) via respiratory burst pathway following bacilli phagocytosis plays an important role in pathogen clearance [4]. Some trace elements have been identified to play important roles in macrophage phagocytosis, ROI and RNI generation, intracellular killing as well as eventual bacterial clearance [5]. Vitamins A, C, D and E have been described as immune enhancers in different infectious diseases including TB, and supplementation of these vitamins has been shown to boost immunity [6]. But the mechanism by which this is achieved is largely unclear. Iron and copper propagate the formation of toxic hydroxyl radical in a Fenton and Fenton-like chemistry, respectively [7,8] and their deficiencies have been associated with modulation of immune responses [5]. Furthermore, the immune modulatory effects of zinc are well documented [9].

There is epidemiological evidence of an association between malnutrition and development of active TB in latently infected individuals [10]. Active tuberculosis is associated with wasting as a result of anorexia, reduced food intake and mal-absorption [11]. Before the advent of anti-tuberculosis (anti-TB) chemotherapy, a diet rich in calories, proteins, fats, minerals and vitamins was considered in the treatment of tuberculosis [12]. However, introduction of anti-TB drugs led to reduced emphasis on the importance of nutritional support in the management of TB patients. In Nigeria, newly diagnosed TB patients are treated for at least 6 months with anti-TB therapy without reference to the micronutrient status of these patients pre-, during and post-therapy.

Therefore, the objective of this study is to determine the levels of nutritionally essential trace elements (Fe, Zn and Cu) and vitamins (Vit A, C, D and E) in plasma of TB patients before and during drug regimen. The aim is to establish micronutrient malnutrition in TB patients and to establish for the first time which duration (months) post commencement of anti-TB drug therapy is in the micronutrient level most affected. It is the opinion of the authors that the outcome will improve TB patients' management or reduce advancement of pulmonary tuberculosis (PTB) to drug resistant TB.

## Participants and methods

Forty-four (44) participants were recruited for the study which comprised of twenty-four (24) newly diagnosed pulmonary tuberculosis (PTB) patients and twenty (20) non-PTB apparently healthy subjects after obtaining written informed consent. The study protocol was reviewed and approved by the University of Ibadan/University College Hospital joint Institutional Research Ethics Committee. All patients were recruited from the Medicine Out-patient Clinic, University College Hospital, Ibadan, Nigeria by a consultant Chest Physician after laboratory tests, chest X-ray and clinical history.

Five milliliters of blood was withdrawn from the anti cubital fossa vein into lithium heparin tubes at diagnosis, 2 months of anti-TB therapy, 4 months of anti-TB therapy and at completion of duration of anti-TB therapy (6 months). Blood samples were centrifuged and plasma collected were analyzed.

### *Micronutrient analysis*

Plasma levels of micronutrient vitamins (A, C, D and E) were determined by high performance liquid chromatography method using WATERS 616/626 (USA) machine as previously carried out [13].

Plasma concentrations of trace metals (Fe, Zn and Cu) were determined using atomic absorption spectrophotometry (Buck Scientific, 210, Atomic Absorption Spectrophotometer, Connecticut, USA) as previously described [14].

### *Statistical analysis*

The data obtained were analyzed using statistical package for social sciences (SPSS) version 17.0. Independent Student *t*-test was used to compare the mean values between PTB patients and controls while paired *t*-test was used to compare the mean values of PTB patients at diagnosis, 2 months, 4 months and 6 months of anti-TB regimen. Values were considered significant at $p < 0.05$.

## Results

Plasma concentrations of the micronutrients iron, zinc, copper, vitamin A, vitamin C, vitamin D and vitamin E were significantly reduced in TB patients at diagnosis and throughout the period of treatment when compared to controls (Table 1).