



Vitamin C Supplementation and Sputum Conversion in Pulmonary Tuberculosis Patients: A Randomized Controlled Study

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Abstract

Background: Pulmonary tuberculosis (TB) patients frequently present with compromised nutritional and antioxidant status, which may impair immune clearance of *Mycobacterium tuberculosis*. Vitamin C (ascorbic acid) has antioxidant and immune-supportive properties and has been proposed as a low-cost adjunct to standard anti-tuberculosis treatment (ATT).

Objective: To evaluate the effect of vitamin C supplementation, given alongside standard ATT, on the rate of acid-fast bacilli (AFB) sputum smear conversion in newly diagnosed pulmonary TB patients during the intensive phase of treatment.

Methods: A randomized, parallel-group study was conducted in 80 newly diagnosed, sputum-smear-positive, ATT-naïve pulmonary TB patients aged 20–65 years. Participants were allocated to receive either vitamin C (1000 mg/day) plus standard ATT (n=40) or placebo plus standard ATT (n=40). Sputum AFB smears were examined every two weeks for two months. Categorical outcomes were compared using the chi-square test; continuous outcomes (serum vitamin C levels) were compared using an independent-samples t-test. Significance was set at $P < 0.05$.

Results: All 40 patients (100%) in the vitamin C group achieved sputum conversion within the first month, compared with 8 of 40 (20%) in the placebo group; the remaining placebo patients converted in the second month. The difference in conversion rate between groups was statistically significant ($P < 0.05$). Mean serum vitamin C levels rose substantially more in the vitamin C group than in the placebo group over the study period.

Conclusion: Vitamin C supplementation during the intensive phase of ATT was associated with significantly faster AFB sputum conversion in pulmonary TB patients. Given its low cost and mild side-effect profile, vitamin C may be a useful, inexpensive adjunct to standard TB treatment, though confirmation in larger, multi-centric trials is warranted.

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Introduction

Pulmonary tuberculosis (TB), caused by *Mycobacterium tuberculosis*, remains one of the leading infectious causes of morbidity and mortality worldwide. According to the WHO Global Tuberculosis Report 2025, an estimated 10.7 million people developed TB and 1.23 million died of the disease in 2024 globally, with India alone accounting for approximately one-quarter of the global

caseload despite a 21% decline in incidence since 2015.^[1] Patients with active TB often exhibit compromised nutritional status compared with healthy individuals, and undernutrition is both a risk factor for progression to active disease and a consequence of it.^[2] Nutrient deficiencies and inadequate nutrition can impair the host immune response required to combat *M. tuberculosis*. Vitamin C supplementation may help address these deficiencies by enhancing appetite and improving iron absorption, both of which support the body's defense against TB.

Vitamin C, or ascorbic acid, is well known for its antioxidant and immune-supporting properties. It is essential for collagen synthesis, wound healing, and maintenance of a robust immune system. In the context of TB management, vitamin C has been investigated for its potential to enhance the effectiveness of anti-TB drugs and to mitigate oxidative stress in affected tissues, through three principal mechanisms:

Antioxidant activity: Vitamin C neutralizes free radicals and reduces the oxidative stress that accompanies chronic TB-related inflammation, thereby supporting immune function.

Immune support: Vitamin C enhances the function of neutrophils, lymphocytes, and phagocytes, aiding effective clearance of *M. tuberculosis*. Notably, a vitamin C-induced Fenton reaction has been shown to render *M. tuberculosis* extraordinarily sensitive to killing.³ **Synergy with anti-TB drugs:** Vitamin C may enhance the bactericidal activity of key anti-TB drugs such as isoniazid and rifampicin,^{4,5} potentially accelerating sputum conversion.

Despite this biological plausibility, clinical evidence on vitamin C as an adjunct to standard ATT remains limited, and existing studies vary in design, sample size, and outcome definitions. This study was therefore undertaken to examine the effect of vitamin C supplementation, given alongside standard ATT, on the rate of AFB sputum conversion in patients with pulmonary TB during the intensive phase of treatment.

Objectives

Primary objective: To compare the rate of AFB sputum smear conversion between patients receiving vitamin C plus standard ATT and those receiving placebo plus standard ATT during the two-month intensive phase.

Secondary objective: To compare the change in serum vitamin C levels between the two groups over the same period.

Materials and Methods

Study Design and Setting

This was a randomized, parallel-group, placebo-controlled study conducted in the Department of Respiratory Medicine, Saraswathi Institute of Medical Sciences.

Study Population

Newly diagnosed, sputum-smear-positive pulmonary TB patients presenting to the department during the study period were screened for eligibility.

Inclusion Criteria

Patients with a positive sputum smear who had not previously received anti-tuberculosis treatment (ATT-naïve); aged 20–65 years; HIV-negative; without gastrointestinal or hepatic

disease; non-diabetic; not on immunosuppressive therapy; and not pregnant or breastfeeding.

Exclusion Criteria

Patients with known hypersensitivity to vitamin C, chronic kidney disease, a history of nephrolithiasis, or those unwilling/unable to provide informed consent were excluded. Patients who had previously received anti-tuberculosis treatment, were HIV-positive, had gastrointestinal or liver disease, diabetes mellitus, were receiving immunosuppressive drugs, or were pregnant or breastfeeding were excluded. Patients outside the age range of 20–65 years and those unwilling or unable to provide informed consent were also excluded.

Sample Size

A total of 80 eligible patients were enrolled and randomly allocated into two groups of 40 each.

Randomization and Blinding

Participants were randomly allocated in a 1:1 ratio to the vitamin C or placebo arm. Participants were randomly allocated in a 1:1 ratio to either the vitamin C plus standard anti-tuberculosis treatment group or the placebo plus standard anti-tuberculosis treatment group, with 40 participants in each group. The specific method of sequence generation, allocation concealment, and blinding was not documented in the available study details.

Intervention

Group A (n=40) received vitamin C supplementation (1000 mg/day, oral) in addition to standard ATT under the intensive-phase regimen. Group B (n=40) received an identical-appearing placebo in addition to standard ATT.

Outcome Assessment

The primary outcome was AFB sputum smear conversion (positive to negative), assessed by microscopy every two weeks for a total duration of two months. Serum vitamin C levels were measured as a secondary outcome.

Statistical Analysis

Descriptive statistics were used to summarize demographic characteristics. The chi-square test was used to compare categorical outcomes (AFB conversion rates) between the two groups. An independent-samples t-test was used to compare continuous outcomes (change in serum vitamin C levels) between groups. A 95% confidence interval was used throughout, with statistical significance set at $P < 0.05$.

Ethical Considerations

The study was conducted after obtaining approval from the Institutional Ethics Committee of Saraswati Institute of Medical Sciences. Written informed consent was obtained from all participants prior to enrolment, and the study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

Results

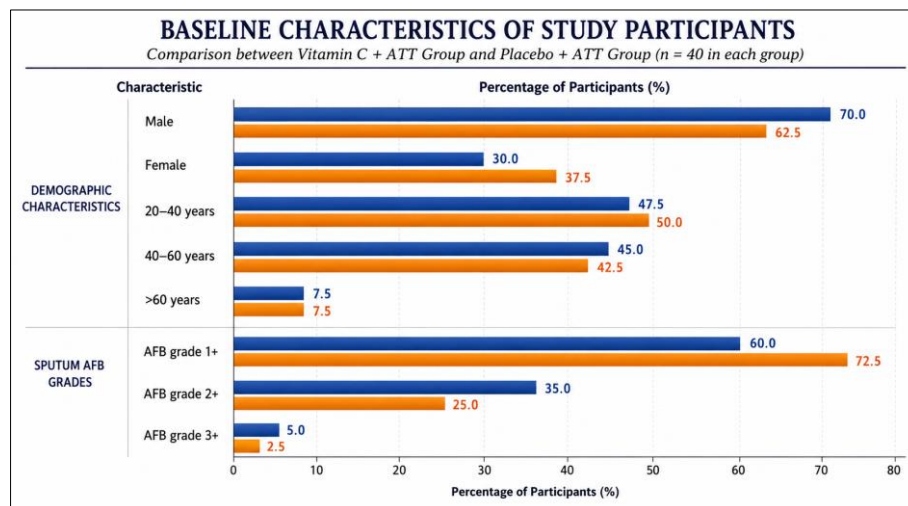
The demographic and baseline AFB grading characteristics of the two groups are presented in Table 1. No significant differences were observed between groups in sex, age distribution, or baseline AFB positivity grade.

Table 1: Demographic and Baseline Characteristics

Characteristic	Vitamin C + ATT (n=40)	Placebo + ATT (n=40)
Male	28 (70.0%)	25 (62.5%)
Female	12 (30.0%)	15 (37.5%)
20–40 years	19 (47.5%)	20 (50.0%)
40–60 years	18 (45.0%)	17 (42.5%)
>60 years	3 (7.5%)	3 (7.5%)
AFB grade 1+	24 (60.0%)	29 (72.5%)
AFB grade 2+	14 (35.0%)	10 (25.0%)
AFB grade 3+	2 (5.0%)	1 (2.5%)

AFB sputum conversion at one and two months is summarized in Table 2. All 40 patients (100%) in the vitamin C group converted within the first month, compared with 8 of 40 (20%) in the placebo group; the remaining 32 placebo

patients (80%) converted during the second month. The difference in conversion rate between groups was statistically significant ($P<0.05$).

**Fig 1:** Baseline Characteristics of Study Participants**Table 2:** AFB Sputum Conversion at One and Two Months

Group	1st Month n (%)	2nd Month n (%)	Total n (%)
Vitamin C + ATT	40 (100.0%)	0 (0.0%)	40 (100.0%)
Placebo + ATT	8 (20.0%)	32 (80.0%)	40 (100.0%)
Combined (n=80)	48 (60.0%)	32 (40.0%)	80 (100.0%)

Table 3 presents the same conversion outcomes broken down by two-week interval. In the vitamin C group, conversion was concentrated in the first four weeks (62.5% by week 2, a

cumulative 82.5% by week 4), whereas in the placebo group conversion occurred predominantly later (62.5% at week 6 alone).

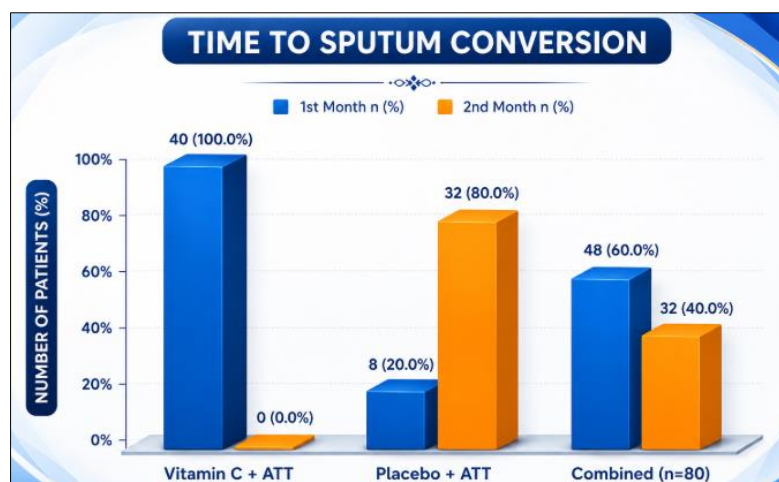
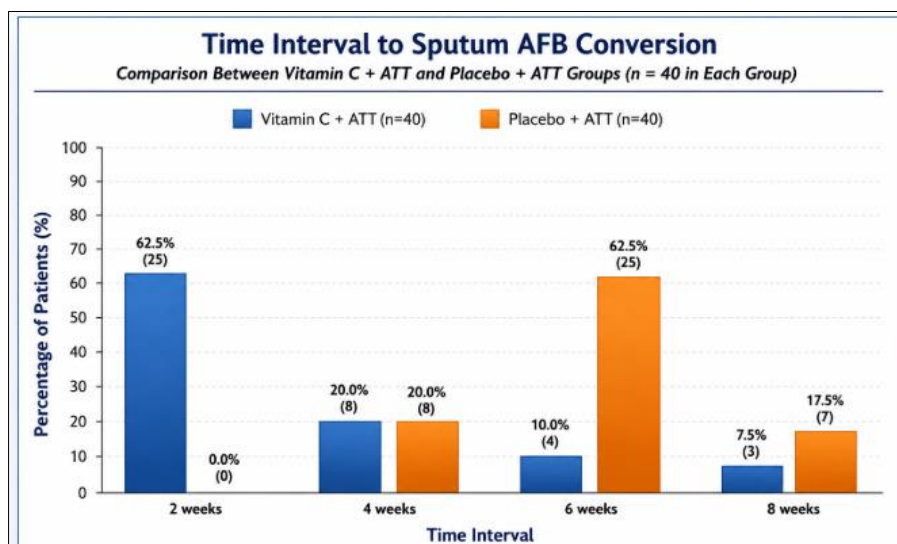
**Fig 2:** Time to Sputum AFB Conversion.docx

Table 3: AFB Sputum Conversion by Two-Week Interval

Interval	Vitamin C + ATT n (%)	Placebo + ATT n (%)
2 weeks	25 (62.5%)	0 (0.0%)
4 weeks	8 (20.0%)	8 (20.0%)
6 weeks	4 (10.0%)	25 (62.5%)
8 weeks	3 (7.5%)	7 (17.5%)
Total	40 (100.0%)	40 (100.0%)

Serum vitamin C levels increased significantly in both groups over the two-month period ($P < 0.05$), but the increase was substantially greater in the vitamin C group (mean increase

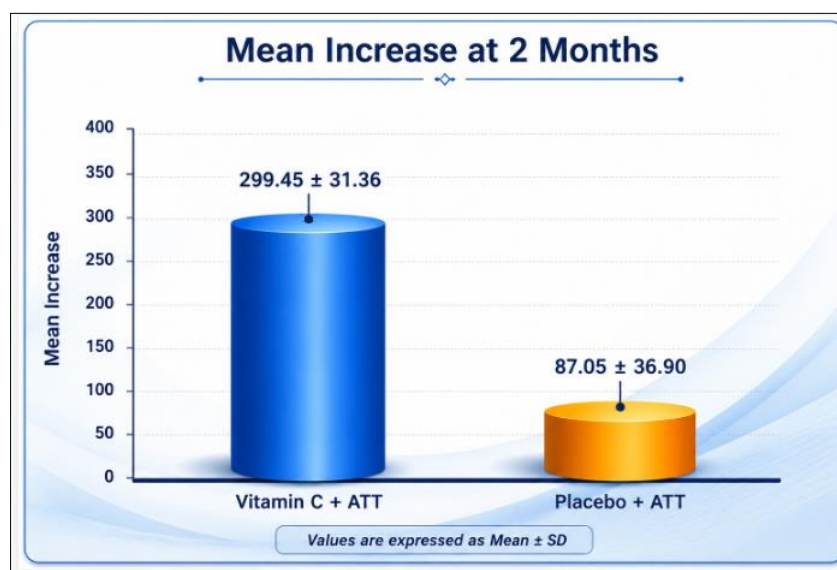
299.45 ± 31.36) compared with the placebo group (mean increase 87.05 ± 36.90).

**Fig 3:** Time Interval to Sputum AFB Conversion in Vitamin C + ATT and Placebo + ATT Groups**Table 4:** Mean Increase in Serum Vitamin C Level at Two Months

Group	Mean Increase at 2 months
Vitamin C + ATT	299.45 ± 31.36
Placebo + ATT	87.05 ± 36.90

At two months, the mean increase in serum vitamin C level was higher in the Vitamin C + ATT group (299.45 ± 31.36) compared with the Placebo + ATT group (87.05 ± 36.90). The mean increase was approximately 3.4-fold greater in the

Vitamin C + ATT group, indicating a substantially greater improvement in serum vitamin C levels with vitamin C supplementation along with antitubercular therapy.

**Fig 4:** Mean Increase in Serum Vitamin C Levels at 2 Months

Discussion

In this study, the majority of participants were in the 20–40-year age group (48.75% of the total sample), with a higher proportion of males in both the vitamin C group (70%) and the placebo group (62.5%), consistent with the demographic pattern typically reported in TB cohorts.

AFB sputum conversion occurred significantly earlier in the vitamin C group than in the placebo group. By two weeks, 62.5% of patients receiving vitamin C had converted, compared with none in the placebo group. This gap persisted throughout the study, with a statistically significant difference in overall conversion rates by the end of the eight-week period ($P < 0.05$).

These findings are consistent with the study by Susanto *et al.* [6], conducted in Indonesia, which similarly reported higher and earlier sputum culture conversion among rifampicin-susceptible TB patients receiving vitamin C compared with controls. Bozonet *et al.* [7] demonstrated that vitamin C supplementation through vitamin C-rich kiwifruit increased plasma vitamin C levels from a mean of 26 $\mu\text{mol/L}$ to over 70 $\mu\text{mol/L}$ within one week, with improved neutrophil chemotaxis and increased oxidant generation, supporting a plausible immunological mechanism for the faster sputum conversion observed in the present study.

Vilchèze *et al.* [3] demonstrated that vitamin C can promote killing of *Mycobacterium tuberculosis* through a Fenton reaction, while Vilchèze *et al.* [4] subsequently showed that vitamin C potentiated the activity of first-line antitubercular drugs, including isoniazid and rifampin, in a murine model. Further, Sikri *et al.* [5] reported that vitamin C induces multifaceted remodeling of *M. tuberculosis* subpopulations and enhances their susceptibility to combination antitubercular therapy. These findings provide a biological rationale for the enhanced treatment response observed in the vitamin C group.

Vitamin C serves as a cofactor for hydroxylation reactions, contributes to nitric oxide and heparan sulfate metabolism, and helps maintain redox balance during mitochondrial respiration. TB patients frequently show reduced levels of key antioxidants, including glutathione, ascorbic acid, and α -tocopherol, due to both inadequate dietary intake and increased free-radical production during the immune response to *M. tuberculosis*. Vijayamalini and Manoharan [8] reported alterations in lipid peroxidation and antioxidant levels, including vitamins C and E and reduced glutathione, among patients with pulmonary tuberculosis. This oxidative burden may worsen the underlying disease process and potentially delay recovery.

AFB sputum conversion is a key marker of treatment response in TB, and nutritional status at diagnosis is one of several factors known to influence conversion. Chang *et al.* [9] demonstrated alterations in gut hormones and appetite regulation in patients with pulmonary TB, including appetite suppression and cachexia, which may reduce nutrient intake and compound caloric and protein deficits. This provides a plausible pathway through which nutritional supplementation, including vitamin C, may support treatment response.

Reported side effects of vitamin C supplementation are generally mild and may include heartburn, nausea, and vomiting.

Given the low cost of vitamin C (approximately ₹0.50–1.00 per capsule), its inclusion in TB treatment regimens could represent a cost-effective adjunct, with the potential public-

health benefit of reducing the duration of infectiousness and, consequently, community transmission.

Overall, these findings suggest that vitamin C supplementation may have potential as an adjunct to standard antitubercular therapy. However, larger, adequately powered randomized controlled trials are needed to confirm its efficacy, establish optimal dosing and duration, and determine its potential role in routine TB treatment protocols before broader clinical or health-policy recommendations can be made.

Strengths and Limitations

This study's principal strength lies in its randomized, placebo-controlled, parallel-group design with a well-defined intensive-phase follow-up schedule, including fortnightly AFB sputum examination over two months, allowing direct comparison of sputum conversion between the two groups. However, several limitations should be noted. First, this was a single-centre study, which may limit generalizability. Second, there was a relatively small number of patients with AFB 3+ smears compared with those graded 1+ or 2+, limiting subgroup analysis at higher bacillary loads. Third, the specific method of randomization and blinding was not documented in the available study details, which may affect the interpretation of the observed effect size. Larger, multicentric studies with greater representation of AFB 3+ cases and a more systematic assessment of adverse effects are recommended to confirm these findings.

Conclusion

Vitamin C supplementation during the intensive phase of anti-tuberculosis treatment was associated with significantly faster conversion of AFB sputum smears in patients with pulmonary tuberculosis. Given its low cost and favorable safety profile, vitamin C merits consideration as an adjunct to standard TB treatment, pending confirmation in larger, adequately powered trials.

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Author Contributions

D.B.: Study conception, data collection, and manuscript drafting. S.G.: Study supervision, critical revision of the manuscript, and final approval. R.R.: Data collection and statistical analysis. V.G.: Data collection and literature review. All authors read and approved the final manuscript.

Ethical Approval

The study was conducted after obtaining approval from the Institutional Ethics Committee of Saraswathi Institute of Medical Sciences. Written informed consent was obtained from all participants prior to enrolment. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

Conflict of Interest: "The authors declare no conflict of interest."

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Data Availability

The data supporting the findings of this study are available from the corresponding author on reasonable request.

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