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Research Article

Effects of Antioxidant Nutraceutical and Functional Foods on Protein Profile of Tuberculosis Patients in Jos Metropolitan, Nigeria

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Abstract

Introduction: Tuberculosis (TB) is a significant global cause of morbidity and mortality, especially when combined with the HIV pandemic. Nutritional deficiencies have long been linked to a higher risk of contracting infectious diseases. TB and HIV infections frequently co-occur and can cause extreme wasting. The study's objective was to evaluate the possible effect of antioxidant nutraceuticals and functional foods on the protein profile of tuberculosis patients.

Methods: Subjects were given a ready-to-use form of processed soybean seeds (Glycine max.) and Date fruits for six months. Blood samples were collected at baseline, midline (3 months into the intervention), and endline (6 months into the intervention) to test for serum total protein, albumin, and C-reactive protein.

Results: The findings indicated a gradual rise in serum total proteins and albumin levels, along with a gradual decline in C-reactive protein levels. Almost all intervention groups displayed a statistically significant difference from the baseline to the midline and endine ($p < 0.05$).

Conclusion: In conclusion, after six months of consuming functional foods and antioxidant nutraceuticals, most subjects showed a notable improvement in their serum protein profile compared to both the control group and their baseline values.

Keywords: Antioxidant Nutraceutical; Foods; Protein; Tuberculosis Patients

Introduction

The End TB Strategy seeks to cut tuberculosis (TB) incidence and mortality by 80% and 90%, respectively, by 2030 (World Health Organization [WHO], 2020a). However, this strategy is falling short of its goals. Despite a target of 20% fewer TB cases between 2015 and 2020, TB cases only decreased by 11% [1]. Furthermore, despite a global decline in TB incidence and mortality, TB mortality actually increased in recent years, going from 1.4 million to 1.5 million deaths, marking the first increase in ten years (WHO, 2020b). People living with HIV (PLHIV) and other high-risk groups bear a disproportionately heavy disease burden [2].

Significant advancements have been made in the field of TB care recently, but direct costs associated with diagnosis and treatment still account for the majority of investments (World Health Organization [3]. Despite the fact that these are important investments in lowering TB-related mortality and morbidity worldwide, concentrating research funding on testing and treatment advancements runs the risk of ignoring undernutrition, one of the primary factors accelerating the TB pandemic [3].

In most of the underdeveloped parts of the world, malnutrition and tuberculosis are serious issues, and these two issues often interact with one another (World Health Organization [4]. The rates of tuberculosis mortality in a community's various socioeconomic groups typically exhibit inverse relationships with their economic status [4].

Similarly, patients with active tuberculosis have significantly worse nutritional status than healthy controls [5]. Notably, there is compelling evidence that suggests there is an inverse relationship between serum albumin levels and TB patient mortality, indicating that these levels, a key nutritional status indicator, may be relevant to TB monitoring [6]. Deficit in cellular immunity, which can be influenced by nutritional status, is another element that may adversely affect the effectiveness of anti-tubercular treatment [7].

The immune system is affected by nutritional imbalances, both deficiencies and excesses [8]. In the past, studies have primarily focused on the link between malnutrition and immunity in developing countries [9]. The extent of immune system impairment not only depends on the severity of malnutrition but also on other factors, such as infections [10]. Reduced immune competence has been associated with deficiencies in protein, certain amino acids, and vitamins [8].

Dates are consumed fresh or in the dried form and are categorized as intermediate foods [11]. In comparison to other fruits and vegetables, dates are regarded as functional foods and have higher amounts of proteins than most fruits [12]. Studies have shown that consuming dates may have potential health benefits, such as reducing inflammation and improving brain function [13,14]. Additionally, dates are a great source of natural sugars and can be used as a healthier alternative to processed sugars in baking and cooking [15].

Materials and Methods

Selection and collection of antioxidant nutraceuticals and functional foods

The study utilized LYCOSET, an antioxidant nutraceutical produced by Akums Drugs and Pharmaceuticals Ltd India and marketed in Nigeria by Pharma Ethics Ltd [16]. Additionally, the West African and Nigerian food composition tables [17] were consulted to identify fruits and legumes that were both rich in macronutrients and minerals, affordable, and had functional properties. The study selected Date fruit (Phoenix dactylifera) and Soya beans (Glycine max) as the functional foods to be processed into a ready-to-use form [16].

Processing of ready-to-use foods

- **Date fruit:** The dates were carefully cleaned and sorted to ensure that no unwanted material was present. Date fruits that were of poor quality or had been eaten by insects were removed. Next, the dates were deseeded using a hammer mill, then cleaned once more, washed, and drained using a mesh before being air-dried. Finally, the processed dates were weighed and packaged into 50g sachets [16].
- **Soybeans Mix:** The soybeans underwent cleaning, washing, and peeling. Then, they were partially boiled, placed in a mesh to drain, shade-dried, partially roasted, properly weighed, mixed, and finally milled into a uniform, fine powder [18]. The soy flour was sieved through a locally made fine mesh and kept in bags [16].

Study design

The study utilized a quasi-experimental design and recruited participants from five hospitals located in Plateau State, namely Plateau Specialist Hospital Jos, Faith Alive Foundation, Our Lady of Apostles Hospital, APIN-JUTH, and Bingham University Teaching Hospital [19]. To ensure proportional representation, systematic random sampling was employed, with Probability Proportional to Size (PPS) used to allocate the number of participants in each site [19]. A total of 161 consenting adults (aged 18 to 65 years) attending TB clinics were enrolled and categorized into four groups labeled A-D based on the different interventions (A= Antioxidant Neutraceutical, B=Date fruit, C=Soya Mix, D = Control) [19]. Over a period of six months, the participants received weekly interventions, and regular follow-up assessments and testing were conducted on all groups [19].

Blood sample collection

Sterile syringes were used to collect 2ml of blood through venepuncture with minimal stasis [20]. The collected blood was transferred into chemically cleaned, dried, and labeled containers. The samples were allowed to clot, then retracted and centrifuged at 3,000 rpm for 5 minutes (Smith., *et al*., 2010). The serum was then carefully transferred into clean and well-labeled vials for further analysis (Smith., *et al*., 2010). Blood samples were collected at three stages: baseline (0 months), midline (3 months), and end line (6 months) [20].

Serum protein analysis

The concentration of Total Serum Proteins (TSP) was determined using the modified Biuret method [21]. Similarly, the concentration of Serum Albumin (SA) was determined using the method developed by Doumas., *et al*. [22].

Statistical analysis

Statistical analysis of the data involved descriptive analysis, as well as bivariate and multivariate analysis using techniques such as student t-test and ANOVA (Johnson., *et al*., 2018). The software used for this analysis was SPSS version 18 [23]. Significance was determined based on P-values < 0.05 [23].

Results

Acceptability and sensory evaluation analysis of functional foods

Figure 1 presents the results of sensory evaluation using a 9-point hedonic scale for the processed foods. The sensory qualities of Date fruit and Soya beans were well accepted, with ratings of 8 and 8.8, respectively. The sensory panellists gave a score of 7.8 for the color of Date fruit and 9 for Soya beans flour among the processed food samples. The color of Soya bean flour was highly liked, with a score of 9. The taste of Dates fruit and Soya beans received scores of 9 and 8, respectively. The mouth feel rating of the samples was 8.3 for Soya beans and 7.9 for Date fruit because the latter had to be chewed. Overall, the TB patients found processed functional foods to be highly acceptable, allowing for their administration.

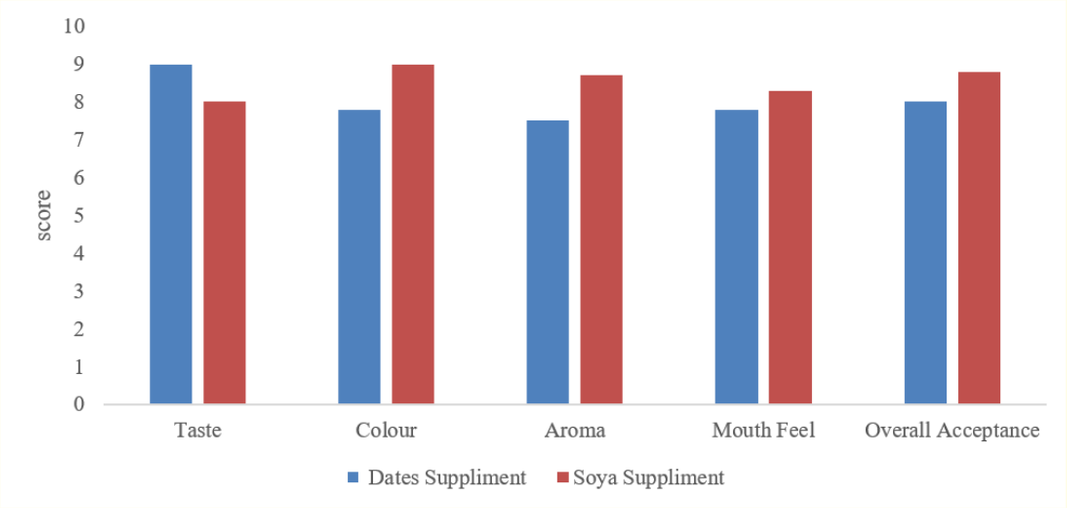

Figure 1: Sensory Evaluation of Functional Foods using Hedionic scale.
Hedionic scale: [1=dislike extremely, 2=dislike very much, 3=dislike moderately, 4=dislike slightly, 5=neither like nor dislike, 6=like slightly, 7=like moderately, 8=like very much, 9=like extremely]

Number of respondents per health facility

In figure 2, the number of clients recruited per hospital is shown using a proportionate-to-size sampling method. Faith Alive Foundation Hospital recruited the highest number of clients with 58 subjects, followed by Plateau Specialist Hospital with 42 recruited. Bingham University Teaching Hospital and Jos University Teaching Hospital recruited 36 and 15 persons respectively, while the least number of clients, 11 persons, were recruited from Our Lady of Apostles Hospital. This data is in agreement with the unpublished 2018 Plateau State data on Tuberculosis and indicates that these hospitals serve as referral centres, providing a picture of the tuberculosis burden in Plateau.

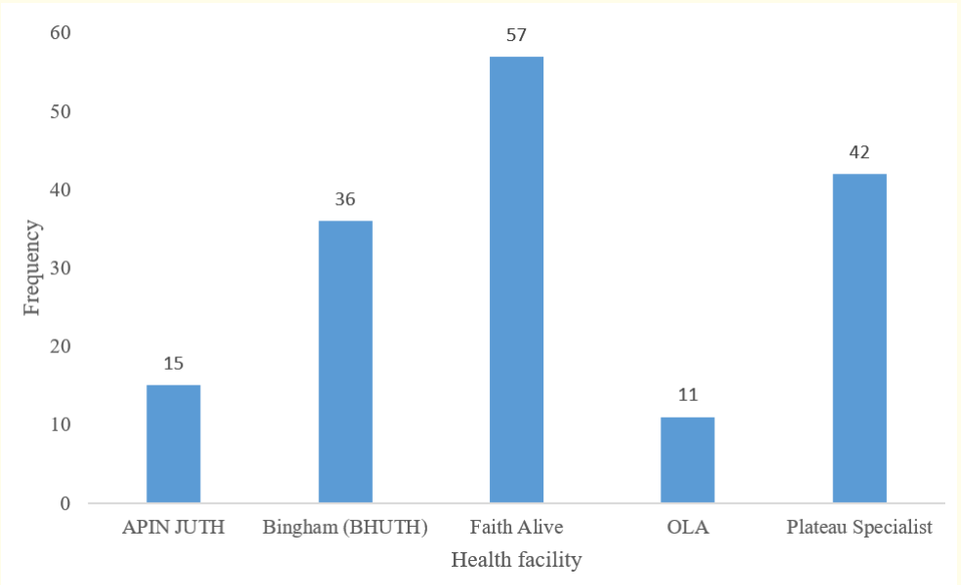

Figure 2: Number of Respondents Per Health Facility.

Socio-demographic of human subjects

Table 1, shows the social and demographic characteristics of the individuals who participated in the study, categorized by gender, occupation, and marital status. Of those who volunteered, males were 69.6%. On average, the participants were 36.4 years old with a standard deviation of 10.7 years. The youthful productive age group made up 58% of the participants, and 47.8% of them were single. The Married represented 42.2%, while widowed and divorced individuals accounted for only 5% each. Among the participants, 28.7% were low-income artisans, 23.6% did not have regular jobs, and 18% were farmers.

Variable	Group	Frequency (n = 161)	Percentage (%)
Age (Years)	15-24	21	13.0
Mean ± SD	25-34	50	31.1
	35-44	58	36.0
(36.4 ± 10.7)	45-54	24	14.9
	55-64	5	3.1
	65 +	3	1.9
Gender	Male	112	69.6
	Female	49	30.4

Table 1: Socio-demographic Characteristics of the Human Subjects.

Serum proteins

The following tables, namely 1a, 1b, and 1c, display the results of the total protein (TP), Albumin (Alb), and C-reactive protein (CRP). The findings in tables 1a and 1b indicate that the mean serum TP and Alb were mostly below their respective reference ranges (62 - 80 mg/dl and 35 - 55 mg/dl, respectively) for all study groups at the start, but there was a gradual increase in the mean TP at midline and endline of groups A, B (HIV positive), and C (irrespective of HIV). On the other hand, Group D had almost identical mean values for total protein at baseline, midline, and endline. Nevertheless, there was a statistically significant difference ($P < 0.05$) when the baseline Alb was compared with the midline and endline outcomes of all groups except group A (HIV positive).

In table 1c, it can be seen that the CRP levels of all study groups were higher than the normal standard reference range of 1 - 15 mg/ml at baseline. However, study groups A, B, C, and D had a positive decrease in this inflammatory protein, which had a statistically significant difference ($p < 0.05$) when compared to the baseline results. In addition, Group A and D (HIV Positive) also showed a positive decrease in the serum level of CRP, although it was not statistically significant ($p > 0.05$).

Group (Intervention)	HIV Status	Baseline (mg/dl)	Midline (mg/dl)	Endline (mg/dl)	F-test	P-value
		M ± SD	M ± SD	M ± SD		
Group A (AN)	Positive	59.9 ± 12.9	62.3 ± 8.9	71.9 ± 5.5	5.384*	0.009
	Negative	57.5 ± 6.7	62.5 ± 10.7	65.3 ± 9.0	4.494*	0.015
Group B (Date)	Positive	52.5 ± 12.1	65.8 ± 12.4	70.7 ± 13.5	10.711*	0.000
	Negative	69.6 ± 8.7	73.9 ± 9.5	67.7 ± 8.5	1.533	0.226
Group C (Soya)	Positive	54.8 ± 7.9	76.8 ± 5.3	69.8 ±8.5	24.951*	0.000
	Negative	61.9 ± 11.0	75.2 ± 10.9	71.6 ± 11.4	10.930*	0.000
Group D (Control)	Positive	70.50 ± 5.2	68.2 ± 6.1	69.3 ± 3.8	0.623	0.543
	Negative	68.2 ± 7.7	66.0 ± 6.9	65.4 ± 6.4	0.948	0.393

Table 1a: Serum Concentrations of Total Protein (TP) of Subjects.

Reference value: Total protein (66-88g/l = Normal range). Group A (AN: Antioxidant Neutriceutical), Group B (DF: Dates Fruits), Group C (SF: Soya beans mix) and Group D (C: Control with no intervention). n: 161; *p < 0.05 was considered statistically significant. Key: TOTPR = Total protein; M=mean, and SD= Standard Deviation.

Group (Intervention)	HIV Status	Baseline Alb (mg/dl)	Midline Alb (mg/dl)	EndlineAlb (mg/dl)	F-test	P-value
		M ± SD	M ± SD	M ± SD		
Group A (AN)	Positive	31.7 ± 6.2	48.3 ± 3.9	45.2 ± 5.3	1.289	0.287
	Negative	30.3 ± 3.5	47.9 ± 4.3	49.1 ± 4.4	16.083*	0.000
Group B (Date)	Positive	35.3 ± 11.0	46.1 ± 3.8	42.0 ± 13.0	6.525*	0.003
	Negative	32.3 ± 4.2	43.0 ± 2.4	43.2 ± 13.7	11.307*	0.000
Group C (Soya)	Positive	34.1 ± 4.8	44.0 ± 5.6	44.7 ±2.0	28.380*	0.000
	Negative	31.7 ± 6.2	45.2 ± 3.6	47.2 ± 4.7	78.222*	0.000
Group D (Control)	Positive	31.0 ± 0.9	47.8 ± 4.7	46.5 ± 10.3	24.947	0.060
	Negative	31.2 ± 3.4	46.4 ± 4.1	44.7 ± 2.9	129.655	0.130

Table 1b: Serum Albumin (Alb)of Subjects.

Reference value: Albumin (30-53g/l=Normal range). Group A (AN=Antioxidant Neutriceutical), Group B (DF Dates fruits), Group C (SF=Soya beans flour) and Group D (C=Control with no intervention). n: 161; *p < 0.05 was considered statistically significant. M=mean, and SD Standard Deviation.

Group (Intervention)	HIV Status	Baseline (mg/ml)	Midline (mg/ml)	Midline (mg/ml)	F-test	P-value
		M ± SD	M ± SD	M ± SD		
Group A (AN)	Positive	17.5 ± 3.4	10.8 ± 3.4	12.0 ± 13.0	3.226	0.051
	Negative	15.9 ± 1.6	14.0 ± 2.9	11.9 ± 12.5	1.919	0.155
Group B (Date)	Positive	29.0 ± 1.3	19.0 ± 5.6	11.6 ± 15.8	17.674	0.000*
	Negative	29.0 ± 2.1	19.3 ± 5.6	6.2 ± 4.3	16.052	0.000*
Group C (Soya)	Positive	17.5 ± 3.4	10.8 ± 3.9	12.2 ± 0.8	101.076	0.000*
	Negative	15.9 ± 1.6	14.0 ± 2.9	28.5 ± 2.3	283.124	0.000*
Group D (Control)	Positive	17.5 ± 3.3	14.8 ± 3.4	15.5 ± 19.1	0.169	0.845
	Negative	18.6 ± 2.1	16.0 ± 5.7	6.9 ± 3.4	44.384	0.340

Table 1c: Serum C - reactive protein (CRP) of Subjects.

Reference value: CRP (1-15mg/ml= Normal range). Group A (AN=Antioxidant Neutriceutical), Group B (DF=Dates fruits), Group C (SF= Soya beans flour) and Group D (C=Control with no intervention). n: 161; *p < 0.05 was considered statistically signifit. M=mean, and SD=Standard Deviation.

Discussion

This study aims to determine the relationship between nutrition and tuberculosis infection and clinical outcomes by examining the effect of consuming antioxidant nutraceuticals and functional foods on TB patients [24]. The study involved adult Nigerians who were newly diagnosed with TB and a control group of patients who did not receive any nutritional intervention [24]. The participants' ages ranged from 18 to 65 years old [24]. The majority of affected individuals were within the 20 to 40 age group, which is consistent with previous reports from developing countries [24]. In contrast, developed countries have reported that the majority of infected individuals are over 50 years old [24].

This study demonstrated that providing nutritional supplements can reduce the incidence of TB and enhance treatment effectiveness. Like a study conducted in Brazil revealed that patients who received a monthly food basket in addition to the standard treatment regimen achieved a cure rate of 87.1%, whereas those who did not receive food baskets had a cure rate of only 69.7% [25]. Similarly, a study conducted in India showed that participants who were provided with a monthly supply of rice and lentils had a success rate of 91%, whereas those who did not receive the nutritional intervention had a success rate of only 79% ($p < 0.001$) [26].

Patients with TB have been found to experience hypoalbuminemia, which is characterized by elevated gammaglobulins and a simultaneous decrease in albumin. This change in serum protein levels has been linked to TB in previous studies [27-31]. One possible explanation for hypoalbuminemia is poor nutritional status. This study indicates that hypoalbuminemia increases the risk of treatment failure significantly. This finding is consistent with a previous study from Indonesia, which found that low serum albumin levels at the time of hospital admission were an independent predictor of in-hospital death among TB patients [32]. In South Korea, low serum albumin levels have also been associated with treatment failure in patients with extensively drug-resistant TB [33]. These results suggest that serum albumin level is a sensitive indicator of a patient's nutritional status and immune response to TB, which in turn can impact the effectiveness of anti-TB treatment.

Our study also found that low serum albumin levels may promote TB progression by impairing host immunity against MTB. Animal experiments have shown that hypoalbuminemia can alter the absolute and relative numbers of total T-lymphocytes and various immune system cell subpopulations [34], which can weaken the immune response against TB [35]. Therefore, serum albumin level may be a useful indicator during early anti-TB treatment to identify patients who are at high risk for treatment failure due to poor immune status. Interestingly, our study found that successful treatment outcomes were associated with increased serum albumin levels in TB patients. This may be because reduced serum albumin levels are generally associated with inflammatory conditions [36] which are common in active TB cases with a higher load of tubercle bacilli at pulmonary sites [37].

Studies have shown that the CRP levels increase in response to IL-6 mediated pyogenic infections like active TB [38]. It is highly sensitive to TB, and HIV status does not affect the TB-related increases in its levels [38,39]. The baseline levels of C-reactive protein were higher, but they decreased in all intervention groups at midline and endline, which is consistent with other studies that suggest tuberculosis can cause an increase in its levels [40]. CRP is considered an acute phase reactant and is found in the area between the beta and gamma components, according to Jacoby and Cole [41].

The consumption of functional foods, particularly date palms, has been shown to strongly reduce the concentration of C-reactive protein (CRP) [42]. Date palms are known to contribute significantly to the neutralization of free radicals, suppressing the development

and progression of various diseases [43]. Previous investigations have found that palm has a potent ability to suppress free radicals, and aqueous extracts of dates have antioxidant, antimicrobial, and anti-mutagenic activity [42,43]. Dates are also a good source of antioxidants, with the highest concentration of polyphenols among dried fruits [43]. The antioxidant activity of phenolic compounds is a result of their redox properties, which can play an important role in absorbing and neutralizing free radicals [43]. Phytochemicals have significant antioxidant capacities and can help in lowering the prevalence and mortality rates of diseases [42].

The human body uses inflammation as a defense mechanism against various factors such as infection, burns, toxic chemicals, allergens, and other stimuli [44]. However, an imbalanced inflammatory process can contribute to the development and progression of various diseases. Transcription factors LOX and NF-kB play significant roles in inflammation, cancer, diabetes, and other diseases. Proper regulation of transcription factors is crucial in preventing disease. Inhibitors of transcription factors have proven effective in preventing their actions, but current inhibitors have adverse effects and are expensive [45].

Natural products, including phenolics and flavonoids found in plants, have anti-inflammatory properties and can suppress NF-kB [45]. Dates are particularly effective in reducing inflammation. Studies have shown that Ajwa dates, in particular, contain ethyl acetate, methanolic, and water extracts that inhibit lipid peroxidation and cyclooxygenase enzymes COX-1 and COX2 [46]. Phoenix dactylifera pollen has also shown potential protective effects through modulation of cytokine expressions [47]. Additionally, the methanolic extract of the edible portion of the date fruit has been found to reduce foot swelling and plasma fibrinogen [46], while date leaves are a good source of natural antioxidant and anti-inflammatory drugs [48].

Conclusions

According to this study, individuals with TB show a significant decrease in almost all measured parameters. However, after a six-month intervention with functional foods, their clinical and nutritional outcomes noticeably improved.

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