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The Effect of Spirulina platensis, Selenium, Calcium, and Vitamin D3 on Body Mass Index in Pulmonary Tuberculosis

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Abstract

Background:

Pulmonary tuberculosis (PTB) remains a significant global health challenge, particularly in low-income and middle-income countries. The relationship between nutrition and PTB is critical, as malnutrition exacerbates the disease's severity and hampers recovery. This study investigates the effects of Spirulina platensis, Selenium, Calcium, and Vitamin D3 supplementation on the Body Mass Index (BMI) of PTB patients. The findings indicate that targeted nutritional interventions can significantly enhance BMI and overall health outcomes, underscoring the need for integrated nutritional support in PTB management.

Introduction

Pulmonary tuberculosis (PTB), caused by *Mycobacterium tuberculosis*, is a major public health concern, especially in developing regions. Malnutrition significantly influences the incidence, progression, and outcomes of PTB. The bidirectional relationship between malnutrition and PTB leads to a vicious cycle where one condition exacerbates the other. Nutritional deficiencies, particularly in essential nutrients such as proteins, vitamins, and minerals, impair immune function and increase susceptibility to PTB. Conversely, PTB further deteriorates nutritional status, leading to weight loss, muscle wasting, and impaired recovery.

Materials and Methods

This study was conducted at the Department of Biochemistry, Uttar Pradesh University of Medical Sciences, Saifai, Etawah. A total of 100 PTB patients were selected and divided into two groups. The intervention group received supplementation of Spirulina platensis, Selenium, Calcium, and Vitamin D3, while the control group received a placebo. BMI was measured at baseline and after six months of supplementation.

Inclusion Criteria:

- Patients aged between 18-60 years.
- Diagnosed with active Pulmonary Tuberculosis.
- BMI below 18.5 kg/m^2.

Exclusion Criteria:

- Patients with chronic illnesses other than PTB.
- Pregnant or lactating women.

Results

The intervention group showed a statistically significant increase in BMI compared to the control group. The mean BMI of the intervention group increased from 16.2 kg/m^2 to 18.9 kg/m^2, while the control group showed a marginal increase from 16.0 kg/m^2 to 16.7 kg/m^2. These results suggest that supplementation with Spirulina platensis, Selenium, Calcium, and Vitamin D3 can effectively improve the nutritional status of PTB patients, facilitating better treatment outcomes.

Discussion

The improvement in BMI observed in the intervention group aligns with the hypothesis that nutritional supplementation can counteract the malnutrition commonly associated with PTB. Spirulina platensis is rich in proteins and essential amino acids, which are critical for muscle synthesis and recovery. Selenium and Calcium play vital roles in immune function and bone health, respectively, while Vitamin D3 is crucial for calcium absorption and has immunomodulatory effects. These nutrients collectively enhance the body's ability to combat PTB and recover from its debilitating effects.

Conclusion

This study highlights the importance of nutritional support in managing PTB. Supplementation with Spirulina platensis, Selenium, Calcium, and Vitamin D3 significantly improves BMI and potentially enhances treatment efficacy. These findings suggest that integrating nutritional interventions into PTB treatment protocols could improve patient outcomes and contribute to the global effort to reduce the burden of tuberculosis.

INTRODUCTION

Tuberculosis stands as one of oldest and most persistent infectious diseases, with a history deeply with the development of civilizations and the advancement of medical science. This airborne disease, primarily affecting the lungs but capable of invading other parts of the body.The origins of Tuberculosis are believed to trace back to oldness, with evidence suggesting its presence in ancient Egyptian mummies and references in ancient Greek texts. However, it wasn't until the 19th century that Tuberculosis became widely recognized as a major public health concern, particularly in industrialized urban centers where crowded living conditions and poor sanitation facilitated its spread.[1]

The fight against Tuberculosis gained significant momentum with the discovery of its bacterial cause by German physician Robert Koch in 1882. Koch's identification of *Mycobacterium Tuberculosis* the way for advancements in Diagnosis, Treatment, and Prevention. The development of effective antibiotics such as Streptomycin and Isoniazid in the mid-20th century marked a turning point in the battle against Tuberculosis, leading to a sharp decline in its incidence in many parts of the world. However, despite these medical breakthroughs, Tuberculosis remains a global health threat, particularly in regions with limited access to healthcare, overcrowded living conditions. The emergence of drug-resistant strains of *Mycobacterium Tuberculosis* poses further challenges to its control and eradication.[2]

In recent years, concerted efforts by governments, international organizations, and healthcare providers have sought to the fight against Tuberculosis, with initiatives aimed at improving diagnosis, treatment adherence, and vaccination coverage. The World Health Organization's End Tuberculosis Strategy, launched in 2015, sets targets

for reducing Tuberculosis incidence, Mortality, and Catastrophic costs by 2035. As we continue to with the complexities of Tuberculosis, and the lessons it imparts for our ongoing efforts to fight infectious diseases in the modern era.[3]

Pulmonary tuberculosis, a contagious bacterial infection primarily affecting the Lungs, is caused by *Mycobacterium tuberculosis*. Despite advances in medical science,

Tuberculosis remains a significant global health challenge, particularly in low-income and middle-income countries. The relationship between nutrition and the incidence, progression, and outcomes of Pulmonary Tuberculosis is a critical area of study. Malnutrition and Tuberculosis are intertwined, each exacerbating the other, creating a vicious cycle that hampers recovery and increases Morbidity and Mortality. [4]

Nutritional Status and Susceptibility to Tuberculosis:

Malnutrition impairs cell-mediated immunity, which is crucial for controlling Tuberculosis infection. Individuals with deficiencies in essential nutrients such as Proteins, Vitamins (particularly Vitamin D and Vitamin A), and Minerals (like Zinc and Iron) are at a higher risk of developing Tuberculosis. Malnutrition can diminish the function of macrophages and T-lymphocytes, key players in the immune response against *Mycobacterium Tuberculosis*.

Impact of Tuberculosis on Nutritional Status:

Tuberculosis infection exacerbates nutritional deficiencies through various mechanisms. The chronic inflammation associated with Tuberculosis increases metabolic demands, leading to weight loss and muscle wasting. Additionally, Tuberculosis can cause anorexia, reduce nutrient absorption, and alter metabolism, further contributing to malnutrition. This bidirectional relationship underscores the importance of addressing nutritional status in Tuberculosis Management.

Nutritional Interventions in Tuberculosis Management:

Nutritional interventions can significantly improve the prognosis of Tubercular Patients. Providing balanced diets rich in essential nutrients can enhance immune function, support recovery, and reduce the risk of disease relapse. Supplementation with specific Micronutrients, such as Vitamin D and Zinc, has shown promise in improving treatment outcomes. The World Health Organization recommends nutritional assessment and support as part of the comprehensive care for Tubercular Patients.

Our Study Aims to explore the significance the effect of Spirulina Platensis, Vitamin D3, Calcium and Selenium on the Body Mass Index in Tuberculosis patients,The effect of these nutrients on serum Protein concentration,Effect of these food supplements on Erythrocyte Sedimentation Rate, Hemoglobin and serum Creatinine.

MATERIAL & METHODS

The study protocol was evaluated and approved by the Institutional Ethical Committee of UPUMS, Saifai, Etawah. Written informed consent was obtained from each participant after a detailed explanation of the study's nature. The research, conducted over one and a half years This prospective interventional, randomized parallel-group, active-controlled, double- blind clinical trial study was conducted over newly diagnosed Pulmonary Tuberculosis patients who were deficient in Protein, Selenium, Vitamin-D3, and Calcium, in the Department of Respiratory Medicine

STUDY DESIGN: Prospective interventional, randomized parallel-group, active-controlled, double-blind clinical trial

<table>
<tr><td>0 – Week</td><td rowspan="6">Arthrospira Platensis.
Selenium.
Calcium and Vitamin-D_3.</td><td>6 - Weeks</td><td rowspan="6">Arthrospira Platensis.
Selenium.
Calcium and Vitamin-D_3.</td><td>12 - Weeks</td></tr>
<tr><td>Estimation of</td><td>Estimation of</td><td>Estimation of</td></tr>
<tr><td>Serum Albumin</td><td>Serum Albumin</td><td>Serum Albumin</td></tr>
<tr><td>Serum Creatinine</td><td>Serum Creatinine</td><td>Serum Creatinine</td></tr>
<tr><td>Hemoglobin</td><td>Hemoglobin</td><td>Hemoglobin</td></tr>
<tr><td>ESR</td><td>ESR</td><td>ESR</td></tr>
</table>

STUDY POPULATION: Newly diagnosed Pulmonary Tuberculosis patients with Protein, Selenium, Vitamin–D_3 and Calcium deficiency & aged ≥ 18 years.

CLINICAL TRIAL REGISTRATION:

This trial is registered with with clinical trials

Registry – INDIA (http://ctri.nic.in) with CTRI

Registration no. – CTRI/2023/10/059041

EXPECTED OUTCOMES:

As discussed above, Vitamin-D_3 has an Immunomodulatory and Anti-Mycobacterial effect. Therefore, from this study, we can expect that Vitamin-D_3 can prevent the progression of the disease process and also can fasten the recovery process in Tuberculosis patients.

SAMPLE SIZE[110]:

The *formula for* calculating sample size:

$N = (Z\alpha + Z\beta)^2 \times [(\delta 1)^2 + (\delta 2)^2] / (\mu 1 - \mu 2)^2$

N= number of subjects for each group $Z\alpha$ = Type I error, at 5%, = 1.96

$Z\beta$ = Type II error, at 90% power = 1.2816 $\delta 1$ = Standard deviation of control =3.9

$\delta 2$ = Standard deviation of study group = 4.3 $\mu 1$ = mean of control = 22.31

$\mu 2$ = mean of study group =24.66

$N = (1.96+1.28)^2 \times [(3.9)\ 2 + (4.3)^2] / (22.31-24.66)^2$

$N = (3.24)^2 \times (15.21+18.49) / (-2.35)^2$

$N = 10.5 \times 33.7 / 5.52$

$N = 64.1$

Therefore, we took a sample size, of 70 for each group, and a total of 140 patients were enrolled

STATISTICAL ANALYSIS:

The randomization sequence was generated using a random number table. All patient data were analysed using Statistical Package for Social Sciences (SPSS) version 23.0 for Windows.

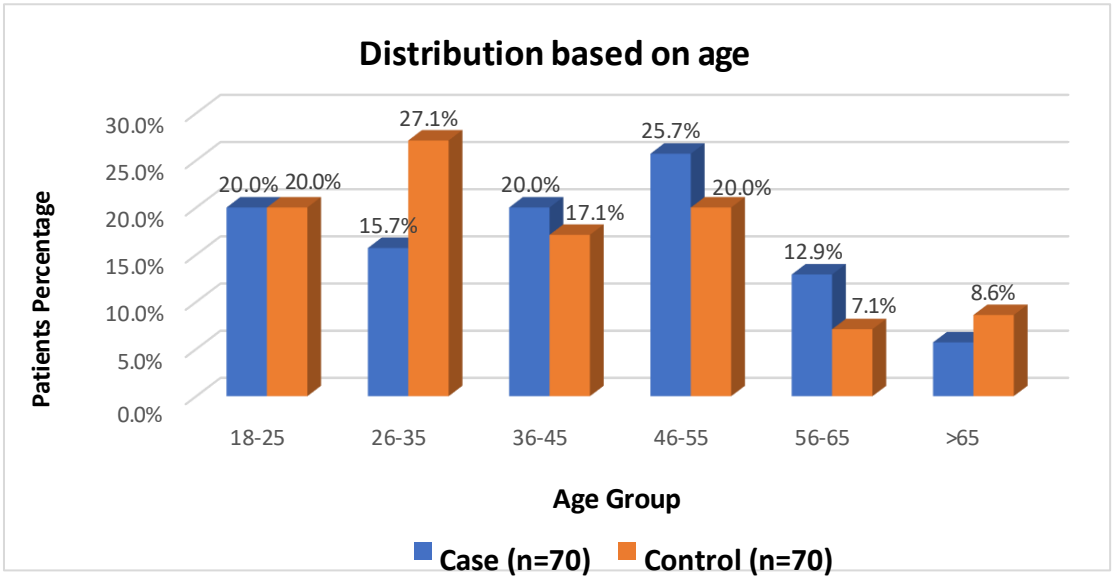
RESULT:

Table 1. shows the age distribution of 70 cases and 70 controls. Among cases, the largest age group was 46-55 years, with 18 patients (25.7%), followed by the 18-25 and 36-45 age groups, each with 14 patients (20.0%). In the control group, the largest age group was 26-35 years, with 19 patients (27.1%), followed by 18-25 and 46-55 age groups, each with 14 patients (20.0%). The mean age was 41.30±15.42 years for cases and 40.29±16.24 years for controls. The Chi-square value was 4.330 and the p-value > 0.05, indicating no significant difference between the age distributions of the two groups.

Table 1: Distribution of the studied patients based on age group:

Age Group (Years)	Group		Chi-square value	p-value
	Case (n=70)	Control (n=70)		
18-25	14 (20.0%)	14 (20.0%)	4.330	0.503
26-35	11 (15.7%)	19 (27.1%)		
36-45	14 (20.0%)	12 (17.1%)		
46-55	18 (25.7%)	14 (20.0%)		
56-65	9 (12.9%)	5 (7.1%)		
>65	4 (5.7%)	6 (8.6%)		
Mean±SD	41.30±15.42	40.29±16.24	0.379	0.705

Figure 1: Distribution of the studied patients based on age group:



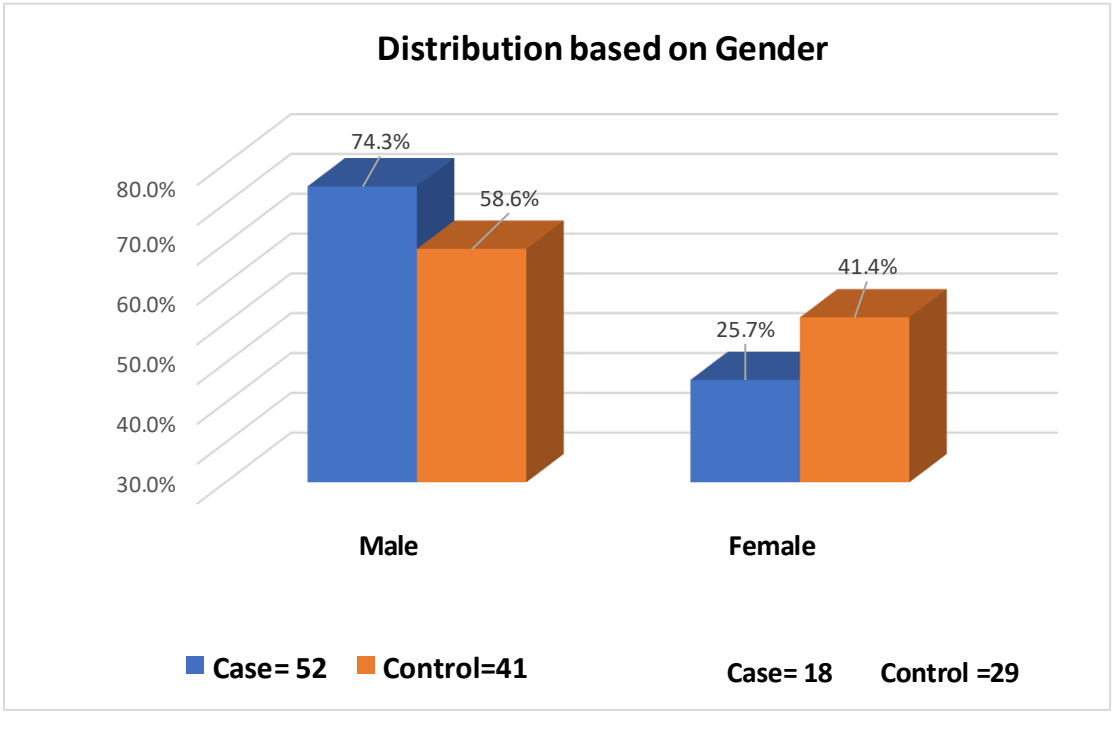
Among the 70 cases, the majority 52 (74.3%) were male and 18 (25.7%) were female. In the control group, the majority 41 (58.6%) were male and 29 (41.4%) were female. The Chi-square value was 3.876, with a p-value > 0.05, indicating that the difference in sex distribution between the cases and controls groups was not statistically significant.

Table 2: Distribution of the studied patients based on Gender:

Gender	Group		Chi-square value	p-value
	Case (n=70)	Control (n=70)		
Male	52 (74.3%)	41 (58.6%)	3.876	0.073
Female	18 (25.7%)	29 (41.4%)		

Figure 2: Distribution of the studied patients based on Gender:

Figure 2: Distribution of the studied patients based on Gender:

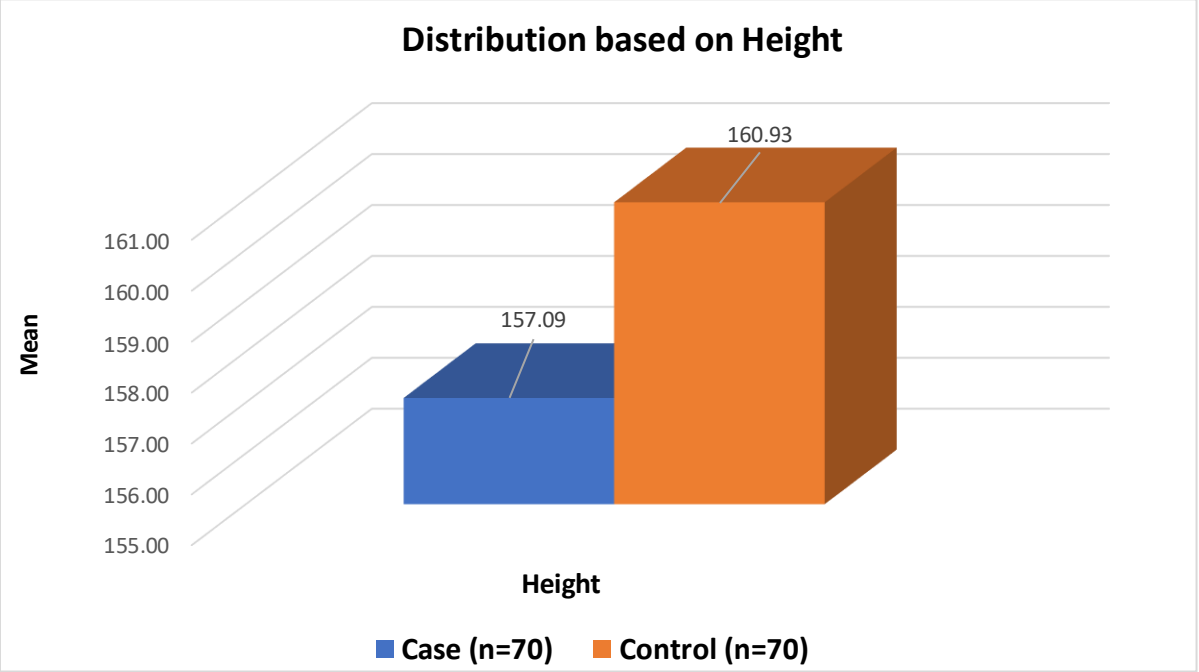


Among the 70 cases, the average height was 157.09±7.91 cm, while for the 70 controls, the average height was significantly greater 160.93±6.86 cm. The t-value was -3.070, with a p-value < 0.05, indicating a statistically significant difference in height between the cases and controls group.

Table 3: Distribution of the studied patients based on Height:

	Group		t-value	p-value
	Case (n=70)	Control (n=70)		
Height (cm)	157.09±7.91	160.93±6.86	-3.070	**0.003**

Figure 3: Distribution of the studied patients based on Height

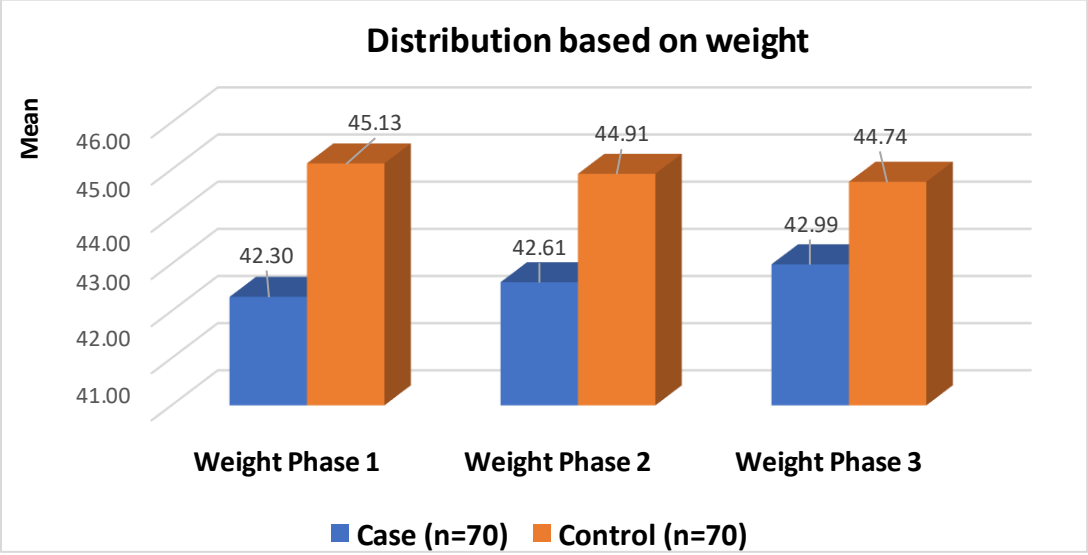


The mean weight for cases was 42.30±8.04 kg at 0-week, 42.61±8.03 kg at follow-up 6-weeks, and 42.99±8.04 kg at follow-up 12-weeks. In the interval of 6-weeks the differences in mean weight=wt_{6week}-wt_{0week} = 42.61±8.03 - 42.30±8.04 = 0.31±0.01 kg for case group. When treatment started and when treatment end total differences in mean weight= wt_{12week} -wt_{0week} = 42.99±8.04 - 42.30±8.04 =0.69±0.00 kg for cases group. For controls, the mean weight was 45.13±9.63 kg at 0-week, 44.91±9.33 kg at follow-up 6-week, and 44.74±9.04 kg at follow-up 12-week. In the interval of 6-weeks difference in mean weight=wt_{6week}-wt_{0week} = 44.91±9.33 - 45.13±9.63 = -0.22±0.30 kg for control group.Total differences in mean weight= wt_{12week} -wt_{0week} = 45.13±9.63 – 44.74±9.04 = -0.39±0.59 kg for control group. Our study result showed that increase of mean weight was statistically significant with small effect at 6 weeks and 12 weeks for cases group. In control group decrease of mean weight was statistically significant with small effect at 6 weeks and 12 weeks. The t-values and p-values at each follow-up (t = -1.886, p = 0.061; t = -1.563, p = 0.120; t = -1.213, p = 0.227) indicated no significant differences in weight between cases and controls at each follow-up. One Way ANOVA showed no significant changes in weight over time within each group (F = 0.129, p = 0.879 for cases; F = 0.031, p = 0.970 for controls). The majority of patients in both groups did not show significant weight differences at each follow-up.

Table 4: Compare the weight at each follow-up in both groups:

Weight (kg)		**Group**		**Independent t-test**	
		Case (n=70)	**Control (n=70)**	**t-value**	**p-value**
Phase 1 (0-week)		42.30±8.04	45.13±9.63	-1.886	0.061
Phase 2 (6-weeks)		42.61±8.03	44.91±9.33	-1.563	0.120
Phase 3 (12-weeks)		42.99±8.04	44.74±9.04	-1.213	0.227
One Way ANOVA	**F-value**	0.129	0.031		
	p-value	0.879	0.970		

Figure 4: Compare the weight at each follow-up in both groups:



The mean BMI for cases was 17.13±2.90 kg/m^2 at 0-weeks, 17.26±2.90 kg/m^2 at follow-up 6-weeks, and 17.41±2.90 kg/m^2 at follow-up 12-weeks. In the interval of 6-weeks the differences in mean BMI= BMI_{6week}-BMI_{0week} = 17.26±2.90-17.13±2.90 = 0.13±0.00 kg/m^2 for case group. When treatment started and when treatment end total differences in mean BMI= BMI_{12week} -BMI_{0week} = 17.41±2.90 - 17.13±2.90 = 0.28±0.00 kg/m^2 for case group. For controls, the mean BMI was 17.39±3.23 kg/m^2 at 0-week, 17.31±3.14 kg/m^2 at follow-up 6-weeks, and 17.25±3.06 kg/m^2 at follow-up 12-weeks. In the interval of 6-weeks the differences in mean BMI=BMI_{6week}-BMI_{0week} = 17.31±3.14 - 17.39±3.23 = -0.08±0.09 kg/m^2 for controls.Total differences in mean BMI= BMI_{12week} -BMI_{0week} = 17.25±3.06 – 17.39±3.23 = -0.14±0.17 kg/m^2 for controls. Our study result showed that increase of mean BMI was statistically significant with small effect at 6-weeks and 12-weeks for case group. In control group decrease of mean BMI was statistically significant with small effect at 6-weeks and 12-weeks. The t-values and p-values at each follow-up (t = -0.500, p = 0.618; t = -0.100, p = 0.921; t =

0.327, p = 0.744) indicated no significant differences in BMI between cases and controls at any follow-up. One Way ANOVA showed no significant changes in BMI over time within each group (F = 0.163, p = 0.849 for cases; F = 0.035, p = 0.966 for controls).

Table 5: Compare the BMI level at each follow-up in both groups:

BMI (kg/m^2)		Group		Independent t-test	
		Case (n=70)	Control (n=70)	t-value	p-value
Phase 1 (0-week)		17.13±2.90	17.39±3.23	-0.500	0.618
Phase 2 (6-weeks)		17.26±2.90	17.31±3.14	-0.100	0.921
Phase 3 (12-weeks)		17.41±2.90	17.25±3.06	0.327	0.744
One Way ANOVA	F-value	0.163	0.035		
	p-value	0.849	0.966		

For cases, the mean Serum Albumin levels were 2.67±0.53 gm/dl at 0-week, 2.93±0.84 gm/dl at follow-up 6-weeks, and 3.03±0.52 gm/dl at follow-up 12weeks. In the interval of 6-weeks the differences in mean Serum Albumin =S. $Albumin_{6week}$ - S. $Albumin_{0week}$ = 2.93±0.84 - 2.67±0.53 = 0.26±0.31 gm/dl for case group. When treatment started and when treatment end total differences in mean Serum Albumin =S. $Albumin_{12week}$ - S. $Albumin_{0week}$ = 3.03±0.52 - 2.67±0.53 = 0.36±0.01 gm/dl for case group. For controls, the mean Serum Albumin levels were 2.80±0.51 gm/dl at 0-week, 2.67±0.46 gm/dl at follow-up 6-weeks, and 2.62±0.50 gm/dl at follow-up 12-weeks. In the interval of 6-weeks the differences in mean Serum Albumin= S. $Albumin_{6week}$ - S. $Albumin_{0week}$ = 2.67±0.46 - 2.80±0.51= -0.13±0.05 gm/dl for controls.Total differences in mean Serum Albumin =S. $Albumin_{12week}$ - S. $Albumin_{0week}$ = 2.62±0.50 – 2.80±0.51 = -0.18±0.01 gm/dl for controls. Our study result showed that increase of mean serum albumin was statistically significant with small effect at 6 weeks and 12 weeks for case group. In

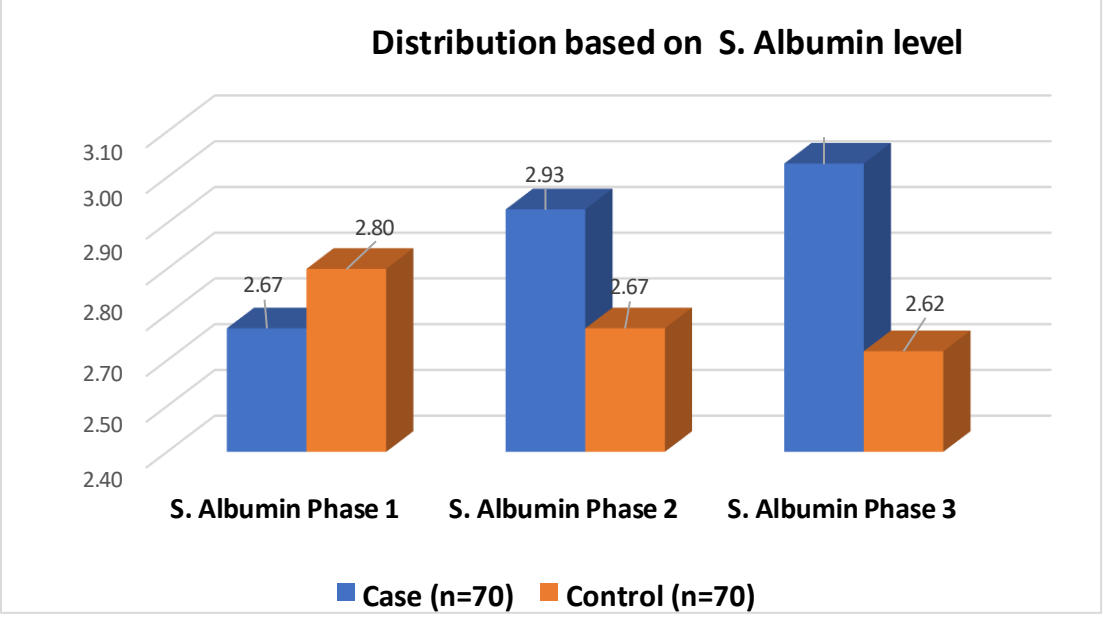
control group decrease of mean serum albumin was statistically significant with small effect at 6 weeks and 12 weeks. The t-values and p-values ($t = -1.479$, $p = 0.141$; $t = 2.275$, $p = 0.024$; $t = 4.717$, $p < 0.001$) indicated a significant differences in Serum Albumin levels at follow-ups 6-weeks and 12-weeks. One Way ANOVA showed no significant changes in Serum Albumin levels over time within each group ($F = 0.272$, $p = 0.762$ for both groups).

Table 6: Compare the Serum Albumin level at each follow-up in both groups:

Mean

S. Albumin (gm/dl)		Group		Independent t-test	
		Case (n=70)	Control (n=70)	t-value	p-value
Phase 1 (0-week)		2.67±0.53	2.80±0.51	-1.479	0.141
Phase 2 (6-weeks)		2.93±0.84	2.67±0.46	2.275	**0.024**
Phase 3 (12-weeks)		3.03±0.52	2.62±0.50	4.717	**<0.001**
One Way ANOVA	**F-value**	0.272	0.272		
	p-value	0.762	0.762		

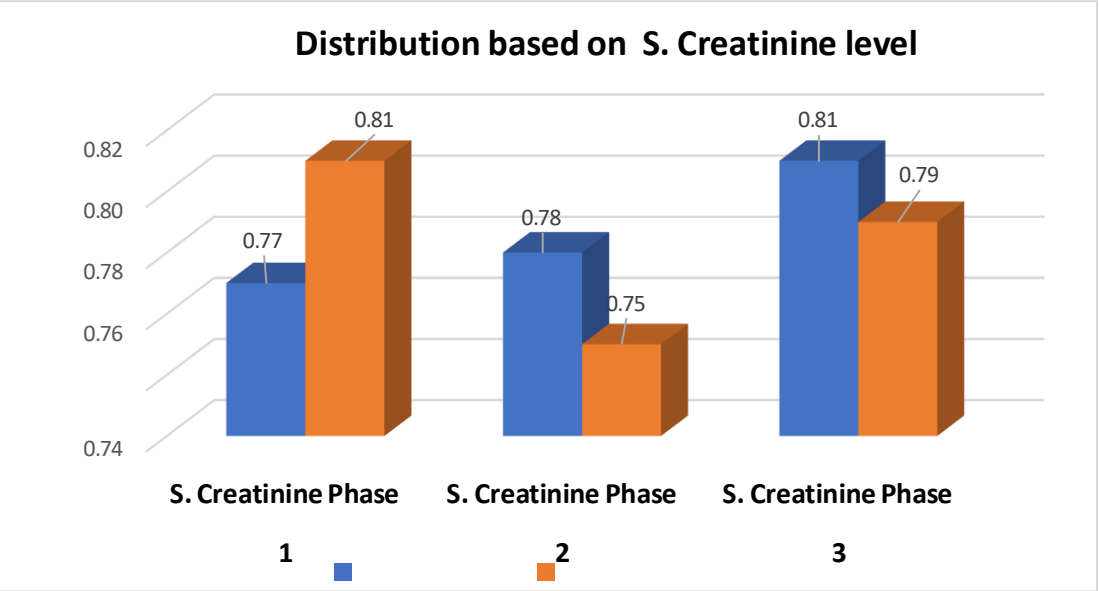
Figure 6: Compare the Serum Albumin level at each follow-up in both groups:



For cases, the mean Serum Creatinine levels were 0.77±0.42 mg/dl at 0-week, 0.78±0.37 mg/dl at follow-up 6-weeks, and 0.81±0.40 mg/dl at follow-up 12-weeks. In the interval of 6-weeks the differences in mean Serum Creatinine =S. $Creatinine_{6week}$ - S. $Creatinine_{0week}$ = 0.78±0.37 - 0.77±0.42 = 0.01±0.05 mg/dl for case group. When treatment started and when treatment end total differences in mean Serum Creatinine =S. $Creatinine_{12week}$ - S. $Creatinine_{0week}$ = 0.81±0.40 - 0.77±0.42 = 0.04±0.02 mg/dl for case group. For controls, the mean Serum Creatinine levels were 0.81±0.50 mg/dl at 0-week, 0.75±0.46 mg/dl at follow-up 6-weeks, and 0.79±0.51 mg/dl at follow-up 12-weeks. In the interval of 6-weeks the differences in mean Serum Creatinine =S. $Creatinine_{6week}$ - S. $Creatinine_{0week}$ = 0.75±0.46 - 0.81±0.50 = -0.06 ± 0.04 mg/dl for controls. Total differences in mean Serum Creatinine =S. $Creatinine_{12week}$ - S. $Creatinine_{0week}$ =0.79±0.51 – 0.81±0.50 =-0.02 ± 0.01 mg/dl for controls. Our study result showed that increase of mean serum creatinine was statistically significant with small effect at 6-weeks and 12-weeks for case group. In control group decrease of mean serum creatinine was statistically significant with small effect at 6-weeks and 12-weeks. The t-values and p-values (t = -0.570, p = 0.569; t = 0.337, p = 0.737; t = 0.240, p > 0.05) indicated no significant differences in Serum Creatinine levels between the groups at any follow-ups. One Way ANOVA showed no significant changes in Serum Creatinine levels over time within each group (F = 0.192, p = 0.825 for cases; F = 0.272, p > 0.05 for controls).

Table 7: Compare the Serum Creatinine level at each follow-up in both groups:

S. Creatinine (mg/dl)		Group		Independent t-test	
		Case (n=70)	Control (n=70)	t-value	p-value
Phase 1 (0-week)		0.77±0.42	0.81±0.50	-0.570	0.569
Phase 2 (6-weeks)		0.78±0.37	0.75±0.46	0.337	0.737
Phase 3 (12-weeks)		0.81±0.40	0.79±0.51	0.240	0.810
One Way ANOVA	F-value	0.192	0.272		
	p-value	0.825	0.762		

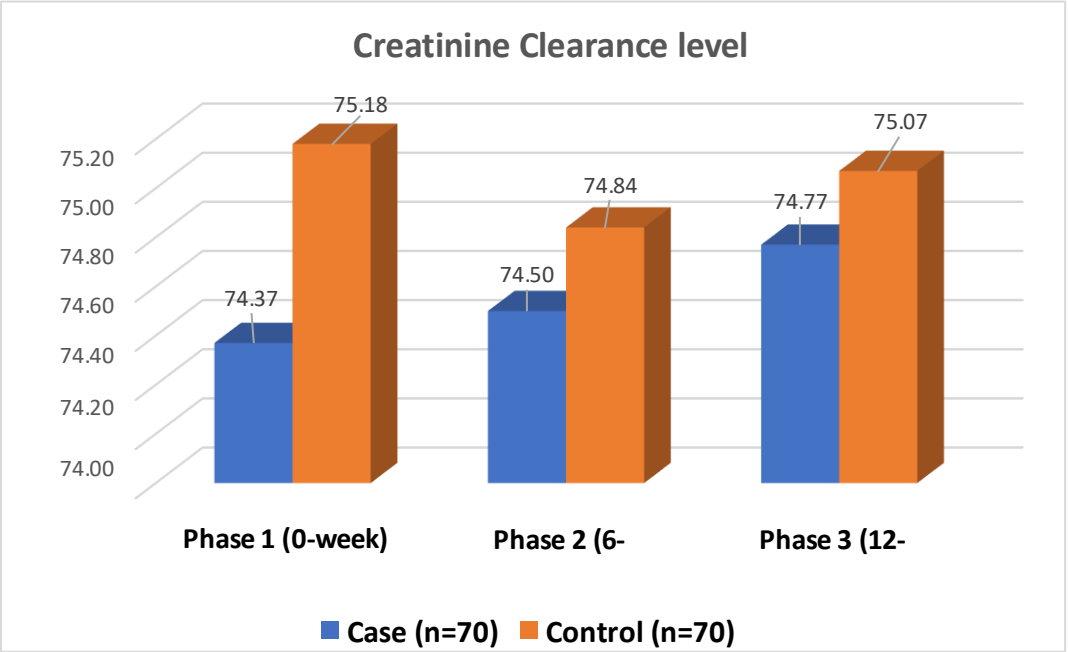

Distribution based on S. Creatinine level
0.82
0.80
0.78
0.76
0.74
0.77
0.81
0.78
0.75
0.81
0.79
S. Creatinine Phase 1
S. Creatinine Phase 2
S. Creatinine Phase 3

During Phase 1 (0-week), the creatinine clearance levels were slightly lower in the case group (74.37 ± 2.69) compared to the control group (75.18 ± 2.93). However, the difference was not statistically significant, as indicated by a t-value of 1.703 and a p-value of 0.090. At the 6-week follow-up (Phase 2), the creatinine clearance levels in the case group (74.5 ± 2.77) remained slightly lower than those in the control group (74.84 ± 2.92). The difference between the groups was even smaller and statistically non-significant, with a t-value of 0.706 and a p-value of 0.480. By the 12-week follow-up (Phase 3), the creatinine clearance levels in the case group had slightly increased to 74.77 ± 2.80, while in the control group, they were 75.07 ± 2.88. Again, the difference was not statistically significant, with a t-value of 0.624 and a p-value of 0.533. A one-way ANOVA was conducted to analyze the differences within each group across the three phases. The F-values were 0.384 for the case group and 0.249 for the control group, with p-values of 0.681 and 0.780, respectively, indicating no significant changes in creatinine clearance levels over time within either group.

Table 7.2: Comparison of Creatinine Clearance level at each follow-up in both groups:

Creatinine Clearance		Group		Independent t-test	
		Case (n=70)	Control (n=70)	t-value	p-value
Phase 1 (0-week)		74.37±2.69	75.18±2.93	1.703	0.090
Phase 2 (6-weeks)		74.5±2.77	74.84±2.92	0.706	0.480
Phase 3 (12-weeks)		74.77±2.80	75.07±2.88	0.624	0.533
One Way ANOVA	F-value	0.384	0.249		
	p-value	0.681	0.780		

Figure 7.2: Comparison of Creatinine Clearance level at each follow-up in both groups:



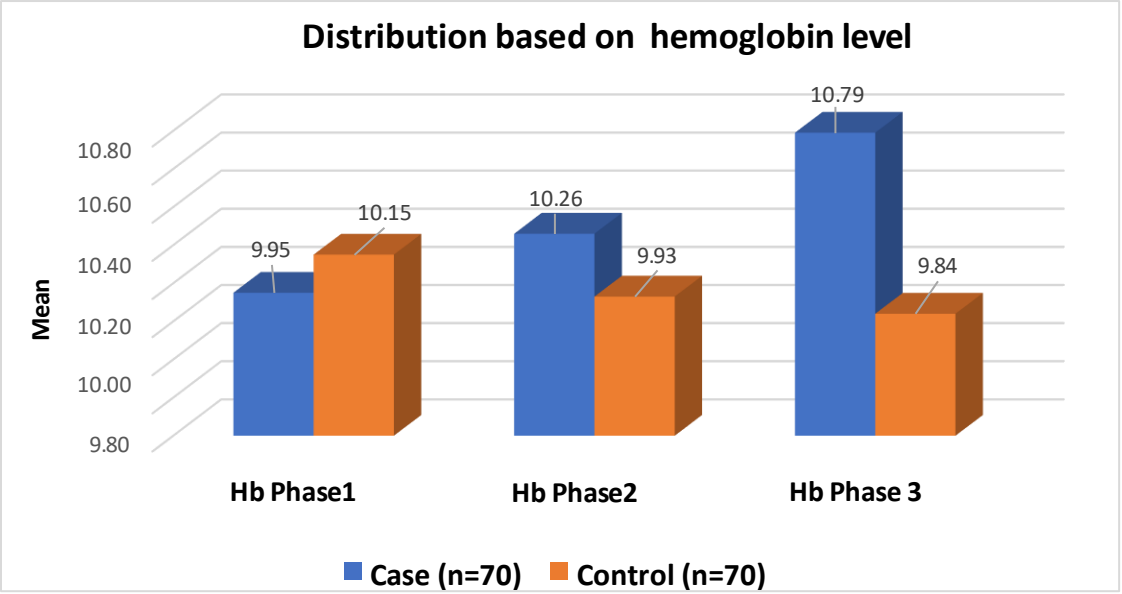
For cases, the mean Hb levels were 9.95±1.86 gm/dl at 0-week, 10.26±1.73 gm/dl at follow-up 6-week, and 10.79±1.64 gm/dl at follow-up 12-week. In the interval of 6-weeks the differences in mean Hemoglobin = Hb_{6week} - Hb_{0week} = 10.26±1.73 - 9.95±1.86 = 0.31±0.13 gm/dl for case group. When treatment started and when treatment end total differences in mean Hemoglobin = Hb_{12week} - Hb_{0week} = 10.79±1.64 - 9.95±1.86 = 0.84±0.22 gm/dl for case group. For controls, the mean Hb levels were 10.15±1.37 at 0-week, 9.93±1.27 at follow-up 6-week, and 9.84±1.23 at follow-up 12-week. In the interval of 6-weeks the differences in mean Hemoglobin =Hb_{6week} - Hb_{0week} = 9.93±1.27 - 10.15±1.37 = -0.22±0.10 gm/dl for controls. Total differences in mean Hemoglobin =Hb_{12week} - Hb_{0week} = 9.84±1.23 - 10.15±1.37 = -0.31±0.14 gm/dl. Our study result showed that increase of mean Hemoglobin was statistically significant with small effect at 6 weeks and 12 weeks for case group. In control group decrease of mean Hemoglobin was statistically significant with small effect at 6 weeks and 12 weeks. The t-values and p-values ($t = -0.721$, $p = 0.472$; $t = 1.294$, $p = 0.198$; $t = 3.882$, $p < 0.001$) indicated

a significant difference in Hb levels at follow-up 12-weeks, with cases showing higher levels. One Way ANOVA revealed a significant change in Hb levels over time within the case group ($F = 4.145$, $p = 0.05$) but not within the control group ($F = 1.068$, $p > 0.05$).

Table 8: Compare the hemoglobin level at each follow-up in both groups:

Hb (gm/dl)		**Group**		**Independent t-test**	
		Case (n=70)	**Control (n=70)**	**t-value**	**p-value**
Phase 1 (0-week)		9.95±1.86	10.15±1.37	-0.721	0.472
Phase 2 (6-weeks)		10.26±1.73	9.93±1.27	1.294	0.198
Phase 3 (12-weeks)		10.79±1.64	9.84±1.23	3.882	**<0.001**
One Way ANOVA	**F-value**	4.145	1.068		
	p-value	**0.017**	0.346		

Figure 8: Compare the hemoglobin level at each follow-up in both groups:



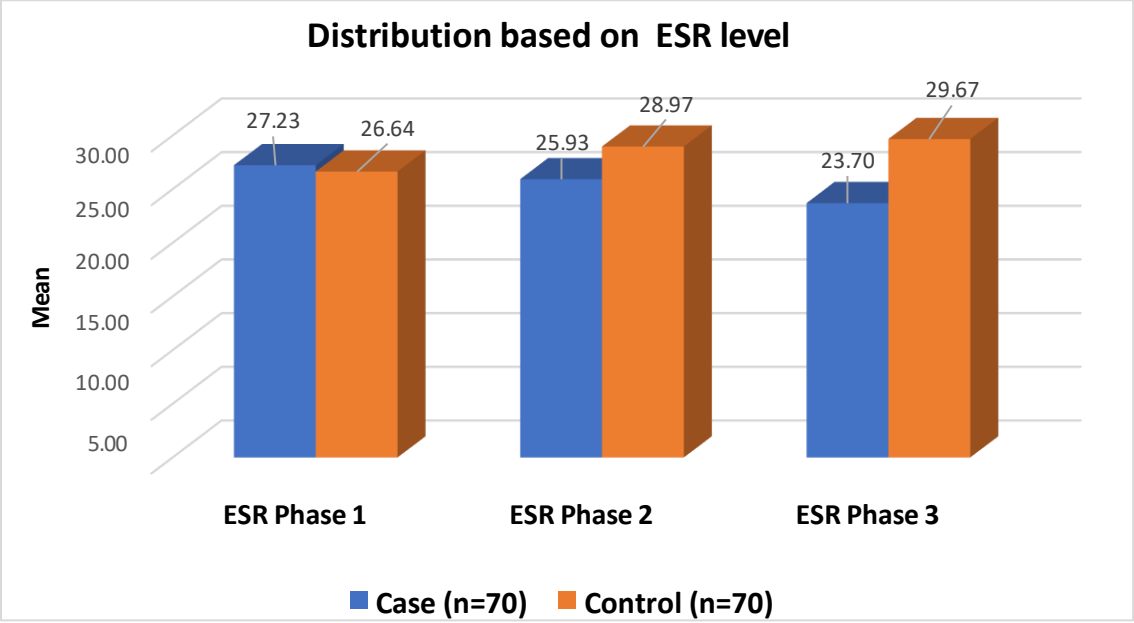
For cases, the mean ESR levels were 27.23±8.40 mm/h at 0-week, 25.93±5.82 mm/h at follow-up 6-weeks, and 23.70±4.97 mm/h at follow-up 12-weeks. In the interval of 6-weeks the differences in mean ESR $=ESR_{6week} - ESR_{0week} =$ 25.93±5.82 - 27.23±8.40 = -1.3±2.58 mm/h for case group. When treatment started and when treatment end total differences in mean ESR $=ESR_{12week} - ESR_{0week} =$ 23.70±4.97 - 27.23±8.40 = -3.53±3.43 mm/h for case group. For controls, the mean ESR levels were 26.64±5.79 mm/h at 0-week, 28.97±5.48 mm/h at follow-up 6-weeks, and 29.67±5.96 mm/h at follow-up 12-weeks. In the interval of 6-weeks the differences in mean ESR $=ESR_{6week} - ESR_{0week} =$ 28.97±5.48 - 26.64±5.79 = 2.33±0.31 mm/h for controls. Total differences in mean ESR $=ESR_{12week} - ESR_{0week} =$ 29.67±5.96 - 26.64±5.79 = 3.03±0.17 mm/h. Our study result showed that decrease of mean ESR was statistically significant with small effect at 6-weeks and 12-weeks for case group. In control group increase of mean ESR was statistically significant with small effect at 6-weeks and 12-weeks. The t-values and p-values ($t = 0.480$, $p = 0.632$; $t = -3.184$, $p = 0.002$; $t = -6.437$, $p < 0.001$) indicated significant differences in ESR levels at follow-up 6-weeks and follow-up 12-weeks,

with cases showing lower levels than controls. One Way ANOVA revealed significant changes in ESR levels over time within both the case group ($F = 5.183$, $p < 0.05$) and the control group ($F = 5.334$, $p < 0.05$).

Table 9: Compare the ESR level at each follow-up in both groups:

ESR (mm/h)		Group		Independent t-test	
		Case (n=70)	Control (n=70)	t value	p-value
Phase 1		27.23±8.40	26.64±5.79	0.480	0.632
Phase 2		25.93±5.82	28.97±5.48	-3.184	**0.002**
Phase 3		23.70±4.97	29.67±5.96	-6.437	**<0.001**
One Way ANOVA	F value	5.183	5.334		
	p-value	**0.006**	**0.006**		

Figure 9: Compare the ESR level at each follow-up in both groups:



Discussion

Spirulina is rich in Proteins, Vitamins, and Minerals, which can help improve the nutritional status of Tuberculosis patients. Studies have shown that Spirulina supplementation can lead to weight gain and improved Body Mass Index in malnourished individuals. Spirulina has anti-inflammatory and antioxidant properties that can support the immune system and potentially improve the overall health of Tuberculosis patients.[123] Selenium is known for its immune-modulating and antioxidant effects. Supplementation with Selenium has been shown to improve clinical outcomes in Tuberculosis patients, including better weight gain and Body Mass Index improvement. Selenium helps reduce oxidative stress, which is beneficial for Tuberculosis patients who often experience high levels of Inflammation and Oxidative damage.[124]

Vitamin D3 plays a significant role in immune function and has been shown to enhance the body's response to Tuberculosis treatment. Supplementation can improve clinical outcomes and support weight gain and Body Mass Index improvement. Vitamin D deficiency is common in Tuberculosis patients, and addressing this deficiency can lead to better health outcomes, including improved Body Mass Index. These supplements can be beneficial as part of a comprehensive treatment plan for Pulmonary Tuberculosis, but it's essential to consult healthcare professionals for personalized advice and monitoring.[125]

Calcium is crucial for bone health and metabolic functions. Tuberculosis patients often have lower serum calcium levels, and supplementation can help improve these levels, potentially leading to better overall health and Body Mass Index. It's important to monitor calcium levels, as can sometimes cause hypercalcemia, which needs to be managed carefully.[126]

In the present study, the mean age of the studied cases was 41.30±15.42 years and for the control group it was 40.29±16.24 years with male predominance in both cases (74.3%) and controls (58.6%). Our findings were comparable to the findings of

Bhargava A et al who did a study on the nutritional Status of Adult Patients with Pulmonary Tuberculosis in Rural Central India and Its Association with Mortality and found that the mean age of the studied cases was 38 years with male predominance (68.0%). In **Pandey A et al** study, the maximum number of patients were in the active age group i.e. 21-60 years (45.0% of patients in the age group of 41-60 years followed by 32.0% in the 21-40 years group) with mean age 42.84±16.50 years and the male-to-female ratio was 1:0.75. **Mahesar S et al[103]** reported that the mean age 45.63±9.87 and 39.63±13.30 years respectively for cases and controls. **Cheng C et al[127]** depicts that there was male predominance in both research and control groups with mean age 44.62±6.41 and 45.66±6.83 years respectively (p>0.05).

Salahuddin N et al[128] reported greater weight gain and accelerated radiological recovery in Pulmonary Tuberculosis patients who received two doses of 600,000 IU Vitamin D3 administered Intramuscularly, in comparison to the placebo group.

In the present study, the mean weight increased slightly in the case group and it decreased in the control group but the difference was insignificant (p>0.05). Similarly, BMI also increases with time in the case group whereas it decreases with time in the control group with insignificant difference (p>0.05). For cases, the mean Serum Albumin levels were 2.67±0.53 at 0-week, 2.93±0.84 at follow-up 6-weeks, and 3.03±0.52 at follow-up 12-weeks. For controls, the mean Serum Albumin levels were 2.80±0.51 at 0-week, 2.67±0.46 at follow-up 6-weeks, and 2.62±0.50 at follow-up 12-weeks (p<0.05). Our findings were supported by **Ramakrishnan K et al[121]** who reported that the mean +/- SD for Body Mass Index, Selenium, and Albumin among the controls, HIV positive, and HIV negative patients were 19.6 +/- 0.6, 18 +/- 0.4 and 18.5 +/- 0.6 kg/m2; 113.1 +/- 4.1, 27.44 +/- 8, and 65.92 +/- 9, microg/dL; and 4.1 +/- 0.6, 2.9 +/- 0.4 and 3.6 +/- 0.7 g/dL, respectively. BMI, serum Selenium, and Albumin levels were found to be significantly lower ($p < 0.004$, $p < 0.0321$, and $p < 0.002$, respectively). **Seyedrezazadeh E et al[87]** reported that in both groups, the BMI showed constant increment during two months of treatment. **Eletreby R et al[129]** reported that higher serum Albumin levels at 2 months and the end of treatment ($p = 0.007$ and $P < 0.001$) which was 3.6 ± 0.3 at baseline at 2 months was 4.2 ± 0.3 and 4.4 ± 0.3

at end of treatment ($p<0.05$)

Low serum Albumin levels are attributed to severe malnutrition associated with Tuberculosis as well as Albumin is a negative acute phase protein, so its concentration decreases in the context of significant inflammation and infection as in Tuberculosis.[130]

When we compared **Hemoglobin**, the mean **Hemoglobin** levels were 9.95±1.86 at 0-week, 10.26±1.73 at follow-up 6-weeks, and 10.79±1.64 at follow-up 12-weeks. For controls, the mean **Hemoglobin** levels were 10.15±1.37 at 0-week, 9.93±1.27 at follow-up 6-weeks, and 9.84±1.23 at follow-up 12-weeks. a significant change in **Hemoglobin** levels over time within the case group ($F = 4.145$, $p = 0.05$) but not within the control group ($F = 1.068$, $p > 0.05$). The mean **Erythrocyte Sedimentation Rate** levels were 27.23±8.40 at 0-week, 25.93±5.82 at follow-up 6-weeks, and 23.70±4.97 at follow-up 12-weeks. For controls, the mean **Erythrocyte Sedimentation Rate** levels were 26.64±5.79 at 0-week, 28.97±5.48 at follow-up 6-weeks, and 29.67±5.96 at follow-up 12-weeks. It revealed significant changes in **Erythrocyte Sedimentation Rate** levels over time within both the case group ($F = 5.183$, $p < 0.05$) and the control group ($F = 5.334$, $p < 0.05$). Our findings were consistent with the findings of **Eletreby R et al**[129] who reported that patients in supplementation group had significantly higher **Hemoglobin** concentration at the end of treatment ($p < 0.001$), higher serum Albumin level at 2 months, and at the end of treatment ($p = 0.007$ and $P < 0.001$), lower CRP level ($p = 0.002$ and $P < 0.001$) and lower **Erythrocyte Sedimentation Rate** at 2 months and the end of treatment ($p = 0.02$ and $P < 0.001$). Several previous studies have demonstrated that Anemia is highly prevalent in active Tuberculosis cases and can be attributed to iron deficiency secondary to Tuberculosis-associated Malnutrition and Iron depletion.[131]

According to **Selmi C et al**[122] over the 12-week study period, there was a steady increase in **Mean Corpuscular Hemoglobin** in subjects of both sexes. Most subjects manifest increased Indoleamine 2,3-dioxygenase activity and white blood cell count at 6 and 12 weeks of Spirulina supplementatio

Martineau AR et al[132] reported that the administration of Vitamin D3 supplementation in four fortnightly doses of 2.5 mg (100,000 IU) did not effect on time to sputum culture conversion. However, Vitamin D supplementation accelerated the normalization of **Erythrocyte Sedimentation Rate** and serum C-Reactive Protein and reduced Chemokine production.[133] Additionally, two randomized-controlled clinical trials conducted by **Wejse C et al**[134] and **Ganmaa D et al[135]** showed that after administration of three doses of 100,000IU Vitamin D2 given at 0, 5 and 8 months and four biweekly doses of 3.5 mg (140,000 IU) Vitamin D3 respectively, no significant difference in the rate of mortality and sputum clearance was recognized in comparison with placebo group. Also, **Ganmaa et al135** reported that no significant effect of Vitamin D supplementation was seen on serum concentrations of the acute-phase reactants **CRP, Albumin**, or **Erythrocyte Sedimentation Rate.**

Chandra H et al[104] reported that Total four doses [each dose of 2.5 mg (100000 IU)] of Vitamin-D3 were given, orally. First dose was given within 7 days second, third, fourth dose were given at 2, 4 and 6 weeks respectively. Decrease in Erythrocyte Sedimentation Rate was statistically significant with small effect sizes at 6 and 8 week and increase of Body Weight in was statistically significant with small effect sizes at 6 and 8 week for intervention group than for control group our finding were consistent with the finding of this because in case group at base line Erythrocyte Sedimentation Rate was 27.23 ±8.40 which was reduced to 25.93 ±5.82 at 6-weeks and 23.70 ±4.97 at the end of treatment for case group than for control group and in case group at base line Body Weight was 42.30±8.04 which was increased to 42.61±8.03 at 6-weeks and 42.99±8.04 at the end of treatment for case group than for control group.

Aghasadeghi MR et al[124] reported that in the non-ICU patients(Less severe illnesses and require a lower level of care) for the Spirulina and control groups, the results of Clinical Laboratory findings on the last follow-up day were as follows: C- Reactive Protein (ARR, 36.84; 95% CI, 21.51 to 52.18, NNT=3; 95% CI, 1.9 to 4.7;

P<0.001), **Erythrocyte Sedimentation Rate** (ARR, 31.58; 95% CI, 16.80 to 46.36,

NNT=4; 95% CI, 2.2 to 6.0; P = 0.003).

Eletreby R et al[129] reported that at baseline the mean **Erythrocyte Sedimentation Rate** was 63.6 ± 12.4 which was reduced to 26.3 ± 4.9 at 2 months and 10 ± 1.5 at the end of treatment ($p<0.05$) our finding were consistent with the finding of this because in case group at base line Erythrocyte Sedimentation Rate was 27.23 ±8.40 which was reduced to 25.93 ±5.82 at 6-weeks and 23.70 ±4.97 at the end of treatment. **Wang J et al**[114] reviewed the efficacy and Safety of Vitamin D Supplementation for Pulmonary Tuberculosis Vitamin D supplementation showed no influence on the improvement of sputum smear-negative conversion rates and BMI, as well as the decrease in **Erythrocyte Sedimentation Rate**. The results of the **Wu H et al**[136] meta-analysis were inconsistent with those of previous meta-analyses, showing that Vitamin D supplementation safely and effectively increases the proportion of sputum smear and culture conversion. A meta-analysis that included four trials did not show any improvement in the clinical parameters of the participants in the Vitamin D arm compared with those in the placebo arm (P=0.05).[137]

Hassanein EG et al[118] demonstrated that administration of single dose of 200,000IU Vitamin D3 during Pulmonary Tuberculosis treatment has resulted in a rapid decline in sputum conversion time compared to the group receiving standard Anti- Tuberculosis treatment alone. **Sato S et al**[138] reported that in cured patients with active Pulmonary Tuberculosis, serum Vitamin D levels showed a significantly negative correlation with time duration until sputum conversion, as well as Platelets count and C-Reactive Protein and a significant positive correlation with serum Albumin. They stated that these correlations reflect the anti-inflammatory effect of Vitamin D and suggest that a low serum Vitamin D level may not only be a risk factor for the development of active Tuberculosis but may also be related to poor treatment outcomes in active Tuberculosis patients.[138]

Selenium functions primarily in the form of Selenoproteins. At least 30 Selenoproteins have been identified including Glutathione Peroxidase, Selenoprotein P, and Thioredoxin reductase that are the major components of the body antioxidant system. Thioredoxin reductase provides reducing power for several biochemical processes and is responsible for degrading Peroxides and Hydroperoxides outside cell membranes.[139] It has been shown that Selenium deficiency increases the risk of

developing Mycobacterial diseases in HIVinfected individuals by 13-folds.[140]

The **Van Lettow M et al**[141] study shows that micronutrient malnutrition and wasting are more severe in adults with Pulmonary Tuberculosis who have high

plasma HIV load. The association between high plasma HIV load and nutrient deficiencies was strongest for the major plasma carotenoids and selenium. Overall in this study population, both HIV-positive and HIV-negative adults with Pulmonary Tuberculosis were extremely malnourished as indicated by Body Mass Index and plasma micronutrient concentrations. About one-third of the adults in this study had a Body Mass Index <17.0, a cut-off that is predictive of mortality in adults co-infected with tuberculosis and HIV.[142]

To the best of our knowledge, this is the first study to evaluate the effect of Spirulina Platensis, Selenium, Calcium Plus Vitamin –D3 on Body Mass Index in Pulmonary tuberculosis supplementation in the treatment course of patients with Pulmonary tuberculosis. However, the study has some limitations, being a single- center study and the small sample size limits the generalizability of the results. Therefore, studies with larger sample sizes that recruit patients with other forms of Extra Pulmonary Tuberculosis are still needed.

STRENTHS OF THE STUDY

The sampling of consecutive patients makes selection bias less likely, though because of the location and low-cost nature of services, the poor might have been over-represented in our cohort.

CONCLUSION

This study showed a high Prevalence of nutritional deficiency among newly diagnosed patients with Pulmonary Tuberculosis. Additionally, Vitamin D3 supplementation has been beneficial in the treatment of Pulmonary tuberculosis, and associated with higher weight gain, as well as better improvement of serum

concentrations of Hemoglobin and acute-phase reactants. Low serum Selenium levels are associated with increased risk of Pulmonary infection caused by Mycobacteria. We also conclude that nutritional support should be considered for severely underweight patients with Pulmonary tuberculosis to decrease their risk of Mortality, although community-based nutritional interventions for such patients in rural India, require further support from the government. Spirulina have a best option for nutritional support due to its high antioxidants content, mainly phycocyanin, its activities on metabolism and detoxification thus the alga may be considered as a coadjuvant agent as it may exhibit a synergistic effect together with **Anti-tuberculosis treatment** drugs.

CONFLICT OF INTEREST: The authors declare that there are no conflicts of interest.

SOURCE OF FUNDING: The study received no external funding.

CONSENT: Written informed consent has been obtained from all participants in accordance with international or university standards and is maintained by the authors.

ETHICAL APPROVAL: Ethical approval was granted in compliance with international or university standards, and the written approval is preserved by the authors.

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