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Percentage and Absolute CD4+ Count and Factors Influencing Their Levels in Tuberculosis Patients in a Tertiary Hospital, Kaduna, Nigeria

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ABSTRACT

Background: The role of CD4+ T cells in immunity against tuberculosis have been widely acknowledged. This study determined CD4+ absolute, CD4 percentage and haemoglobin (HB) levels in tuberculosis (TB) patients undergoing TB treatment and compared these levels with presence of some factors which could modify the quantities of CD4+, CD4% and HB in TB patients.

Methods: A cross-sectional study of eighty-five persons attending TB DOTS clinic in tertiary hospital between 2020 to 2021. Multicolour fluorescence imaging and absorbance spectrometry microscopy was used to enumerate CD4+ absolute count, CD4+ percentage and HB concentration in whole blood. Questionnaire and interviews were used to determine history, demographic data, BCG vaccination, BCG scar, vitamin A supplementation, awareness of zoonotic diseases and zoonotic TB, maternal BCG vaccination status, maternal BCG scar and undernutrition for each respondent.

Results: CD4% significantly differed between forty-seven males (mean age: 33.5) and thirty-eight females (mean age: 32.2) ($p < 0.05$).
T-test indicated no significant difference in CD4+ count, CD4% and HB compared with BCG vaccination status, presence of BCG scar, knowledge of zoonotic diseases, knowledge of zoonotic TB and with vitamin A supplementation ($p < 0.05$). There was also significant difference in CD4% compared with undernutrition and in absolute CD4+ counts compared with drug resistance ($p < 0.05$).

Conversely, there was significant difference in CD4% and absolute CD4+ count when compared with maternal BCG vaccination, presence of maternal BCG Scar.

Pearson correlation coefficient indicated weak negative relationship between CD4%, absolute CD4+ count and age. Also, weak positive relationship between HB and age. Both relationships were not significant ($p < 0.05$).

Conclusion: Undernutrition, gender, maternal BCG vaccination (with or without scaring) and age influence levels of CD4+ in TB patients.

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Introduction
Background
The role of CD4+ T cells in immunity against tuberculosis (TB) have been widely acknowledged [1-5]. Whether as a result of natural TB infection or due to vaccination with bacille Calmette-Guérin BCG, CD4+ cells have an important role in the control of active TB disease. Polyfunctional CD4+ cell express cytokines which include Interferon gamma (IFN-γ), Tumour necrosis factor alpha (TNF-α) and Interleukin-2 (IL-2) on a single cell. CD4 levels deplete in active tuberculosis but improve with treatment and as the disease progresses [6-9]. Individuals who have deficient CD4+ T-cells are prone to severe TB disease [6, 7]. CD4+ level is altered

in HIV TB coinfection [10]. CD4+ count has been identified as a key determinant in TB transmission dynamics [11].

Generally, there are known factors that can influence CD4+ counts in individuals with TB, these include: HIV co-infection, duration and severity of TB, drug-resistant or multidrug-resistant TB (DR-TB or MDR-TB), age, nutritional status, weight, adherence to treatment, concomitant infections, immune response and genetic factors. In individuals with TB, timely and appropriate treatment of both TB and any underlying conditions (such as HIV, diabetes) is crucial for restoring and maintaining immune function. Additionally, supportive care measures, including good nutrition and management of comorbidities, can play a significant role in overall health and immune function.

There is also a clear negative correlation between baseline CD4+ T cell count and incident TB among ART-receiving patients. Patients with baseline CD4+ T cell count < 200 cells/mm³ exhibit a substantially higher risk of incident TB compared to those with count > 200 cells/mm³ [11].

While active TB is more likely in HIV patients with WHO stage 2 or 3, and those with baseline CD4 cell count < 350 cells/mm³, these factors do not significantly predict active TB development after 6 months on ART, as a substantial portion of patients who developed active TB had been on ART for an extended period [12].

Abdullahi et al. (13) highlighted that being above 39 years of age, HIV positivity, low CD4+ cell count (< 456cells/mm3), and low weight (< 42kg) were significant risk factors associated with the death of TB/HIV co-infected patients [13].

Mean CD4+ T-lymphocyte counts in patients with PTB are usually low [14]. CD4+ levels tend to increase with duration of PTB treatment. Higher CD4+ levels were seen at six months of treatment compared to baseline [9]. CD4+ count also plays a pivotal role in various aspects of TB management in individuals co-infected with HIV.

In TB progression, CD4+ count has also emerged as a significant factor associated with the presence of latent TB among HIV-infected persons [15]. CD4+ also plays a role in immune recovery in TB as TB patients may experience suboptimal immune recovery compared to those without active TB. Studies highlight the slow but sustained increase in CD4+ count over time in cohorts with TB [16].

Drug resistance is a major concern in TB control. Although there is report of decreased risk of TB disease in contacts of MDR-TB cases associated with previous BCG vaccination, including in persons with prolonged exposure to MDR-TB cases, more information on BCG protection against drug-resistant strains of TB is still required [2]. In MDR-TB/HIV co-infected treatment-naïve patients, an advanced immunodeficiency with significantly lower CD4+ T cell counts is seen compared to MDR-TB mono-infected treatment-naïve patients [16].

Age and nutrition status have been identified by WHO as factors influencing risk of tuberculosis infection. Vitamin A and vitamin A supplementation have been fingered and studied as influencing immunity against TB infection [19-21]. A study found that supplementing zinc, lysine, and vitamin A for a duration of two months could result in an increase in total CD4+ count and in the levels of IFN- γ in pulmonary tuberculosis patients [20]. Additionally, a 2017 study on effect of Vitamin A and carotenoids on the risk of tuberculosis progression, indicated that Vitamin A deficiency strongly predicted the risk of TB among Household contacts (HHCs) of patients with tuberculosis. This suggests that supplementing Vitamin A for individuals at high risk of tuberculosis may provide an effective means of preventing TB [21]. An investigation on the impact of vitamin A deficiency on TB disease progression, noted that human and animal studies support the role of baseline vitamin A deficiency as a determinant of future TB disease progression [22]. There is therefore need to determine the absolute CD4+ count, CD4% and HB (haemoglobin) levels in TB patients undergoing TB treatment and also determine factors which could modify the values of these parameters.

BCG has for a hundred years now been used as vaccination against tuberculosis [18]. BCG remains the only approved vaccine against TB [19]. Scar formation is usually referenced as evidence of BCG vaccination [2].

There is currently no licensed vaccine that is effective in preventing TB disease (either before or after exposure of TB infection) in adults [19]. BCG protection wanes with age, the duration of protection after neonatal BCG vaccination could last between 10 to 20 years, however, one study reported up to 50–60 years protection against all TB outcomes following neonatal BCG vaccination [2, 25-29]. CD4+ cells also play a role in BCG induced immunity against TB [5, 13-15].

Human TB is caused by *M. tuberculosis*, however, possibility of bovine tuberculosis caused by *Mycobacterium bovis* exists. Unfortunately, Zoonotic TB is poorly monitored. Animals in TB endemic areas may be affected by reverse zoonosis, including multi-drug resistant strains [23-25]. M. bovis is naturally resistant to pyrazinamide which is a first line drug for treating TB in humans. In 2016, there were an estimated 147,000 new cases and 12,500 deaths due to zoonotic TB globally. The heaviest burden of which lies in the African region. It is believed that the true burden of zoonotic TB is probably underestimated, owing to a lack of routine surveillance data from most countries [25]. In 2017, 104,904 new cases of tuberculosis were notified, zoonotic tuberculosis incidence or prevalence in humans is unknown, but Incidence of MDR/RR-TB was about 24,000 [26].

Materials Methods

This was a cross-sectional study of eighty-five consenting HIV negative TB patients, confirmed by GeneXpert and on anti-TB drugs attending TB DOTS clinic at Barau Dikko Teaching Hospital in Kaduna State Nigeria between September 2020 to August 2021. Convenient sampling was used to select patients that attended the clinic during this period and consented to the study. All enrolees filled and signed consent forms after the study was explained to them.

Self-administered questionnaire and interview were used for the collection of demographic data, history, and factors influencing CD4+T lymphocytes count in tuberculosis, like BCG vaccination status, BCG scar, knowledge of zoonotic diseases knowledge of zoonotic tuberculosis, vitamin A supplementation, undernutrition (nutrition status), maternal BCG vaccination status and presence of maternal BCG from each consecutive consenting patient.

Three (3) millilitres (mls) of blood was collected by venipuncture from the 85 patients into sterile recommended vacutainers by qualified phlebotomists. Whole blood in EDTA was used for serological assay to determine absolute CD4+T lymphocytes count and CD4 percent levels and haemoglobin concentration immediately after collection. Multicolour fluorescence imaging and absorbance spectrometry microscopy using the Becton Dikinson (BD) FACSPresto™ was used to enumerate CD4+ absolute count (in cells/µL), CD4+ percentage (in %) and haemoglobin concentration (in g/dl) in whole blood. Handling and analysis of all data were in strict confidentiality. Enrolees were assigned numbers as codes for identification. Data were expressed in frequencies and percentages. Statistical analysis was done using Chisquare and Pearson correlation coefficient, significant at $p<0.005$. Excel spreadsheet (2010) and IBM SPSS® Statistics 26.0 were used for data statistical analysis. Ethical clearances were obtained from the Kaduna State Ministry of Health and Barau Dikko Teaching Hospital, Kaduna.

Results

Age of Respondents

The respondents were mostly between 17 to 65 years of age. Mean age of respondents was approximately 34 years, most of the respondents were either 20 or 21 years old, standard deviation was approximately 14 years (Table 1). There was no significant difference between the mean age of male and female respondents ($p <0.05$).

Table 1: Analysis of Age of Respondents

Statistic	Age (years)
Minimum age	17
Maximum age	65
Mode	20 and 21
Mean age	34
Standard deviation	14

Comparison of CD4 and HB Parameters between Male and Female Respondents

CD4+ count was assessed for all 85 respondents, however CD4% and HB was assessed for only 84 of the respondents as data for one respondent was not available for CD4% and HB.

The mean CD4+ count, CD4% and HB for males and females are shown in table 2.

There was significant difference in the CD4% between males and females ($p <0.05$) (Table 2).

Table 2: Comparison between CD4+, CD4% and HB between Males and Females

	Gender	N	Mean	Std. Deviation	Std.Error Mean	df	tcal	p-value
CD4	Male	47	697.23	305.353	44.540	83	-0.920	0.360
	Female	38	759.08	311.619	50.551			
CD4 %	Male	47	35.5889	9.39946	1.37105	82	-2.220	0.029
	Female	37	40.3711	10.29186	1.69197			
HB	Male	47	12.3270	2.31971	.33836	82	0.624	0.553
	Female	37	12.0257	2.02771	.33335			

Comparison of CD4+, CD4% and HB with Influencing Factors

About 67.0% of the respondents had been previously vaccinated with BCG and 58.82% had BCG scars, 20% reported that their birth mothers had BCG and 15.29% reported that their birth mothers had BCG scars. When assessed for their knowledge of zoonotic diseases and zoonotic TB, 49.41% reported that they were aware of zoonotic diseases and 42.35% reported awareness of zoonotic TB.24.71% of the respondents were taking vitamin A supplementation (Figure 1).

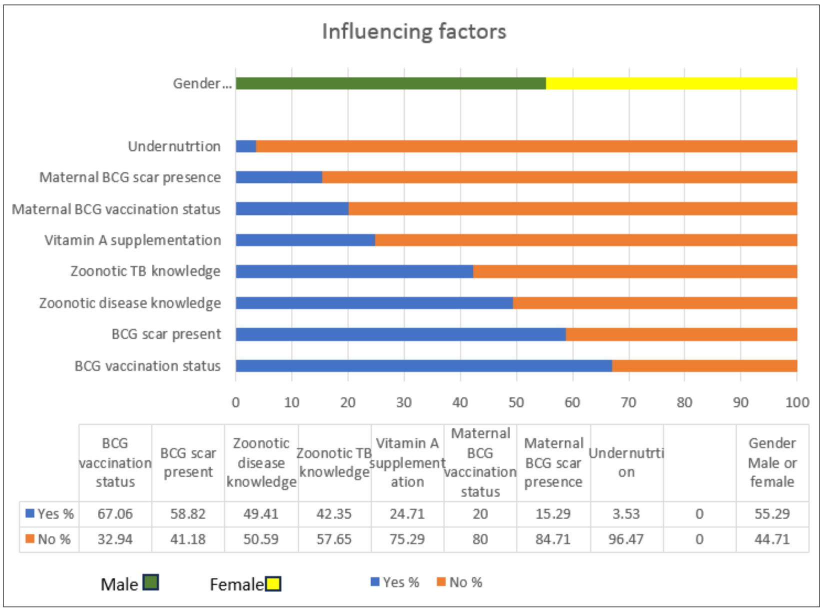

Figure 1: Influencing Factors for CD4+, CD4% and HB

BCG vaccination status, presence of BCG scar, knowledge of zoonotic diseases, knowledge of zoonotic tuberculosis and vitamin A supplementation showed no significant difference in the mean values of absolute CD4+ count, CD4% and HB ($p>0.05$) as shown in table 3.

Table 3: Comparison between CD4+, CD4% and HB with BCG Vaccination Status, BCG scar, Knowledge of Zoonotic Diseases, Knowledge of Zoonotic Tuberculosis and Vitamin A Supplementation

Influencing Factor	Parameter	Yes/No	N	Mean	Std. Deviation	Std. Error Mean	df	tcal	p-value
BCG Vaccination Status	CD4+	Yes	57	745.98	326.736	43.277	83	0.9	0.37
		No	28	681.93	265.758	50.224			
	CD4 %	Yes	56	38.0791	11.01101	1.47141			
		No	28	36.9279	7.83551	1.48077	82	0.494	0.623
	HB	Yes	56	12.0861	2.13155	0.28484	82	-639	0.525
BCG Scar	CD4+	Yes	50	731.78	352.188	49.807	83	0.245	0.807
		No	35	715.03	235.07	39.734			
		Yes	49	36.8451	11.82773	1.68968			
	CD4 %	No	35	38.8857	6.75355	1.14156	82	-0.918	0.361
		Yes	49	11.8867	2.1474	0.30677			
	HB	No	35	12.6249	2.20267	0.37232	82	-1.537	0.128
Knowledge of Zoonotic Disease	CD4+	Yes	42	676.79	338.66	52.256	83	-1.432	0.156
		No	43	771.86	270.272	41.216			
	CD4 %	Yes	41	36.4107	10.24148	1.59945			
		No	43	38.9202	9.78708	1.49252	82	-1.148	0.254
	HB	Yes	41	11.7993	2.24857	0.35117	82	-1.632	0.107
		No	43	12.5709	2.08559	0.31805			
Knowledge of Zoonotic Tuberculosis	CD4+	Yes	36	709.72	348.075	58.012	83	-0.387	0.7
		No	49	736.02	277.921	39.703			
	CD4 %	Yes	36	35.6175	11.79469	1.96578			
		No	48	39.2538	8.2639	1.19279	82	-1.662	0.1
	HB	Yes	36	11.8158	2.11197	0.35199			
		No	48	12.4781	2.22314	0.32088	82	-1.38	0.171
Vitamin A Supplementation	CD4	Yes	21	809.52	299.025	65.253	83	1.462	0.148
		No	64	697.11	307.943	38.493			
	CD4 %	Yes	21	37.1438	10.70595	2.33623			
		No	63	37.8792	9.87819	1.24453	82	0.289	0.773
	HB	Yes	21	12.3476	2.5244	0.55087			
		No	63	12.1432	2.08418	0.26258	82	0.369	0.713

Factors which have Significant Difference in CD4+, CD4% and HB Using Independent Sample T-Test

Conversely, maternal BCG vaccination status and presence of maternal BCG scar significantly affected the CD4% and absolute CD4+ count. There was significant difference in CD4+ count and CD4% compared with undernutrition ($p<0.05$) as shown in table 4.

Table 4: Comparison of CD4+, CD4% and HB with Maternal Immunization, Maternal BCG scar and Undernutrition

Influencing Factor	Parameter	Yes/No	N	Mean	Std. Deviation	Std. Error Mean	df	tcal	p-value
Maternal Immunization	CD4+	Yes	17	542.65	297.874	72.245	83	-2.841	0.006
		No	68	770.44	295.159	35.793			
	CD4 %	Yes	17	32.44	12.562	3.04673	82	-2.494	0.015
		No	67	39.0288	8.90797	1.08828			
	HB	Yes	17	11.4218	1.61885	0.39263	82	-1.647	0.103
		No	67	12.3903	2.27894	0.27842			
Maternal BCG Scar	CD4+	Yes	13	499.23	301.489	83.618	83	-3.005	0.004
		No	72	765.63	292.876	34.516			
	CD4 %	Yes	13	29.9585	13.4379	3.727	82	-3.188	0.002
		No	71	39.112	8.6711	1.02907			
	HB	Yes	13	11.2054	1.8645	0.51712	82	-1.796	0.076
		No	71	12.3754	2.20606	0.26181			
Undernutrition	CD4+	Yes	3	322	89.062	51.42	83	-2.37	0.02
		No	82	739.62	303.106	33.472			
	CD4 %	Yes	3	27.6133	7.96078	4.59616	82	-1.797	0.076
		No	81	38.0688	9.94218	1.10469			
	HB	Yes	3	11.7	0.2	0.11547	82	-0.396	0.693
		No	81	12.2126	2.22651	0.24739			

Relationship between age, CD4+ count, CD4% and HB

Table 5: Pearson Correlation - Relationship between Age, CD4 count, CD4% and HB

		Age	CD4	Absolute CD4	HB
Age	Pearson Correlation	1	-.051	-.047	.015
	Sig. (2-tailed)		.641	.670	.889
	N	93	85	84	84
CD4	Pearson Correlation	-.051	1	.535**	.128
	Sig. (2-tailed)	.641		.000	.247
	N	85	85	84	84
Absolute CD4	Pearson Correlation	-.047	.535**	1	.060
	Sig. (2-tailed)	.670	.000		.586
	N	84	84	84	84
HB	Pearson Correlation	.015	.128	.060	1
	Sig. (2-tailed)	.889	.247	.586	
	N	84	84	84	84

**. Correlation is significant at the 0.01 level (2-tailed).

Pearson correlation coefficient indicated weak negative relationship between CD4%, absolute CD4+ count and age (Table 5), suggesting that older people tend to have lower percentages of CD4+ T cells and lower absolute CD4+ count in the blood. Also, there was a weak positive relationship between HB and age. Indicating that older people tend to have higher hemoglobin levels in the blood, however, this correlation is not significant and may be influenced by other variables. The relationships betweenCD4%, absolute CD4+ count and HB were not statistically significant (p>0.05).

Discussion

In our study, the age groups which had the greatest number of respondents were ages 20 and 21 years. This is similar to what was reported in another study in Akwa Ibom state [14]. This age range are potentially at higher risk of TB due to transitional lifestyles post-adolescence. They are more itinerant than other age groups and having just come out of adolescence, may engage in activities and lifestyles which make them more at risk of getting tuberculosis. The age distribution pattern seen in our study agrees with the WHO 2022 report, that tuberculosis mostly affects adults [19]. However, in contrast to WHO 2020 report which stated that, the elderly (those 65 years and older) was the largest group of people living with TB infection, particularly in developed countries , in our study, only 2 respondents (3.2%) were up to 65years of age [25]. The majority of the TB cases in a study carried out in Delta state, were in the age group 31-45 years age, which is in variance with what we have reported [33]. However, since the next age group in their study was 16 – 30, this age group (20 and 21 years) should be of interest in TB preventive interventions, the difference in age prevalence in the two studies may be a context of location and lifestyle.

In our study, 55.29% of the respondents were male; this also agrees with the WHO report for 2022 and other reports that more men than women are affected with tuberculosis and in contrast with a report of higher prevalence of TB in females [13, 19, 33]. Nigeria's country profile for 2019 published by WHO in 2020, shows that out of the 440,000 people who fell ill with tuberculosis, a little more than half (55%) of them were men (25). In 2021, 56.5% of all TB cases globally were men, 32.5% of the cases were women while children accounted for the remaining 11% of the cases [19].

We report that the mean absolute CD4+ count and CD4% levels of the males and females in this study were noted to fall within the normal reference values of absolute CD4+count (500 to 1500 cells/μL) and CD4% (25% to 65%) (reference values used in the study location lab.). This may be because all respondents were HIV naïve, hence their mean CD4+ counts and CD4% were within acceptable limits. Overall, the mean HB values for both males and females were also within the acceptable range of HB 12 to 15.5g/dl, however, the mean value for males (12.32g/dl) seen in our study is lower than minimum reference value of 13g/dl for this clinic (reference values used in the study location lab).). That the mean CD4+ count reported in our study are closer to the lower limit, may be an indication of confirmation that CD4+ counts are lower in individuals infected with TB. Though not directly assessed in our study, TB treatment and TB disease progression also affect CD4+ count [9, 16]. A study in Nigeria which followed CD4+ counts from baseline through a course of six months of treatment, reported much lower mean CD+ counts at baseline compared to after six months of treatment [9]. Another study in Delta state, Nigeria reported higher mean CD4+ in females compared to males however, mean CD4+ for males was lower than what we observed in this study and the value they reported for females was slightly higher than what we observed [33].

From our results, absolute CD4+ count, CD4% and HB have a statistically linear relationship. The values for these variables tend to increase together (i.e., greater CD4+ count is associated with greater CD4% and greater HB). The magnitude, or strength, of the association was approximately moderate ($.1 < | r | < .4$).

In our study, although there was no significant difference between mean age of males and females, indicating a balanced age distribution in both gender groups, absolute CD4+ count significantly differed between male and female respondents.
Our study reported more than half (58.8%) of the respondents had BCG scars, this is consistent with another study outside Nigeria, where most (68.1%) subjects with TB who had been vaccinated with BCG had BCG scars [5]. Usually when children are vaccinated with BCG a scar usually forms from a papule with induration which appears at the site of intradermal administration of BCG [2, 29-32]. Even though the presence of a scar has been associated with evidence of BCG vaccination, this is not always a reliable evidence of BCG vaccination against tuberculosis. The scar also does not determine whether an individual is fully immune to tuberculosis [18]. In our case, finding BCG scars in more than half of the respondents suggests that the BCG programme in this population is active and has a wide reach. However, since the respondents were all confirmed TB patients undergoing treatment, having individuals who had previously been vaccinated with BCG (with evidence of scars) in this group suggests that the conclusion that BCG protection wanes with age may be true [25-29]. This gives credence to the suggestion that BCG vaccination does not last a lifetime as it does not offer good protection in adulthood [2, 27-29]. This evidence that BCG protection diminishes with age suggests a need for booster vaccinations or alternative interventions for adults. This is further supported by the fact that the results in our study show that there was no significant effect of BCG vaccination status on CD4+, CD4% and HB.

Factors that significantly influenced CD4+, CD4% and HB included maternal BCG vaccination and undernutrition. Reports of better immune cover for children whose mothers have been vaccinated with BCG with or without the presence of a BCG scar are available [29-30, 34].

It is known that undernutrition is a risk factor for the probability of developing TB disease [19, 35-37]. Many of the people who are already at high risk of TB infection, such as impoverished people living in crowded, unsanitary housing, are also likely to be undernourished. In our study, three (3.5%) respondents were undernourished. Undernutrition reduces the body's immune defenses against TB and encourages the transition from latent infection to active disease. The disease can also impair the body's ability to absorb nutrients and micronutrients, leading to malnutrition and wasting [19]. Undernutrition increases the likelihood of developing TB, particularly in individuals living in impoverished and unsanitary conditions [38].

24.71% of the respondents were taking vitamin A supplements. Vitamin A supplementation has shown potential benefits in boosting CD4+ counts and immunity in TB patients [20]. Also, vitamin A may be associated with decreased TB risk, poor treatment compliance and outcomes [20, 38]. Unfortunately, our study found no significant difference in the mean values of CD4, CD4%, and HB between those taking vitamin supplements and those who were not. This may be because of the sample size or number respondents on vitamin A supplementation or presence of other influencing factors such as age, gender, nutrition status, infection history, genetic factors, or other interventions.

Our results showed that only about half (49.41%) of the respondents were aware of zoonotic diseases and less than half (42.35%) reported awareness of zoonotic TB. Also, 27% of respondents reported that they suspected they might have zoonotic TB, potentially linked to their occupations or dietary habits. This is either because they were animal health workers, butchers or animal farmers. Additionally, 73% reported that they handled raw meat and 58.7% reported that they drank unpasteurised milk. Awareness on zoonotic TB needs to be improved among TB patients as this group of people may be at risk. Zoonotic TB may pose a risk of drug resistance [23].

In summary from our results, while there was no significant difference in mean age between males and females, CD4 counts showed significant variation between genders. The mean CD4+ count was higher in females (759.08cells/μL) compared to males (697.23cells/μL). CD4% count significantly differed between male and female respondents. The gender of the patient also influenced level of CD4% in tuberculosis patients undergoing TB treatment. However, the relationship between CD4%, absolute CD4, and age was weak and not statistically significant, even though there was a weak negative correlation between CD4%, absolute CD4 count, and age. There was a weak positive correlation between hemoglobin levels and age, but it was not statistically significant. CD4, CD4%, and hemoglobin levels showed a statistically significant positive linear relationship, indicating that higher CD4 counts were associated with higher hemoglobin levels. BCG vaccination status, presence of BCG scar, knowledge of zoonotic diseases, knowledge of zoonotic tuberculosis, and vitamin A supplementation did not significantly affect CD4 parameters. Normal absolute CD4+ (500 to 1500cells/µL) and CD4% (25% to 65%) could be altered by presence of some factors. In our study, we have seen that undernutrition, drug resistance, age, gender and maternal immunization (with or without presence of BCG scar) are likely to influence levels of absolute CD4+ count and CD4% than BCG vaccination status, presence of BCG, vitamin A supplementation, knowledge of zoonotic diseases and/or knowledge of zoonotic tuberculosis among TB patients. Pearson correlation coefficient indicated weak negative relationship between CD4%, absolute CD4+ count and age.

Conclusion

Our study suggests that undernutrition, maternal immunization (with or without presence of maternal BCG scar) and gender play roles in immunity against tuberculosis and influence levels of CD4+ and CD4% in TB patients. There is a weak negative relationship between CD4%, absolute CD4+ count and age.

This study highlights the influence of gender, maternal BCG vaccination (with or without presence of scar), vitamin A supplementation, nutritional status (undernutrition) and age as factors influencing TB prevalence and CD4+ levels (as a measure of immune status) in TB patients.

We therefore recommend that TB vaccines development targeting CD4+ T cells should consider these factors as they could influence outcome of such efforts.

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