The Relation Between Active Pulmonary Tuberculosis Patients and Level of Serum Calcium

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Conflict of interest
None declared by author

Abstract

Background: Tuberculosis is a bacterial infection caused by Mycobacterium tuberculosis, usually characterized pathologically by the formation of granulomas. The most common site of infection is the lung, but other organs may be involved. It is spread through the air when people who have the disease cough, sneeze, or spit.

Objective: To assess the level of serum calcium in adult patients with active pulmonary tuberculosis.

Patients and method: A case control study was carried out in respiratory and chest disease specialized center/medical city complex from the 1st of December 2017 to the end of May 2018. (80) Respondents were included in the current study and divided into 2 groups: 40 patients with pulmonary Tuberculosis and other group contain 40 healthy controls. TB patients were previously diagnosed in the Respiratory and chest center.

Results: The range of age regarding to the Tuberculosis group were from 17- 59 years old with the mean age of 36.95±12.6 years. The main age group is between 30-39 age group. Male were dominant than female in which it represents 22(55%) in the cases group. Serum calcium level in studied groups, it varied from (6.6 -10.4 mg/dl) in Tuberculosis group with a mean level of 8.99±0.64 mg/dl. In control group, serum calcium level varied from 8.2 to 10.0 mg/dl with a mean reading of 9.01±0.43 mg/dl. There was no significant difference in mean levels between TB patients and comparison group according to this study (P > 0.05) VIII.

Conclusion: Serum calcium levels tend to be lower in active pulmonary tuberculosis patients than normal (control) group but with no statistically significant differences.

Keywords: Active pulmonary Tuberculosis, Serum calcium levels, Case control study

1. INTRODUCTION

Tuberculosis is a bacterial infection caused by Mycobacterium tuberculosis, usually characterized pathologically by the formation of granulomas. The most common site of infection is the lung, but other organs may be involved (1). It is spread through the air when people who have the disease cough, sneeze, or spit (2). Tuberculosis (TB) remains a major health problem in the world it causes ill health among millions of people each year and ranks as the second leading cause of death from an infectious disease worldwide (3). About one third of the human population (about 1.86 billion people) Worldwide are infected with Mycobacterium tuberculosis (MTB), the bacterium that causes tuberculosis; and 10% of these progress to develop active tuberculosis disease (4). In addition, 95% of these reported TB cases and 98% of the resulting deaths are from developing countries, of which 23% and 55% of these death having been documented to come from south Asia and Sub-Saharan Africa respectively (5). Global burden The WHO estimates that over 4 000 people die of TB every day and 3 million TB cases are missed by health care systems (6). The TB burden is most significant in developing countries, with developed countries having the lowest TB prevalence. In Iraq the National Tuberculosis Program (NTP) reports that the total number of TB patients exceeded 8,000 individuals. Of those, 29 percent Introduction pg. 2 were completely cured, 62 percent successfully completed treatment, and 3 percent (240 people) died from TB (7). Iraq is an upper middle-income country in the Eastern Mediterranean Region. The Region accounts for 25% of the global burden in 2014. TB is a public health priority in Iraq. The country is among 7 of the countries of the Region with a high burden of TB, and accounts for 3% of the total number of cases. There are an estimated 20 000 TB patients in Iraq. Estimated deaths due to TB are more than 4000 annually (8). Calcium is the fifth most abundant element in the human body, it plays a key role in skeletal mineralization, as well as a wide range of biologic functions (9). In some individuals, particularly the elderly, calcium supplements may be needed to achieve the recommended dietary calcium intake. (10). Calcium plays a key role in a wide range of biologic functions, either in the form of its free ion or bound complexes. One of the most important functions as bound calcium is in skeletal mineralization. (11). Serum calcium ranges from 8.8 to 10.4 mg/dl in healthy subjects.

It comprises free ions (51%), protein-bound complexes (40%), and ionic complexes (9%). Nonionized calcium is bound to a variety of proteins and anions in both the extra- and intracellular pools. The main calciumbinding proteins include albumin and globulin in serum and calmodulin and other calcium-binding proteins in the cell. The major ionic complexes in serum are calcium phosphate, calcium carbonate, and calcium oxalate (12).

2. METHODOLOGY

A case control study was carried out in respiratory and chest disease specialized center/medical city complex from the 1st of December 2017 to the end of May 2018. Patients: 80 respondents were included in the current study and divided in to 2 groups: 40 patients with active pulmonary TB and other group contain 40 healthy controls.

Inclusion criteria:

All patients diagnosed to have pulmonary TB, who previously diagnosed either by sputum for acid fast bacilli positive, sputum culture or Xpert / RIF test.

Exclusion criteria:

1. History of neoplastic disease

2. History of thyroid

3. History of parathyroid disease

4. History of adrenal disease

5. History of renal disease

6. Patients taking cortisone, anticoagulant, diuretic, calcium supplement, vit D tablet. Patients and method pg. 6 Method: Serum calcium measurement performed for all sample of study (TB and control) groups. Ethical consideration: The purpose and procedures explain to all participants and were give the right to participate or not, verbal consent was taken with reassurance that interpret gained will be kept confidentially and not to be used for other research object.

Statistical analysis: All patients' data entered using computerized statistical software; Statistical Package for Social Sciences (SPSS) version 21 was used. Descriptive statistics presented as (mean ± standard deviation) and frequencies as percentages.

3. RESULTS

This study enrolled 80 persons, 40 persons are TB patients (50%) as TB group and 40 persons (50%) as a control group. Age varied in TB group from 17 to 59 years with a mean age of 36.95±12.6 y. In the control group, age varied from 17 to 55 y with a mean age of 34.95±9.4 year. The smallest age group on both study groups is under 20 year. Numbers of males were 22 (55%) in TB group and 16 (40%) in comparison group. Numbers of females were 18 (45%) in TB group and 24 (60%) in comparison group. Regarding serum calcium level in studied groups, it varied from 6.6 to 10.4 mg/dl in TB group with a mean level of 8.99±0.64 mg/dl. In control group, serum calcium level varied from 8.2 to 10.0 mg/dl with a mean reading of 9.01±0.43 mg/dl. There was no significant difference in mean levels between TB patients and comparison group according to this study ($P > 0.05$). Mean calcium levels did not vary significantly between age groups within study group and control group and between the same age groups from the two groups ($P > 0.05$). Mean calcium levels did not vary significantly between both genders within study group and control group, at the same time it did not vary significantly as well between the same genders from the two groups ($P > 0.05$), all findings are demonstrated in (Table 1 and Figures 1 , 2 & 3)

Table 1. Age and sex characteristics of sampled patients and serum calcium levels according to study group

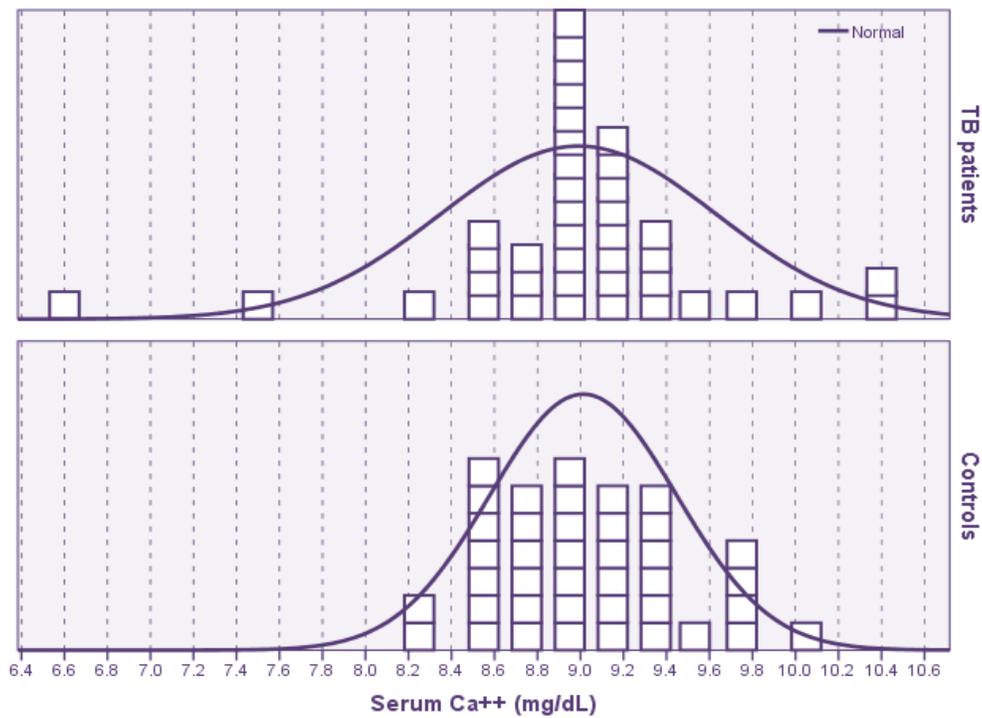| Variable	Category	TB patients (n=40)		Controls (n=40)		P. value
		No	%	No	%	
Age (year)	<20	2	5.0	1	2.50	0.455
	20-29	10	25.0	11	27.50	
	30-39	11	27.5	17	42.50	
	40-49	8	20.0	7	17.50	
	≥50	9	22.5	4	10.00	
	Mean ±SD	36.95±12.6		34.95±9.4		
	Range	17-59		17-55		
Gender	Male	22	55.0	16	40.0	
	Female	18	45.0	24	60.0	
S. Calcium (mg/ dL)	Mean ±SD	8.99±0.64		9.01±0.43		0.855
	Range	6.6-10.4		8.2-10.0		

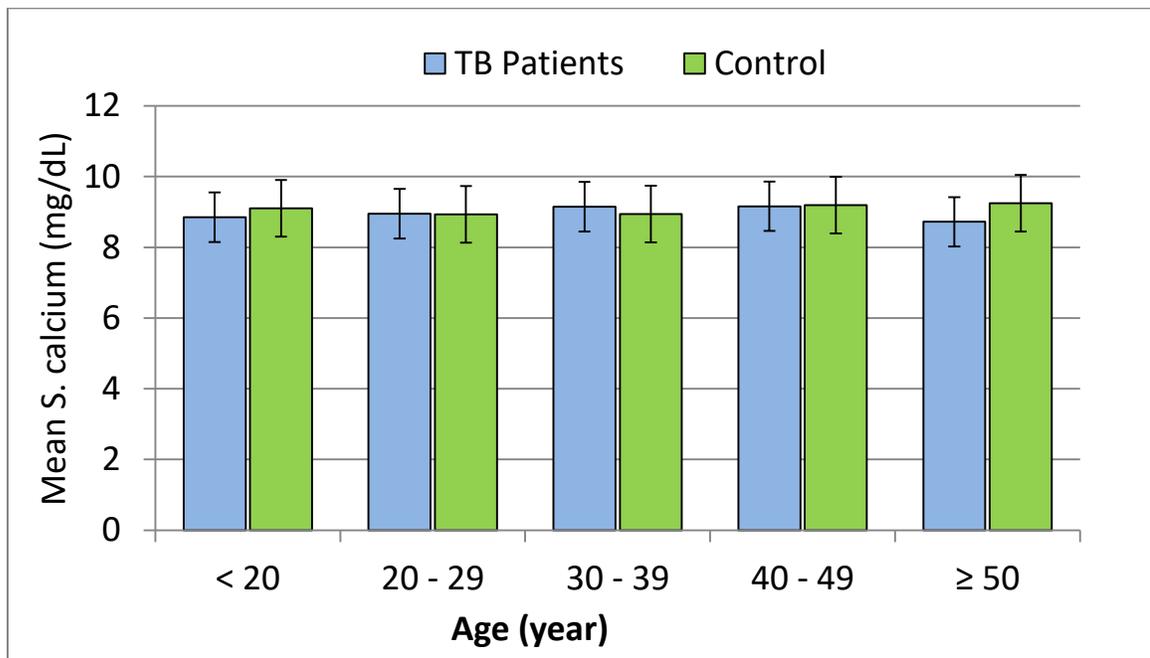Figure 1. Measured levels of serum calcium according to study group and control group.

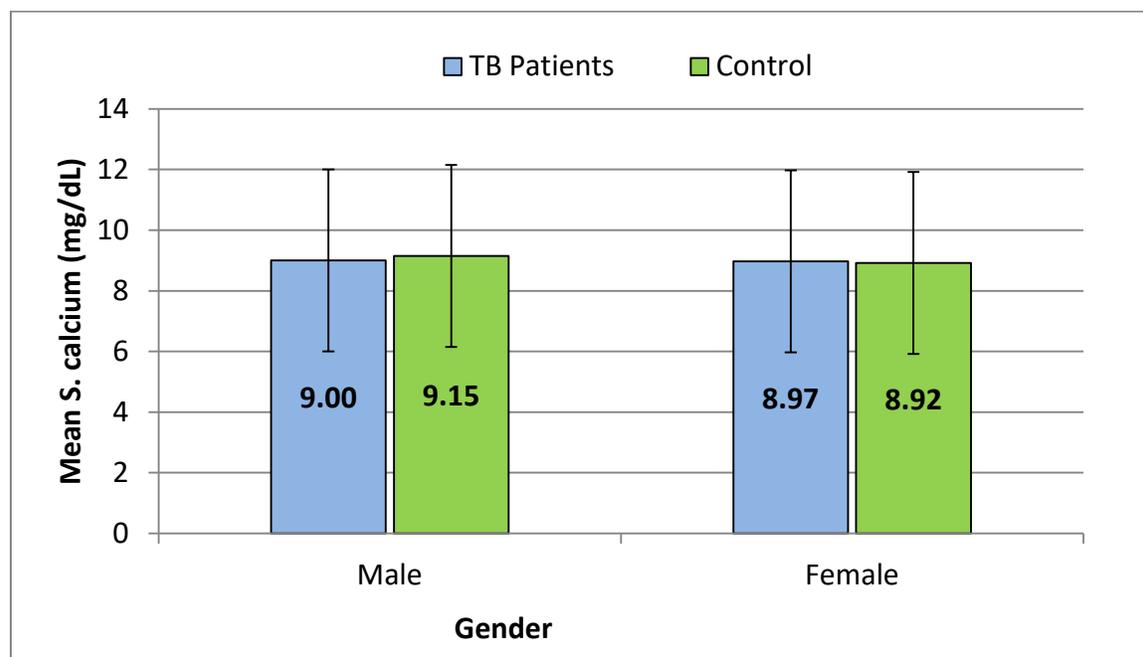Figure 2. serum calcium levels in study and control groups according to Age,(P>0.05)

Figure 3. serum calcium levels in study and control groups according to Gender, (P>0.05)

4. DISCUSSION

Worldwide TB is more common among men and affects mostly adults in the economically productive age groups, around two-thirds of cases estimated to occur among people aged 15–59 years (13). This is similar to that revealed in the current study when male with TB infection were dominant than female, and this is same that mentioned by Yap B et al., 2014 study (14). Moreover In the current study; about two third (77.5%) of the patients were in age < 50 years old which is same that reported by Mukhtar A. et al.(15) in Libya in 2009, who found that majorities of their patients at this age group. Moreover, in Sudan, in 2006, Mohamed A. et al. (16) found that 83.8% of the respondents were below 50 years. Some studies report hypercalcemia associated with tuberculosis (17-23), some others report hypocalcemia as a finding in the disease (24-26). Low serum calcium was not considered the predisposing cause of tuberculosis until the recent past, where different workers from different centers of the world were able to show that tuberculous patients were often associated with hypocalcemia (27, 28). In Rohini K et al, (29) study, the mean serum calcium

in PTB patient before treatment was less (by nearly 1.2-fold) than that of normal controls and this was statistically extremely significant (p <0.001).

Hafiez et al., (25) in their studies attribute the hypocalcemia to impaired intestinal absorption of calcium or deficient intake as a result of anorexia, decreased plasma albumin or decreased active metabolites of vitamin D. Ijaz et al. (26) have attributed their finding of hypocalcemia to malnutrition and malabsorption associated with tuberculosis.

According to Islam et al., tuberculosis is the disease of people who live in underprivileged conditions like dark homes and with poor nutritional intake. It is a well-known fact that poor exposure to sunlight results in vitamin D deficiency that along with low intake of milk leads to hypocalcaemia. Rohini K et al.(29) presume that the decreased physical activity experienced by the patients due to the rest advised in the event of the disease could be a reason for less exposure to sunlight. This could lead to vitamin D deficiency and hence hypocalcemia. Mehto S et al, (30) revealed that hypocalcemia is a problem in tuberculosis which is related to poor nutritional status; therefore, calcium phosphate agents are proposed to be used during anti-TB therapy. Abnormalities in calcium, metabolism have not been studied in our population of Pulmonary TB and this is first study to measure the level of serum calcium done in Iraq. The serum levels of calcium in patients with pulmonary TB in the current study were lower than that in control group but with no significant difference in mean serum calcium level between two groups . Same that found in Iranian study done in 2017 by Sepehri Z et al,(31) when he study the essential and toxic metals in serum of individuals with active pulmonary tuberculosis in an endemic region. The most striking finding of the Ijaz A et al, (26) study was presence of hypocalcemia in pulmonary TB patients. This finding is consistent with earlier studies from Japan (31,32), and Nigeria (27). Surprisingly the percentage of hypocalcemia patients found in Ijaz A et al,(26) study (35%) is also quite close to that reported in Japanese study (38%) (24). The number of pulmonary TB patients with hypercalcemia was found to be very low (5.2 %). This is in contrast to the reports from Sweden (17), US (18) and Greece (19) while closer to that reported from Hong Kong (22). It is well known that alteration of serum Ca levels in various infections (33). In one study from India, hypocalcemia was reported by the investigators, the mean serum Ca levels

were 9.3 ± 0.46 mg/dl, 7.72 ± 1.02 mg/dl, respectively in the smear negative (SN) and SP individuals (29).

In Chandra T study,(34) newly diagnosed PT patients before initiation of ATT were included in the test group, the mean serum Ca was 7.2 mg/dl. In the control group, all were healthy individuals; never had TB and SN for AFB. In the control group, the mean serum Ca level was 9.4 mg/dl. In this study, hypocalcemia was observed among the SP cases and statistically the difference was not significant between the groups (P>0.05). It has been reported that hypercalcemia is more often encountered during the first weeks of antituberculosis treatment, when hypercalcemia may be found in approximately 30–50 % of the patients (35,36). According to Kitrou et al. (37) hypercalcemia in patients with PTB seems to be triggered by chemotherapy although the mechanism(s) by which anti-tuberculosis treatment affects calcium metabolism remains uncertain. An increase in the calcium content of the body tissue and blood apparently tends to lessen capillary permeability, thereby lessening the amount of exudate, preventing an extension of the infecting organisms and tending to limit the destruction by their toxins (38).

Limitation of the study:

1. Small sample size with short period of time for the study

2. Single center study

3. One sample of the blood were taken from the respondents

4. Only serum calcium was evaluated

5. CONCLUSIONS

Serum calcium levels tend to be lower in active pulmonary tuberculosis patients than normal subjects but with no statistically significant differences in mean serum calcium level between two populations.

Ethical Approval:

All ethical issues were approved by the author. Data collection and patients enrollment were in accordance with Declaration of Helsinki of World Medical Association , 2013 for the ethical principles of researches involving human. Signed informed consent was obtained from each participant and data were kept confidentially.

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