

**VITAMIN 'D' AND TUBERCULOSIS****Dr. Laxmikanta Mohanty¹ and Dr. Ambad Ranjit Sidram*²**¹Associate Professor Dept. of Respiratory Medicine CCM Medical College Durg.²Assistant Professor Dept. of Biochemistry CCM Medical College Durg.***Corresponding Author: Dr. Ambad Ranjit Sidram**

Assistant Professor Dept. of Biochemistry CCM Medical College Durg.

Article Received on 20/03/2018

Article Revised on 10/04/2018

Article Accepted on 30/04/2018

SUMMARY

Total 20 TB infected patients were selected for study group and compare with 25 normal healthy control groups. All patients of TB infection are diagnosed by clinician and admitted in our hospital for treatment. Informed consent was taken from all patients, who participated in our study and the study was approved by the hospital ethics committee. TB was defined as microbiological or histological evidence of MTB infection and/or receipt of treatment for TB during the study period, past TB was defined as documentation of having completed treatment for TB, LTBI was defined as a positive test result (diameter, ≥ 10 mm) and a positive QFT-G test result and no evidence of TB or history of TB, any MTB infection was defined as evidence of MTB infection and no MTB infection was defined as a negative test result and neither current TB nor past TB. Patients in the TB and past TB groups were combined for the analysis, because we were interested in those whose infection had progressed to TB.

INTRODUCTION

Tuberculosis (TB) is a respiratory illness that usually affects the lungs, but it also infects kidney, spine and brain. TB is of two types dormant and active. Dormant tuberculosis means that you become infected with bacteria, but you are not sick and you're not contagious. TB becomes activated in weak immune system peoples. People with strong immune systems can live with dormant TB without ever having symptoms. People who have dormant TB are not contagious. TB becomes active when your immune system can't stop the bacteria from growing. A weak immune system means that it will be easier for the TB bacteria to multiply in your body, causing you to become sick. People with active TB are contagious and can spread it to other people.^[1]

Vitamin D is having important role in macrophage activation and the subsequent restriction of MTB growth,^[2] and it has been implicated as a tuberculosis risk (TB).^[3] An association between vitamin D (i.e. 25[OH] D) levels and TB has been already described in several studies.^[4-6] An association between 25(OH) D levels and latent tuberculosis infection (LTBI) has not been well described. Vitamin D is an important part of your immune system. Vitamin D can help to increase the amount of good immune proteins that fight and destroy bacteria. People with low levels of vitamin D are more likely to develop dormant tuberculosis, and are also more likely to progress to active tuberculosis. Having high levels of vitamin D may be a way to help prevent tuberculosis infection, but more experiments need to be done to say for sure. Some authors have shown that people with tuberculosis who take vitamin D

supplements have a faster recovery and fewer symptoms. More experiments are needed to determine whether or not vitamin D can help to treat tuberculosis.^[7]

Symptoms of active TB include.^[1]

- a) A bad cough for more than 3 weeks
- b) Chest pain
- c) Coughing up blood or mucus
- d) Feeling weak
- e) Weight loss
- f) No appetite
- g) Fever, chills, or night sweats.

Before discovering antibiotics for TB, sun therapy was used as treatment for peoples. Physician or clinician thought that something in the sun was helping to TB people, which shows that vitamin D plays important role in curing TB. Vitamin D is synthesized in the skin from sunlight. Vitamin D receptors are found on the surface of a cell, where they receive chemical signals. By attaching themselves to a receptor, these chemical signals direct a cell to do something. Vitamin D receptors found on immune system and respiratory tract, and it can bind with receptor. Vitamin D works in the immune system and lowering levels of bad inflammatory proteins, while at the same time increasing amounts of good antimicrobial proteins that can destroy TB bacteria. Vitamin D helps to immune system to kill the TB bacteria.^[8]

Macrophages are good cells in the immune system. Macrophages "eat" invading bacteria and viruses, which protects your body from TB infection and illnesses. The

TB bacteria try to attack on your macrophages and infect your body. Vitamin D helps your immune system by making macrophages stronger and fights the TB bacteria [9-10]. Many studies show that people with low levels of vitamin D are more likely to get TB than people with higher levels of vitamin D.^[7] Another major determinant to the free and total circulating 25(OH) D concentration is the vitamin D binding protein (DBP); in circulation it binds 85–90% of the 25(OH) D and in circulation increases the half-life of 25(OH) D as a vitamin D reservoir, and aids in reabsorbing vitamin D filtered in the kidney.^[11-13]

Some studies have showed a role for vitamin D in promoting the environment associated with antibacterial activity. Autophagy is the cellular process of degrading cytosolic components including decaying organelles and nonfunctional proteins, and has also been linked to immune processes and TB disease. It is therefore interesting to note studies showing that 1,25D promote autophagy in monocytes, with inhibitors of autophagosome formation suppressing antibacterial activity.

MATERIAL AND METHODS

Total 20 TB infected patients were selected for study group and compare with 25 normal healthy control groups. The study will be conducted in the patients admitted in the Department of TB and Chest in collaboration with Dept. of Biochemistry, Intensive Coronary Care Unit at Chandulal Chandrakar Memorial Medical College, Kachandur, Durg. All patients of TB infection are diagnosed by clinician and admitted in our hospital for treatment. Informed consent was taken from all patients, who participated in our study and the study was approved by the hospital ethics committee.

Tb Status was classified as Follows

TB was defined as microbiological or histological evidence of MTB infection and/or receipt of treatment for TB during the study period, past TB was defined as documentation of having completed treatment for TB, LTBI was defined as a positive test result (diameter, ≥ 10 mm) and a positive QFT-G test result and no evidence of TB or history of TB, any MTB infection was defined as evidence of MTB infection and no MTB infection was defined as a negative test result and neither current TB nor past TB. Patients in the TB and past TB groups were combined for the analysis, because we were interested in those whose infection had progressed to TB.

Collection of Blood sample

5 ml fasting blood sample was collected in a dry, clean, plane tube from TB patients. After clotting of blood, it is centrifuged at 3000 r.p.m. for 10 minutes. Serum will separate for the analysis of Vit D.

The activity of Vit D measured by using 25-hydroxyvitamin D (25OHD) assays used for determination of vitamin D status.^[14]

Control Group

Total 25 normal healthy 20-64 years adult, age & sex matched subject comprises for control group.

Data Analysis

Data were expressed as mean \pm SD. Mean values were assessed for significance by unpaired student $-t$ test. A statistical analysis was performed using the Stastical Package for the Social Science program (SPSS, 21.0). Frequencies and percentages were used for the categorical measures. Probability values $p < 0.05$ were considered statistically significant.

Table 1: Showed mean value of Age in patients with TB compared with control groups.

Age group	20-25	26-30	31-35	36-40	41-45	46-50	51-55	56-60	Above 60
No of Normal subjects	3	3	7	2	3	2	2	2	1
No of TB Patients	1	2	2	4	7	1	1	1	1

Table 2: Showing sex wise distributions in TB patients and control group.

Age group	20-25	26-30	31-35	36-40	41-45	46-50	51-55	56-60	Above 60
Male	2	2	5	2	2	2	2	1	1
Female	1	1	2	0	1	0	0	1	0
Total Control	3	3	7	2	3	2	2	2	1
Male	1	2	2	3	4	0	1	1	0
Female	0	0	0	1	3	1	0	0	1
Total Patients	1	2	2	4	7	1	1	1	1

RESULT AND DISCUSSION

The study was conducted in Dept. of Respiratory medicine in collaboration with dept. of Biochemistry from June 2017 to March 2018 at Chandulal Chandrakar Memorial Medical College Kachandur, Durg. Patient group included 14 (70%) males and 6 (30%) females. Sex-matched controls were selected from the hospital registry where 19 (76%) males and 6 (24%) females were included in group II. In patient group, mean \pm SD

age was 46.60 ± 21.87 years. Age-matched controls were selected as group II from the registry with a mean \pm SD age of 44.72 ± 19.94 years. There was no statistically significant difference between the studied groups regarding age ($p = 0.8$). Patient group included 11 (55%) smokers and 9 (45%) non-smokers. control included 15 (60%) non-smokers and 10 (40%) smokers. There was no statistically significant difference between the two groups regarding smoking status ($p = 0.5$).

Our study shows in patient group, on commencing the anti-TB treatment, Serum vitamin D deficiency was defined in 19(95%) patients, serum vitamin D insufficiency was detected in a single (5%) patient while there were no single case found where serum vitamin D toxicity was found. Mean serum vitamin D level at the start of treatment was 8.73 ± 4.38 ng/dl. After 2nd month's treatment, serum vitamin D deficiency was detected in 4 (20%) patients, serum vitamin D insufficiency was traced in 11 (55%) patients, serum vitamin D sufficiency was found in 5 (25%) patients, and there is no serum vitamin D toxicity. Mean serum vitamin D level after second month treatment was 21.76 ± 6.83 ng/dl and in case control groups the level of Vit D were 37.91 ± 4.28 ng/dl. On the basis of activity of Vit D found that there was a statistically significant difference between the control group and patient group at the start of treatment and the end of 2nd month anti-TB treatment. Similar findings were found in Essam Gouda Hassanein *et al.* Studies,^[15] and shows that the improvement observed in vitamin D supplemented TB therapy. Vitamin D is safe when added to anti-tuberculous drugs. Vitamin D deficiency is common among TB patients. In the study of Sutaria *et al.* was used vitamin D for treat TB patients during the pre-antibiotic era, trials in recent years have continued to assess its role in the treatment and prevention of TB and concluded that individuals with TB had lower vitamin D status (lower serum levels of 25(OH) D) than healthy, age-matched, and sex-matched controls.^[16]

At the start of TB treatment, patients group included 14 patients who were hypocalcemic, 6 were normocalcemic, and there were no patients with hypercalcemia. After 2nd month of TB treatment, 4 patients were hypocalcemic, 10 patients were normocalcemic and 6 patients were hypercalcemia. The mean serum calcium level after 2nd month of TB treatment was 3.94 ± 0.63 mg/dl and before treatment it was 9.16 ± 2.83 mg/dl. There was a statistical significant difference in serum calcium level at the beginning and after 2nd month of treatment.

Martineau *et al.*^[17] showed that serum calcium level declined in both intervention and control arms after initiation of antimicrobial treatment. Such a decline might have resulted from a reduction in granulomatous burden in patients responding to treatment, leading to a decrease in extra-renal 1-alpha hydroxylation of 25-hydroxy-vitamin D and a fall in serum 1, 25-dihydroxyvitamin D concentrations.

In a research carried out in Jakarta The effect of vitamin D as supplementary treatment in patients with moderately advanced pulmonary tuberculous lesion the group treated with vitamin D had higher sputum conversion and radiological improvement (100%) as compared to the placebo group.

CONCLUSION

On the basis of our result and supportive findings of some studies concluded that vitamin D used as a supplementation during tuberculosis therapy. It increases activity of cell-mediated immunity and reduces bacterial growth. Because there is no risk of supplementation it is safe.

REFERENCES

- Centers for Disease Control and Prevention. Tuberculosis (TB), 2012.
- Chandra G, Selvaraj P, Jawahar M *et al.* Effect of vitamin D3 on phagocytic potential of macrophages with live Mycobacterium tuberculosis and lymphoproliferative response in pulmonary tuberculosis, J Clin Immunol, 2004; 24: 249-57
- Chan T. Vitamin D deficiency and susceptibility to tuberculosis, Calcif Tissue Int, 2000; 66: 476-8.
- Chan T, Poon P, Pang J, *et al.* A study of the calcium and vitamin D metabolism in Chinese patients with pulmonary tuberculosis, J Trop Med Hyg, 1994; 97: 26-30.
- Davis P. A possible link between vitamin D deficiency and impaired host defence to Mycobacterium tuberculosis, Tubercle, 1985; 66: 301-6.
- Sasidharan P, Rajeev E, Vijayakumari V. Tuberculosis and vitamin D deficiency, J Assoc Physicians India, 2002; 50: 554-8
- Martineau A. Old wine in new bottles: vitamin D in the treatment and prevention of tuberculosis. Proceedings of the Nutrition Society, 2012; 71: 84-89.
- Ralph AP, Lucas RM & Norval M. Vitamin D and solar ultraviolet radiation in the treatment of tuberculosis. Lancet, 2013; 13: 77-88.
- Nnoaham KE & Clarke A. Low serum vitamin D levels and tuberculosis: a systematic review and meta-analysis. International Journal of Epidemiology, 2008; 37: 113-119.
- Arnedo-Pena A, Juan-Cerdan JV, Romeu-Garica A, *et al.* Latent tuberculosis infection, tuberculin skin test and vitamin D status in contacts of tuberculosis patients: a cross-sectional and case-control study. BMC Infectious Diseases, 2011; 11(349): 1-8.
- Wang T.J., Zhang F., Richards J.B., Kestenbaum B., van Meurs J.B., Berry D. Common genetic determinants of vitamin D insufficiency: a genome-wide association study. Lancet, 2010; 376(9736): 180-188.
- Chun R.F., Peercy B.E., Orwoll E.S., Nielson C.M., Adams J.S., Hewison M. Vitamin D and DBP: the free hormone hypothesis revisited. J Steroid Biochem Mol Biol., 2014; 144PA: 132-137.
- Safadi F.F., Thornton P., Magiera H., Hollis B.W., Gentile M., Haddad J.G. Osteopathy and resistance to vitamin D toxicity in mice null for vitamin D binding protein. J Clin Invest., 1999; 103(2): 239-251.

14. Tsugawa, N., Suhara, Y., Ka mao, M. and Okano, T. Determination of 25-hydroxyvitamin D in human plasma using high-performance liquid chromatography tandem mass spectrometry. *Analytical Chemistry*, 2005; 77: 3001-3007.
15. Essam Gouda Hassanein, Enas Elsayed Mohamed, Ayman Ibrahim Baess. Eman Tayae EL-Sayed, Ahmad Madi Yossef. The role of supplementary vitamin D in treatment course of pulmonary tuberculosis. *Egyptian Journal of Chest Diseases and Tuberculosis*, 2016; 65: 629-635.
16. Sutaria N., Liu C.-T., Chen T.C. Vitamin D status, receptor gene polymorphisms, and supplementation on tuberculosis: a systematic review of case-control studies and randomized controlled trials. *J Clin Transl Endocrinol*, 2014.
17. A.R. Martineau, P.M. Timms, G.H. Bothamley, Y. Hanifa, K. Islam, A.P. Claxton, et al, High-dose vitamin D(3) during intensive-phase antimicrobial treatment of pulmonary tuberculosis: a double-blind randomised controlled trial, *Lancet*, 377(2011): 242–250.