Prevalence and clinical impact of vitamin D deficiency on abdominal tuberculosis

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Abstract

Background: Vitamin D is recognised to have multiple actions, including role in immune modulation. The prevalence and impact of vitamin D deficiency (VDD) in abdominal tuberculosis is unknown.

Methods: We report the prevalence and clinical impact of VDD in patients with abdominal tuberculosis. The patients were divided into two groups: VDD (<20 ng/ml) or vitamin D sufficient (VDS) (⩾20 ng/ml). Groups were compared for extent (abdominal alone or extra-abdominal also) of disease and pattern of involvement (intestinal, peritoneal or both) and inflammatory response [serum C-reactive protein (CRP)].

Results: Of 63 patients, 53 had complete data (mean age: 36.3 ± 14.43, 31 males). Fourty-five (84.9%) patients had VDD and mean VD levels were 11.1 ± 10.1 ng/ml. Of 8 patients with VDS, 1 (12.5%) had extra-abdominal involvement while 13 (28.9%) with VDD had extra-abdominal involvement ($p = 0.066$). The mean CRP in patients with VDD was 42.9 ± 34.9 mg/dl vis-a-vis 105.38 ± 64.8 in VDS ($p \leqslant 0.05$). All seven patients with both intestinal and peritoneal involvement had VDD.

Conclusion: VDD is common in abdominal tuberculosis and may be associated with more extensive involvement albeit a reduced inflammatory response.

Keywords: abdominal tuberculosis, CRP, inflammation, tuberculosis, vitamin D

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Introduction

Vitamin D is a key steroid molecule which is believed to play numerous biological roles in human body. Apart from its actions on calcium and phosphorus homeostasis, vitamin D is increasingly being recognised to have role in mediating inflammatory disorders.[1] Vitamin D is recognised to play an important role in innate immune response and vitamin D deficiency (VDD) may elevate the risk of acquisition of mycobacterial infection.[2,3] The anti-microbial response of macrophages is mediated by a vitamin D–dependent process.[4] Vitamin D has also been suggested to modulate the adaptive immune response to infection, including activation of T cells.[5]

Vitamin D levels in tuberculosis have been reported to be lower than healthy controls.[6] Also vitamin D levels negatively correlate with the bacterial load in cases with pulmonary tuberculosis.[7] Vitamin D supplementation in tuberculosis has been attempted as an adjunctive therapy. In a recent systematic review, it has been suggested that anti-mycobacterial effects are possible at higher doses and may shorten the duration of therapy albeit at a heightened risk of paradoxical reactions.[8] There is, however, paucity of literature about the prevalence of VDD in abdominal tuberculosis and whether this affects the pattern and extent of involvement in these patients.

Materials and methods

The study is a retrospective study of collected database of patients diagnosed and treated for abdominal tuberculosis. The clinical records were examined for history, physical findings and haematological and biochemical parameters. These were entered in a predesigned format. Vitamin D levels at the time of diagnosis were recorded. The

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Table 1. Differences in patients with abdominal tuberculosis with and without VDD.

Parameters	VDS ($n=8$)	Vitamin D deficient ($n=45$)	p value
Pattern of involvement			
Intestinal	4 (50%)	22 (57.9%)	0.7126
Peritoneal	4 (50%)	16 (42.1%)	
Extra-abdominal involvement	01/8 (12.5%)	13/45 (28.9%)	0.066
Both intestinal and peritoneal involvement	0	7 (100%)	0.50
Mean C-reactive protein value	105.38 ± 64.8 mg/dl	42.9 ± 34.9 mg/dl	<0.05

study included all patients diagnosed to have abdominal tuberculosis (intestinal or peritoneal). We excluded patients with incomplete records or missing information or those who were on vitamin D supplements at the time of diagnosis.

Definitions

A case was defined as confirmed abdominal tuberculosis if the patient had clinical and radiological evidence of tuberculosis with one of the following:

1. Microbiological evidence in form of acid fast bacilli (AFB) positivity on tissue or fluid staining or growth of AFB on culture of tissue or fluid
2. Caseating granulomas on histology of the tissues

A case was labelled as probable abdominal tuberculosis if the patient with clinical and radiological evidence of tuberculosis had one of the following:

1. Consistent histology like granulomas of chronic inflammation;
2. Peritoneal fluid showing high adenosine deaminase (ADA) >32 U/l.

Only those patients with probable abdominal tuberculosis were included in the present study who had demonstrated improvement (ulcer healing on colonoscopy or resolution of ascites) on anti-tubercular therapy (ATT).

The patients were divided into two groups on basis of their levels, that is, vitamin D sufficient (VDS) (⩾20 ng/ml) and vitamin D deficient (<20 ng/ml).[9] We recorded the clinical presentation and biochemical findings available from the records. We recorded the presence of any extra-abdominal tuberculosis (pulmonary, pleural, neurological, etc.) on basis of clinical and radiological findings. The pattern of involvement of abdominal tuberculosis was defined as peritoneal or intestinal or both. The inflammatory response as measured by levels of C-reactive protein (CRP) at the time of diagnosis was also recorded. The two groups were compared for these parameters and for pattern of involvement (intestinal or peritoneal or both) and extent (abdominal or both abdominal and extra-abdominal involvement). The follow-up of patients like the drugs and duration of ATT and the outcome and occurrence of any adverse events (ATT-related hepatitis or intestinal obstruction) or need for surgery was also recorded.

Statistical analysis

We reported continuous variables as mean and discrete variables as percentages. Comparisons of continuous variables will be done with T test and those of discrete variable with chi-square test.

Results

Out of the 63 patients, we had complete data of 53 patients, and these were included in the present report (Table 1). The mean age of the study subjects was 36.3 ± 14.43 years (range: 13–80 years). Out of the 53 patients, 31 were males (58.49%). Most of the patients presented with abdominal pain (52/53, 98.11%), the other features were loss of weight (43/53, 81.13%), loss of appetite (40/53, 75.47%), fever (33/53, 62.26%), intestinal obstruction (18/53, 33.96%), lump abdomen (07/53, 13.20%), bleeding per rectum (04/53, 07.54%) and diarrhoea (02/53, 03.77%). Seventeen of 53 had co-morbidities (32.07%)

with 3 having hypothyroidism, 3 diabetes mellitus, 2 gall stones disease, 2 seizure disorder and 1 each having chronic kidney disease, chronic pancreatitis, chronic obstructive airway disease, nephrotic syndrome (membranous glomerulonephritis), chronic hepatitis B and alcohol-related cirrhosis. Mantoux skin test was positive in 29 (72.5%) of the 40 patients. None of the patients were HIV positive. Ascitic fluid evaluation was available for 22 patients. Nineteen of the 22 patients (86.36%) had ADA values >32 U/l (range 11–174 U/l) and 20 (90.9%) had low serum ascites albumin gradient (SAAG). Of the 53 patients with abdominal tuberculosis, 26 (49.05%) patients had intestinal involvement, 20 (37.73%) had peritoneal involvement, while 7 (13.2%) patients had both intestinal and peritoneal involvement. Fourteen patients (26.41%) had extra-abdominal involvement with seven having pulmonary involvement, five with pleural involvement while one each had combined pulmonary and pleural, and mesenteric and pleural involvement. The mean vitamin D level was 11.1 ± 10.1 ng/ml (range 3–52.5 ng/ml). Among them 45 (84.9%) patients had VDD, while 8 (15.09%) patients had VDS. When the extent of involvement was compared with vitamin D levels, 13/45 (28.9%) with VDD had extra-abdominal involvement while only one out of the eight patients with VDS (12.5%) had extra-abdominal involvement ($p = 0.066$). Also it was observed that of those patients who had both intestinal and peritoneal involvement (7/53), all had VDD suggesting that VDD lead to more extensive involvement. Out of the remaining 38 patients with VDD, 22 (57.9%) had intestinal involvement while 16 (42.1%) had peritoneal involvement, while of the 8 patients with VDS, 4 (50%) each had intestinal and peritoneal involvement ($p = 0.7126$). When the CRP values were evaluated, the mean value in the study subjects was 52.33 ± 45.9 mg/dl (range 1.2–224 mg/dl). Only six patients had normal CRP at baseline. On comparing the vitamin D status and inflammatory response, it was observed that mean CRP value among subjects with VDD was 42.9 ± 34.9 mg/dl, whereas the mean CRP value among those with VDS was 105.38 ± 64.8 ($p < 0.05$).

Discussion

Vitamin D has been implicated to have various immune functions which may impact the manifestations and outcomes of various diseases. It has been related to disease severity in inflammatory bowel disease and lower levels may increase the risk of relapse.[10] For tuberculosis, VDD is believed to be a risk factor for acquisition of infection.[11] Vitamin D supplementation has also been used to improve outcomes in patients with tuberculosis with contradictory results. The reports regarding utility of vitamin D in patients with pulmonary tuberculosis have demonstrated conflicting results. In a trial of vitamin D supplementation in active pulmonary tuberculosis, time to sputum conversion did not reduce with vitamin D supplementation.[12] Another report suggested that even a high dose of vitamin D, while improving Vitamin D levels, does not improve rates of sputum clearance.[13]

Previous reports on VDD in abdominal tuberculosis are sparse. In one such report, of the 44 patients with abdominal tuberculosis, 31 patients had vitamin D levels of <25 nmol/l. However, the levels were not done at the time of diagnosis and the clinical impact of VDD was not reported.[14] Our findings suggest that VDD is associated with more extensive disease and possibly a reduced inflammatory response. However, since the study is a small study and a retrospective report, the findings need replication in larger prospective reports. Future reports may also assess the utility of vitamin D supplementation in these patients, although the intervention has not been of benefit in pulmonary tuberculosis. However, the clinical utility of such vitamin D supplementation should assess not only the healing or cure rates but also any role in reducing the post-tubercular sequel like strictures and intestinal obstruction. Since the effects of vitamin D are multidimensional, it activates innate immunity while also attenuating the pro-inflammatory cytokine response, the exact outcomes of vitamin D in abdominal tuberculosis may not be easy to predict.[15] The supplementation is more likely to be beneficial if the actions of vitamin D are primarily in alleviating immune and fibrotic response, rather than in its anti-mycobacterial action.[16]

To conclude, VDD is fairly common in patients with abdominal tuberculosis and may be associated with patients having more extensive disease albeit with an attenuated inflammatory response.

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