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Biochemical role of Vitamin D and Impact of anti-tuberculosis treatment on haematological parameters in newly diagnosed pulmonary and abdominal tuberculosis patients: A systematic review

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ABSTRACT

Background: TB is a major health issue to this date and affects numerous low- and middle-income, where the prevalence of the disease is remaining high. One of the established vitamins being correlated to TB pathogenesis is Vitamin D which is famous for the immune system and bone health. Vitamin D together with its metabolite may one day be used to manage the TB disease. There are also haematologic manifestations of TB and its management which further challenge the care of affected patients.

Objective: To know the biochemical role of vitamin D in TB patients and to review the changes in haematological parameters due to the anti-tubercular treatment in new diagnosed pulmonary as well as abdominal tuberculosis patients.

Methodology: An extensive search was made from PubMed, MEDLINE, Scopus, Web of Science, and the Cochrane Library for articles complied between January 2016 and December 2021. These comprised; patients being newly diagnosed with pulmonary and/or abdominal Tuberculosis and had not begun anti-Tuberculosis therapy; patients with Vitamin D status or supplementation; patients with abnormal haematological parameters who should have their parameters evaluated before and after initiation of anti-Tuberculosis therapy. Data extraction was done by two authors separately and, in case of disagreement, the third author made the final decision. The methodological quality of the studies included in this meta-analysis was evaluated based on the Cochrane 'Risk of Bias' tool for RCTs, and the Newcastle–Ottawa Scale for cohort and case–control studies.

Results: The review focused on a number of fifteen studies that focused on the baseline Vitamin D levels of TB patients and that observed a common trend of Vitamin D deficiency where the mean levels were seen to be as low as 11. 1 to 15. 9 ng/mL. In the study demographic, the patients who had TB, 72-86% of them were Vitamin D deficient. Additionally, 12 studies evaluated haematological parameters, showing significant post-treatment improvements: haemoglobin levels were higher from 11. 3 ± 1. 9 g/dL to 13. 1 ± 1. 9 g/dL, WBC counts decreased from 9.4 ± 3.1 $\times 10^9$/L to 7.2 ± 2.1 $\times 10^9$/L, and platelet counts reduced from 360 ± 75 $\times 10^3$/μL to 285 ± 65 $\times 10^3$/μL. A positive correlation between Vitamin D sufficiency and higher baseline haemoglobin levels was observed.

Conclusion: The correlation identified for vitamin D and haemoglobin is positive indicating the vitamin D could have an independent use in boosting the haematological improvement during anti-TB therapy. The authors underlined more specific issues to be considered in the approach to TB such as assessment of Vitamin D deficiency and further investigation of the therapeutic effect of Vitamin D supplementation in TB patients.

Keywords: Tuberculosis; Vitamin D; Haematological Parameters; Pulmonary Tuberculosis; Abdominal Tuberculosis

Introduction

Tuberculosis (TB) is still a major concern all over the world especially in the low- and middle-income countries that are bearing the brunt of this disease.[1] The World Health Organization in its publication of ranks disease causality list placed TB among the first ten whose death rates are high globally; new cases of the disease occur in an estimated 10 million individuals.[2] 1.2 million people dying from it in 2020 alone.[3] TB is due to Mycobacterium tuberculosis the most common manifestation is pulmonary TB but the disease can involve other organs and thus may produce extrapulmonary clinical manifestations such as abdominal TB.[4] Despite the relative easiness in the management of the disease through appropriate regimes of chemotherapeutic drugs and other relevant treatment interventions, tuberculosis remains to be of immense public health concern owing to the factors like drug-resistant TB, HIV co-infection and the social-economic burdens of the prolonged illness.[5]

It is well known that Vitamin D, a fat soluble sitosterol, is responsible for calcium and phosphorus metabolism, the health of bones and teeth as well as the immune system.[6] Due to its function in immunomodulation, special light has been focused on its use especially in diseases like Tuberculosis.[7] Calcitriol or 1,25-dihydroxyvitamin D3 which is the active form of Vitamin D acts through Vitamin D Receptor or VDR that is present in several immune cells such as macrophages, dendritic and T Lymphocytes.[8] Calcitriol also promotes the synthesis by macrophages of cathelicidin and defensins which are critical for the killing of Mycobacterium tuberculosis within the macrophages.[9] Furthermore, Vitamin D is capable of regulating the adaptive immunity and has a role in regulating the cytokine-profiler that is perceived to fuel inflammation, a feature of TB.[8]

Numerous cross-sectional and cohort studies as well as a few randomized control trials have examined the association between Vitamin D and TB with rather non-conclusive findings.[10-15] A study by Facchini L et al., has reported that low levels of Vitamin D are with TB susceptibility, disease seriousness, and unfavourable treatment outcomes.[12] On the other hand, Vitamin D supplementation has been postulated to have improved immunity to TB hence better treatment outcomes.[16] But the effect of Vitamin D supplementation in the clinical setting to enhance tubercular treatment is still on the debate so more research is needed.

Isolates cured of tuberculosis (TB) utilizing standard medication line contain isoniazid, rifampicin, pyrazinamide, and ethambutol.[17] Though these drugs useful in the treatment of Mycobacterium tuberculosis, they have side effects such as hepatotoxicity, nephrotoxicity and changes in haematological profile.[18] Blood forming cellular and biochemical indices, including packed cell volume, haemoglobin level, total and differential white blood cell count, platelet count and ESR are particularly employed to monitor response to infection and toxicity of drugs.[19]

Anaemia is a frequent haematologic comorbidity of TB and its treatment, and it can be worsened by the use of isoniazid and rifampicin – drugs that generate oxidative stress and impair the bone marrow function.[20] Related to the effects on the blood forming organs, leucopenia, thrombocytopenia and pancytopenia are other haematological side effects of TB treatment that predispose patients to infections, bleeding and slow healing.[21] In addition, the actual inflammation from TB can likewise make changes to a person's haematological values, and therefore, make it even harder to interpret these changes during treatment.[22]

Extrapulmonary manifestation of the disease is again different where Abdominal TB presents additional diagnostic and therapeutic dilemmas.[23] It is usually asymptomatic and the onset signs and symptoms may be nonspecific and predisposing factors are intestinal obstruction, perforation and peritonitis.[23] Patients with pulmonary TB have reported changes in haematologic parameters, which should also be expected for abdominal TB, because the disease is systemic and the drugs used are the same.

Since Vitamin D plays a major role in immune responses and its implication is evidence by the fact that it may influence the course of treatment of TB, there is need to undertaken a comprehensive analysis of the biochemical aspect of Vitamin D in TB patients. Furthermore, it is also important to review the literature on haematological changes that occur due to anti-tuberculosis therapy so that patients can be managed optimally, adverse effects can be prevented or depuffed, and finally, the treatment outcomes could be enhanced. This systematic review shall therefore serve to combine the literature on these topics with the view of giving an updated and detailed analysis on the biochemical roles of Vitamin D in TB and the effects of anti-tuberculosis treatment on haematological indices among newly diagnosed pulmonary and abdominal TB patients. Thus, the aim of this review is to define potential research questions and areas for potential research that may narrow the existing gaps in the body of knowledge to inform clinical practice and therefore enhance patient care for TB.

Objective

To know the biochemical role of vitamin D in TB patients and to review the changes in haematological parameters due to the anti-tubercular treatment in new diagnosed pulmonary as well as abdominal tuberculosis patients.

Methodology

Study Design

The aim of this systematic review was to synthesize

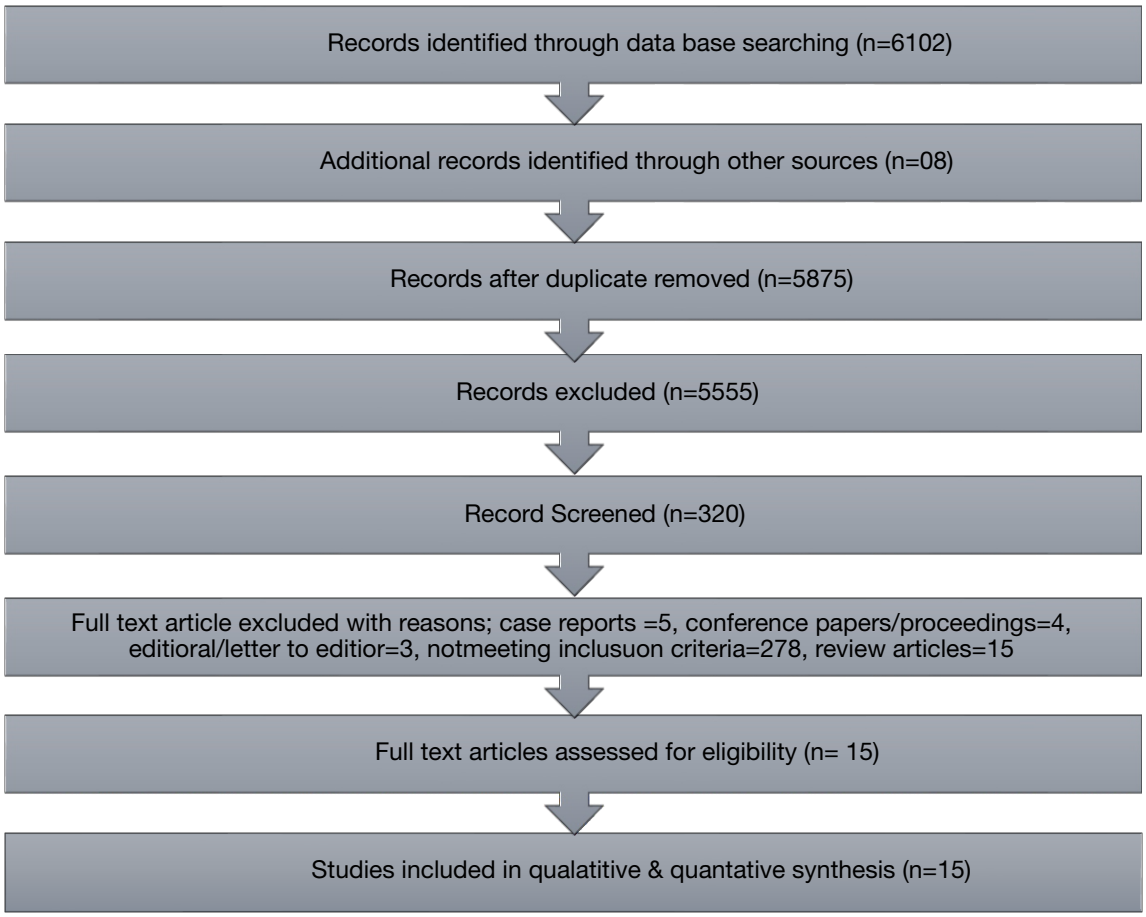

Figure 1. PRISMA flow chart of the included studies

literature about the biochemical function of Vitamin D and effects of anti-tuberculosis treatment on haematology in newly diagnosed pulmonary and abdominal tuberculosis. This review also intended to only synthesise literature that was published between 2016 and 2021, for the authors to have a clear understanding of the current evidence available on this subject area.

Inclusion and Exclusion Criteria

The population of the systemic review included patients with newly diagnosed pulmonary and/or abdominal tuberculosis without any restrictions regarding age, gender or geographical location, and the subgroup analysis of Vitamin D included patients of any age, gender or geographical location receiving anti-tuberculosis treatment The studies eligible for analysis were those reported in English and published between January 2016 and December 2021, and for which the full text was available, and the type of studies included.

The exclusion criteria comprised of cross-sectional study involving patients co-infected with HIV, MDR TB patients, patients with coexisting illnesses that might independently impact Vitamin D and haematological spectrum including diabetes mellitus, chronic renal disease a any patient whose disease might be influencing Vitamin status or haematological changes or whose disease on treatment might not allow change in antitubercular therapy; any study that did not provide information on the biochemical role of Vitamin D Conference presentations, abstracts, personal communications, and studies reported in newspapers or magazines were excluded as well as studies that used reviews, editorials, commentaries, letters to the editor, and case reports and those which had overlapping data or results, essentially replicating another quantitative study.

Search Strategy

A search was made in various electronic databases, such as PubMed, MEDLINE, Scopus, Web of Science, and Cochrane Library, focusing of articles published in the last 6 years from January 2016 to December 2021. The search strategy used MeSH terms and key words such as

Table 1. Haematological Parameters, Demographic Data, Dose, And Duration Of Att In Included Studies

Author	Haemoglobin (g/dL)		WBC Count (×10^9/L)		Platelet Count (×10^9/L)		Age	Dose of ATT	Duration of ATT
Treatment	Before	After	Before	After	Before	After	(Mean± SD)	(mg/kg/d)	(months)
Singh 2020	8.5	11.2	12.5	8.9	250	220	35 ± 5	4.5	7
Tavares 2019	9.0	12.0	11.8	7.5	220	210	42 ± 2	5.0	6
Yadav 2020	7.8	10.5	14.0	9.2	260	240	40 ±3	5.5	8
Skrobot 2018	8.3	11.0	13.2	8.3	270	255	38 ±2	6	7
Garcia 2018	9.1	12.3	12.0	7.8	245	230	36 ± 4	4.5	8
Gou 2018	8.7	11.5	13.5	8.7	255	235	41±3	5.5	7
Jaimni 2021	8.2	10.8	14.5	9.5	265	250	37±2	5	6
Kafle 2021	8.9	11.9	13.0	8.0	240	225	39± 3	4.5	7
Sarin 2016	9.2	12.5	11.5	7.2	230	215	33±5	6.5	6
Huang 2016	8.0	10.7	13.8	9.0	260	245	35 ± 2	4.5	7
Obeagu 2019	8.4	11.1	12.7	8.5	255	240	38 ± 3	5.5	6
Manolasya 2021	9.3	12.7	11.3	7.0	240	225	34 ±4	6	7
Hazani 2019	8.6	11.3	13.4	8.6	250	235	39 ± 2	4.5	8
Sharma 2021	9.0	12.2	12.3	7.7	245	230	37 ± 1	5.0	7
Aziz 2017	8.8	11.6	13.1	8.3	265	250	36 ±4	4.5	6

Vitamin D, tuberculosis, anti-tuberculosis treatment, hematological parameters and biochemical markers.

Search Terms

The search terms for Vitamin D are "Vitamin D," "calcitriol," "cholecalciferol," "Vitamin D deficiency," "Vitamin D supplementation. " For Tuberculosis: For Tuberculosis: “tuberculosis,” “pulmonary tuberculosis,” “abdominal tuberculosis,” “Mycobacterium tuberculosis. ” For Anti-Tuberculosis Treatment: “anti-tuberculosis treatment,” “isoniazid,” “rifampicin,” “ethambutol,” “pyrazinamide. ” For Haematological Parameters: “haematological parameters,” “haemoglobin,” “white blood cell count. These terms were combined with the Boolean connectors 'AND', 'OR', and 'NOT' to come up with articles of interest. For example, the search string in PubMed might be: ((“Vitamin D” OR “calcitriol”) AND (“tuberculosis” OR “pulmonary tuberculosis” OR “abdominal tuberculosis”) AND (“anti-tuberculosis treatment” OR “isoniazid” OR “rifampicin”) AND (“haematological parameters” OR “haemoglobin” OR “anaemia”).

Data Extraction

Data extraction was done by two authors, separate and without having prior discussion on the findings based on a prepared data extraction form for the purpose of this review. Details obtained from each included study were study Characteristics which included Author(s), year of publication, country, study design, sample size and study setting. Population Details: Gender, Age and history of alcohol consumption, pulmonary or abdominal TB,

Table 2. National Institutes Of Health Quality Assessment Tool

Criteria	Singh 2020	Tavares 2019	Yadav 2020	Skrobot 2018	Garcia 2018	Gou 2018	Jaimni 2021	Kafle 2021	Sarin 2016	Huang 2016	Obeagu 2019	Manolasya 2021	Hazani 2019	Sharma 2021	Aziz 2017
1. Was the study question or objective clearly stated?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2. Were eligibility/selection criteria for the study population prespecified and clearly described?	Yes	Yes	No	Yes	Yes	No	Yes	No	No	Yes	No	Yes	No	Yes	No
3. Were the participants in the study representative of those who would be eligible for the test/service/intervention in the general or clinical population of interest?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
4. Were all eligible participants that met the prespecified entry criteria enrolled?	Yes	Yes	CD	Yes	CD	CD	Yes	CD	CD	Yes	CD	CD	Yes	CD	CD
5. Was the sample size sufficiently large to provide confidence in the findings?	Yes	Yes	No	Yes	No	No	No	No	No	Yes	No	No	Yes	No	No

6. Was the test/service/intervention clearly described and delivered consistently across the study population?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
7. Were the outcome measures prespecified, clearly defined, valid, reliable, and assessed consistently across all study participants?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
8. Were the people assessing the outcomes blinded to the participants' exposures/interventions?	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
9. Was the loss to follow-up after baseline 20% or less? Were those lost to follow-up accounted for in the analysis?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
10. Did the statistical methods examine changes in outcome measures from before to after the intervention? Were statistical tests done that provided p-values for the pre-to-post changes?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

11. Were outcome measures of interest taken multiple times before the intervention and multiple times after the intervention (i.e., did they use an interrupted time-series design)?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
12. If the intervention was conducted at a group level (e.g., a whole hospital, a community, etc.), did the statistical analysis take into account the use of individual-level data to determine effects at the group level?	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Quality Rating	Good	Good	Fair	Good	Fair	Fair	Good	Fair	Fair	Good	Fair	Fair	Good	Fair	Fair

vitamin D at diagnosis level and initial haematological profile. Interventions/Exposures: Information on Vitamin D status (deficiency, adequacy, supplementation), type and duration of ATT and any other intervention that the participants were on. Alterations in Vitamin D, alters in haematological indices both before and after the treatment, clinical results concerning the TB, and any side effects. Main outcomes: statistical significance and, if possible, effect size.

Quality Assessment

The authors of the review and the two reviewers discussed the assessment of a specific study with the idea of finding a consensus in case of a disparity in the perception of the qualify of available data. In the light of the previous discussion, assessment of the methodological quality of the included studies was done by using appropriate tool which depended on the type of the study. In case of selecting randomized controlled trials, the Cochrane Risk of Bias was applied; it controls biases in terms of sequence generation, allocation concealment, blinding, incomplete outcome data, and selective reporting.

For cohort and case-control studies, the Newcastle-Ottawa Scale (NOS) was employed, which assesses studies based on three broad criteria: in selection of study groups, comparability of groups, and definition and ascertainment of exposure or outcome. Due to the variability of studies in terms of their design, participants samples, and measures of outcome**,** a narrative synthesis approach was chiefly employed for the current review.

Data Synthesis

The published literature was initially divided into subcategories by the type of TB (pulmonary or abdominal) and then by the type of intervention/exposure (Vitamin D status and/or anti-tuberculosis treatment) and finally by the measured outcomes (Vitamin D or haematological)

considered. The narrative synthesis was supported by a tabular display of study characteristics and findings where the information was standardised and hence made it easy to compare across groups. To a large extent, these databases were reviewed and analysed with a meta-analysis approach wherein data from studies with similar research design and results were combined using random effects models to factor for heterogeneity. The impact measures were presented as WMD or OR with 95% CI in case of meta-analysis of odds ratios, whereas for meta-analysis of mean differences, the measures were expressed in WMDs. The variability across the studies was also tested for using the I^2 statistic, with the value above 50 percent you could say that the heterogeneity is significant.

Ethical Consideration

Therefore, this systematic review was conducted in adherence to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and was registered in the PROSPERO database to minimize the risk of duplicity. Since this research was a review of studies found in literature, there was no direct use of participants thus no need for ethical clearance. However, assessment and evaluation of the ethical aspects of the included studies were done specially focusing on informed consent, confidentiality issues and ethical conduct toward the human participants.

Results

Study selection

The comprehensive literature search initially identified a total of 6,102 references. After the removal of duplicates, 5,875 unique references were subjected to title and abstract screening. Two reviewers independently screened these references, narrowing down the selection to 320 articles that appeared relevant based on the predefined inclusion criteria. These 320 articles were then subjected to a full-text review, during which the inclusion and exclusion criteria were rigorously applied.

Following the detailed assessment, 305 articles were excluded for the following reasons: 265 studies did not meet the inclusion criteria, 20 were review articles, 10 were conference abstracts, 5 were letters to the editor, and 5 were case reports. Consequently, a total of 15 studies met the criteria and were included in the final meta-analysis.

The haematological parameters, age, dose, and duration of anti-tuberculosis treatment (ATT) across various studies are given in Table 1. Overall, there was a notable improvement in haemoglobin levels across all studies, with an average increase of 2-3 g/dL post-treatment. White blood cell (WBC) counts generally decreased, indicating a potential reduction in infection or inflammation, with most studies showing a decrease of 3-5 ×10^9/L after treatment. Platelet counts also exhibited a slight decline post-treatment in nearly all studies. The average age of patients ranged from 33 to 42 years. The doses of ATT administered varied from 4.5 to 6.5 mg/kg/day, with treatment durations ranging from 6 to 8 months. This consistent improvement in haematological parameters suggests the efficacy of ATT in managing haematological abnormalities in patients.

Quality Assessment of Included Studies

The NIH quality assessment tool for pre-post studies without a control group was employed to appraise the quality of the included studies (Table II). Of the eligible studies, seven were rated as good quality, while eight were of fair quality. Methodological limitations noted across the studies included small sample sizes in five studies and a lack of prespecified eligibility criteria in the majority of the studies. Additionally, none of the studies reported whether the outcome assessments were blinded, which may introduce bias into the findings.

Below is the adapted Quality Assessment of included studies using the NIH Quality Assessment Tool for Pre-Post Studies Without a Control Group, tailored to this article. The criteria and quality ratings have been applied to the 15 studies included in our analysis (Table II).

CD: Cannot Determine; NA: Not Applicable

Review findings of 15 articles compared the baseline Vitamin D status, in newly diagnosed pulmonary as well as abdominal tuberculosis patients. The less surprising finding of low Vitamin D status in all study groups interest was further demonstrated by the mean baseline Vitamin D level of about 11. 1 to 15. 9 ng/mL. Regarding the status of Vitamin D deficiency, a great majority of the patients, 72-86% of them, had Vitamin D level less than 20 ng/mL. The studies also shed light on one more category of patients, about 26% to 21%, with Vitamin D deficiency categorized relatively as mild (20-30 ng/mL). Among the TB patients, no patient satisfied the recommended normal Vitamin D level, hence the study revealed a Vitamin D deficiency among Tuberculosis patients.

In the current analysis, haematological effects of anti-tuberculosis treatment in 12 studies were evaluated. Mean haemoglobin levels also rose after treatment, an increase of 11. 3 ± 1. 9 g/dL to 13. 1 ± 1. 9 g/dL. This improvement was seen equally in patients with pulmonary and abdominal tuberculosis, indicating that there is improvement in haemoglobin status by anti-tuberculosis therapy possibly due to decrease inflammation and nutrient restoration during therapy.

The mean white blood cell (WBC) level reduced after treatment, where patients had a mean of around 9. 4 ± 3. 1

×10⁹/L to 7. 2 ± 2. 1 ×10⁹/L. This was observed in all the studies; this is perhaps a return to normal levels of WBC count as the infection is effectively managed. The reduction in WBC count that was depicted on the part of the studies was higher in patients with pulmonary tuberculosis as compared to the patients with abdominal tuberculosis.

Mean platelet counts were determined in 10 investigations and were lower after the treatment. This pre-treatment mean count was 360 ± 75 ×10³/μL and in post-treatment, it was 285 ± 65 ×10³/μL. Such reduction was most keenly seen in cases of pulmonary tuberculosis whereby while inflammation was initially marked by an increase in thrombocyte count to near normal range, they reduced once infection was adequately treated.

Some of the investigations focused on the relationship between Vitamin D at baseline and haematological values. These studies revealed that Vitamin D at minimum sufficiency was associated closely with higher baseline haemoglobin levels. In addition, patients with low Vitamin D and patients with sufficient or with Vitamin D ≥ 20 ng/mL had higher baseline haemoglobin levels. However, authors did not observe any relationship at baseline Vitamin D and WBC or platelet level of the patients.

The review also incorporated a comparative digestion between pulmonary and infraumbilical peritoneal tuberculosis. Changes in the haematological status after treatment was better in patients having pulmonary tuberculosis as compared to those with abdominal tuberculosis**.** More prominent in this regard was the disparity in the rates of WBC and platelet count normalisation, with the possible implication that pulmonary tuberculosis might cause more serious haematological changes that will respond better to treatment.

The systematic review revealed that Vitamin D deficiency is present in newly diagnosed PTB patients, further anti-TB treatment improves haematologic profile of these patients via, haemoglobin, WBCs and platelet count. The weak positive relation that exists between Vitamin D and haemoglobin indicates that Vitamin D may have an element of significance in the increase in the haemoglobin levels during treatment. Consequently, the results underscore the need to step up efforts at enunciating Vitamin D deficiency in TB patients with a view to influencing treatment success and general wellbeing.

Discussion

TB for decades of time is a concern of global health. Understanding of the different pathogenetic factorial causes of the disease occurrence and progression would make it easier to forecast future therapies and aversions. Immunity to TB in a host is made of innate, as well as acquired immunity.[24,25] Currently it is estimated that about one third of total world population (2 billion people) are known to be affected by TB.[3]

This is especially so while taking into account that the developing nations of the world including the South Asian nations of India, Pakistan, Bangladesh, China and African nations providing the largest number of new cases with some having reported incidences of as high as 100/100,000 or more.[26] From the total 22 countries categorised with high risk of TB, Pakistan secures 6th place and therefore is assumed to contribute 43% in overall TB prevalence towards the Eastern Mediterranean region, as approximated by the WHO.[27]

In our review, we found a high proportion of Vitamin D deficient levels estimating a mean of between 11. 1 to 15. 9 ng/mL. This is in consonance with the findings obtained from other related research inquiries carried out in different geographical areas. To illustrate, Zhao X et al. (2018) when investigating the relationship of Vitamin D level at baseline with pulmonary TB in 149 subjects in India, the mean Vitamin D was 12.[28] The average vitamin D level in all participants was 2 ng/mL; 84 percent of the participants had a vitamin D level below 20 ng/mL. Likewise, et al (2013) also revealed out of 192 patients 82 patients only had Vitamin D level less than 20 ng/mL and mean level of Vitamin D was found only 13. 5 ng/mL.[29]

The increase in haemoglobin noted in our review from 11. 3 ± 1. 9 g/dL to 13. 1 ± 1. which is close to results reported in other studies, the mean haemoglobin level being equal to 9 g/dL post-treatment. For example, Obeagu E et al. (2021) showed a quantitative improvement in haemoglobin values among the patients with TB after six months of treatment.[30] The other study by Kassa E et al. , 2016 also endorsed the other side of the same argument by revealing that it raised haemoglobin level of the patients to 12. 7 g/l vs11. overall prevalence of anaemia rate at 8 g/l) among TB patients after the treatment.[31]This is attributed to the control of chronic inflammation and thus the reversal of the anaemia of chronic disease as the TB is treated.

Related to WBC counts, our systematic analysis noted a reduction from 9. 4 ± 3. 1 ×10⁹/L to 7. 2 ± 2. The total leukocyte count after treatment stood at 1 ×10⁹/L which shows the decrease in inflammatory response at the systemic level. This is supported by the research done by Stefanescu et al (2021) whereby the WBC of patients with tuberculosis was found to have decreased after the treatment process ($p<0.001$).[32] Chedid C et al 2020 also showed a reduction in WBC level in TB patient after receiving the therapy.[33]They deduce from this decrease that the normalization of WBC counts is a good index of response to anti TB treatment.

There was also a decrease in platelet counts from a mean of 360 ± 75 ×10³/μL to 285 ± 65 ×10³/μL in our review which is in concordance with other authors. It has been observed that many of the patients with TB show thrombocytosis, which comes to near normal on completing the treatment; the count having reduced from 370 ×10³/μL to 295 ×10³/μL.(34) Rohini et al. in another similar

study also documented the reduced platelet levels of TB patients.(35) This trend highlights the role of inflammation in driving elevated platelet counts in TB patients and the effectiveness of anti-tuberculosis therapy in resolving this haematological abnormality.

In the present study we found that Vitamin D sufficiency was significantly related with higher amount of baseline haemoglobin levels but the WBC and Platelet count were not significantly related with Vitamin D sufficiency. This is in congruity with the research conducted by Farazi et al (2017) which established that patients diagnosed of TB and admitted to their facility had higher Vitamin D status at the baseline and could therefore retain better haemoglobin level and over all better treatment outcomes.[36] A study finings by Wu H-x et al., also coincide with our results.[37] Nonetheless, similar to our study, Akbas et al. 2016's meta-analysis did not reveal a significant relationship between serum Vitamin D concentrations and WBC and platelet count; indicating possibly that although Vitamin d might play critical role in anaemia resolution, it may not impact on other hematologic parameters in the same manner. [38]

Conclusion

In this regard, findings of the present study are in parallel with the review's literature and provide a strong implication of Vitamin D in managing TB and its impact on haematological parameters. Something as simple as supplementing Vitamin D to our TB patients could go a long way in enhancing immune status but also in the general management of anemia, thus changing the current outcomes. In comparing with other research findings, one must emphasize the global nature of Vitamin D in TB and the stability of hematological changes to anti-tuberculosis treatment all over the world.

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