



A STUDY OF CORRELATION BETWEEN VITAMIN B12 LEVELS AND D-DIMER LEVELS - IN COVID-19 POSITIVE PATIENTS AT OUR HOSPITAL

Medical Science

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ABSTRACT

Background: Coronavirus disease 2019 (COVID-19) is a pandemic infectious disease. COVID-19 has associated coagulopathy. Elevated D-dimer is valuable in the diagnosis and the monitoring of thrombus formation in COVID-19. Cases with vitamin B12 deficiency suggest a relationship between vitamin B12 and thrombosis. We wish to find out, if any, correlation between Vitamin B12 deficiency and increased thrombosis (by means of D-Dimer) in the study group.

Results: 94 patients who gave consent for the study were included. 54 (57.5%) were males and 40 (42.5%) were females. Mean age of the study population was 58.88 years. 14 (14.89%) patients were B12 deficient. In the vitamin B12 deficient and non deficient groups, there was no significant statistical difference between the mean initial or mean maximum D-Dimer (p-value = 0.36 and 0.45 respectively). Mean duration of stay and percentage of patients needing oxygen support or anticoagulation was also not significantly different among the two groups. Mortality in vitamin B12 deficient (14.28%) was not significantly different from the non-deficient group (20%, p=0.59). Overall mortality in those who had elevated D Dimer was significant compared to those who had normal D-Dimer (p=0.0062; i.e. <0.05).

Conclusions: Our data shows that there appears to be no correlation of Vitamin B12 deficiency with thrombosis, overall recovery time, morbidity or mortality in COVID-19 patients when compared to non-deficient patients in the same hospital setting. Elevated D-Dimer can be considered to be an independent risk factor for mortality.

KEYWORDS

COVID-19, Vitamin B12, Thrombosis, D-Dimer

INTRODUCTION

COVID-19 and Thrombosis

- Coronavirus disease 2019 (COVID-19) is a pandemic infectious disease caused by a novel coronavirus.
- The pathophysiological mechanisms underlying COVID-19-associated coagulopathy follow Virchow's triad, including (i) diffuse endothelial cell injury (ii) abnormal blood flow dynamics, and (iii) uncontrolled platelet activation^[1].
- Virus infection causes direct endothelial injury, dysfunction, and prothrombotic gene expression^[2].
- In addition to the direct effect, the virus also triggers innate immune responses (including the activation of monocytes and complement cascade), causing massive local release of proinflammatory cytokines and aggravation of endothelial injury and microvascular thrombosis, termed immunothrombosis^[3].
- In the course of COVID-19, high blood concentrations of vWF, cell-free DNA, histones, and viral RNA (which all cause factor XI activation, thrombin generation, and intravascular fibrin formation), lead to abnormal flow dynamics^[4].
- Platelet activation is induced both indirectly by neutrophil extracellular traps (NETs) and directly by virus infection. NETs lead to platelet activation via toll-like receptors on platelets and other cells, therefore integrating pulmonary infection, inflammation, and thrombosis^[5,6].

VITAMIN B-12 AND HOMOCYSTEINE

- Sporadic cases with vitamin B12 deficiency and thrombosis have been reported suggesting a relationship between vitamin B12 and thrombosis. Arterial and venous thrombotic events have been demonstrated.^[7-10]
- Homocysteine (Hcy) rises with either folate or vitamin B12 deficiency because folate and vitamin B12 (methylcobalamin) are intertwined with the metabolism of methionine and Hcy.^[11]
- Elevated plasma homocysteine is a new risk factor for vascular disease. Several lines of evidence suggest that HHcy induces dysfunction and/or injury of the vascular endothelium.^[12] The biochemical mechanisms that have been proposed to explain Hcy pathology include^[13] -
- Oxidative Stress
- Decreased Bioavailability of Nitric Oxide
- Hypomethylation of Proteins and DNA
- Protein Modification and Endoplasmic Reticulum Stress

- Impairment of Vascular Resistance to Thrombosis

D-DIMER

- One of the most consistent findings in COVID19 patients is that of a raised D-dimer^[14]. Although many inflammatory processes can influence D-dimer levels, it almost certainly reflects, to some extent, intravascular thrombosis in patients with COVID-19.
- D-dimer is the degradation product of crosslinked fibrin.
- Since elevated D-dimer assumes activation of the coagulation and fibrinolytic systems, it is valuable in the diagnosis and the monitoring of thrombus formation.

MATERIALS AND METHODS

This is an observational cross-sectional study at a tertiary care hospital. After approval by the ethics committee and due consent of patients, 94 patients were enrolled in the study.

All adult patients of all genders who were COVID-19 positive [by COVID-19 RT-PCR test / rapid antigen test / HRCT chest suggestive of active COVID-19 infection (CORADS III and above)] were included in the study. Patients who were known to have taken Vitamin B12 supplements, patients who might have raised D-Dimer due to other known causes (e.g. heart disease, prolonged bed rest, post surgical, etc) and pregnant and lactating women were excluded from the study.

RESULTS

Out of 94 patients, 54 (57.5%) were males and 40 (42.5%) were females. Mean age of the study population was 58.88 years.

Table 1: Age demographics of the study group

Age distribution	No of patients
<20	0
20-40	6
40-60	45
60-80	39
>80	4

[Normal B12: 211-916 pg/mL; Normal D-Dimer: 200-600 ng/mL (or microgram/L)]

Mean B12 in the study population was 808.71 pg/mL. 14 (14.89%) of the patients were B12 deficient (B12 < 211 pg/mL) while the rest were

non-deficient. Unpaired t tests were done to find out statistically significant differences between the two groups.

Table 2: Comparison of B12 deficient and non-deficient patients with p-value for statistical difference

Parameter	B12 DEFICIENT (14)	NON DEFICIENT (80)	p value
Mean baseline D Dimer (ng/mL)	499.14	587.14	0.36
Mean maximum D Dimer (ng/mL)	2257.5	2367.1	0.45
Mean duration of stay (days)	13.62	11.51	0.14
% having elevated (max) D Dimer (>600 ng/ml)	64.28	55	0.53
% Needing O ₂	71.43	61.25	0.46
% Needing anticoagulation	92.86	78.75	0.11
% Mortality	14.28	20	0.59

Overall mortality in those who had normal D-Dimer was 7.32%, while mortality in those who had elevated D Dimer(>600 ng/ml) was 28.30% (p=0.0062; i.e.<0.05).

DISCUSSION

Our study shows that the overall incidence of Vitamin B12 deficiency in the study group is 14.89%. There was no significant statistical difference between the mean initial(p=0.36) or mean maximum (p=0.45) D-Dimer between the two groups. Percentage of patients with elevated D-Dimer, i.e. above the upper range of normal(>600 ng/ml), was also not significantly different(p=0.53). This disapproves our hypothesis that B12 deficiency may aggravate the thrombosis in COVID-19 even though it is considered to be an independent risk factor for hypercoagulable state.

Mean duration of stay(p=0.14) and percentage of patients needing oxygen support(p=0.46) or anticoagulation(p=0.11) was also not significantly different among the two groups. Mortality in vitamin B12 deficient(14.28%) was not significantly different from the non-deficient group(20%, p=0.59). Hence the morbidity or end outcome in B12 deficient patients cannot be said to be worse than non-deficient patients.

Overall mortality in those who had elevated D Dimer was 28.30%, while in those who had normal D-Dimer was 7.32% (p=0.0062; i.e.<0.05). Hence elevated D-Dimer can be considered to be an independent risk factor for mortality.

Other studies testing Vitamin B12 and its role in COVID-19 are limited. A clinical study of 43 patients conducted in Singapore showed that COVID-19 patients who were given vitamin B12 supplements (500 µg), vitamin D (1000 IU) and magnesium ("DMB") had reduced clinical deterioration requiring oxygen support and/or intensive care support^[15]. A recent study hypothesised that methylcobalamin supplements have the potential to reduce COVID-19-related organ damage and symptoms^[16].

Further prospective, longitudinal, and well-designed cohort studies are needed. There is the possibility of new research avenues and treatment modalities in this context.

CONCLUSION

Our data shows that there appears to be no correlation of Vitamin B12 deficiency with thrombosis, overall recovery time, morbidity or mortality in COVID-19 patients when compared to non-deficient patients in the same hospital setting. Elevated D-Dimer can be considered to be an independent risk factor for mortality.

Conflicts of Interest

There are no conflicts of interest.

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