

# Journal of Coastal Life Medicine

## Metformin Causes Vitamin B12 Deficiency

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### Abstract

Metformin is a first drug of choice of oral diabetic drug for hyperglycemia in diabetes is generally regarded as having few cause vitamin B12 deficiency. It has been reported that an average of 6% to 30% of patients could show vitamin B12 deficiency due to metformin use. The 2017 American Diabetes Association treatment guidelines now recommend regular monitoring of vitamin B 12 levels in patients with diabetes taking metformin. Metformin so causes Vit B12 deficiency which is a rare side effect of prolonged metformin therapy. Many studies showed the inverse relationship between the prolonged usage and dosage of metformin usage and B12 serum levels.

### 1. Introduction

Metformin is an universally approved drug, which suppress the glucose produced in liver and improves insulin activation mainly in muscle, liver and adipose tissue. But the drug is known to cause gastrointestinal disturbance such as diarrhoea and vomiting, and also hypoglycaemia and lactic acidosis. On further use, apart from anemia, it leads to Vitamin B12 deficiency which itself is an essential nutrient for brain function, nerves and for the formation of blood and its components. <sup>1</sup> This study aims to provide knowledge and describe the Vitamin B12 deficiency induced by Metformin among T2DM patients, aggravating

peripheral neuropathy.

### 2. Case History

A 77yr old male came to Sree Balaji medical college and hospital general medicine department with complaints of easy fatigability for the past 2 months with history of recurrent thrombocytopenia for the past 2 months he also gives a history of covid infection in January following covid booster vaccination. Fatigability started during covid infection. He also complains of profuse sweating all over the body after eating since two months. He gives a history of chills for the last two months not associated with fever and

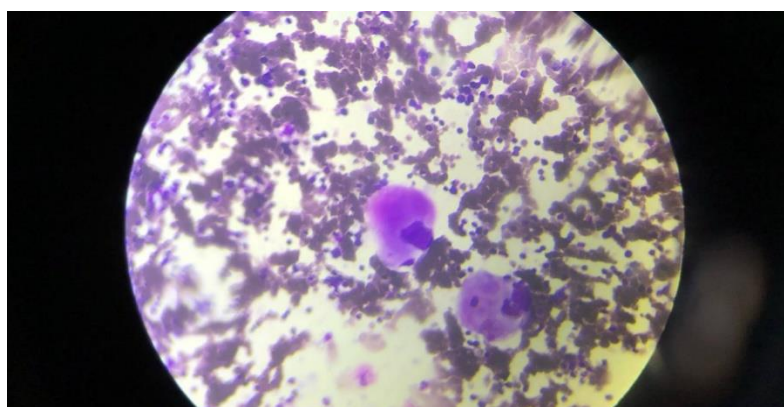
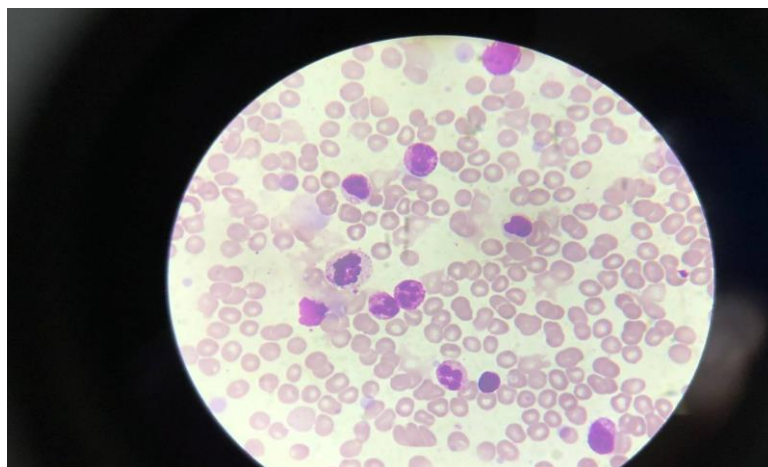
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rigor associated with joint pain since twenty years, pain which is pricking type of pain, localised more to the knee not radiating aggravated on work and no relieving factors. No history suggestive of other system system involvement. He is a known case of type 2 diabetes mellitus for the past 10 yrs. on T. Metformin 500 mg and known hypertensive for the past 10 yrs on oral anti hypertensive agents. No other known comorbidities. He is an alcoholic for the past 30 yrs and a smoker for the past 20 yrs. On examination the patient is conscious oriented and afebrile. General physical examination is normal. Vitals are stable. On Systemic examination no abnormalities detected. During the course of stay in the hospital vitals were monitored the patient was started on symptomatic treatment with BP and CBG monitoring.

### 3. Results

All routine investigations were done results which showed platelet count 30,000, Haemoglobin-10g/dl, PCV -29%, MCV MCH-97.0,-33.3, MCHC-34.2, ESR-47, peripheral smear showed hyper segmented neutrophils, normocytic normochromic anaemia with thrombocytopenia, CRP-8.60, PT-16.5, INR-1.21, protein electrophoresis-normal, LFT-Total bilirubin-1.10, Direct bilirubin-0.42, SGOT-25U/L, SGPT-31U/L, alkaline phosphatase-121U/L, Hematology reports, fibrinogen -363mg/dl, D-Dimer-0.34ugm, FBS-129mg/dl, PPBS-338mg/dl, TFT, FT3-2.49, FT4-1.07, TSH-6.07. Bone marrow aspiration was done which showed hyper cellular bone marrow with erythroblasts-40%, myeloblasts-3%, band forms-4%, neutrophils-27%, megakaryocytes-5%. Impression-megaloblastic erythropoiesis, hyper segmented neutrophil with giant stab forms, hypolobated megakaryocytes with decreased platelet budding. Mild increase in megakaryocytes

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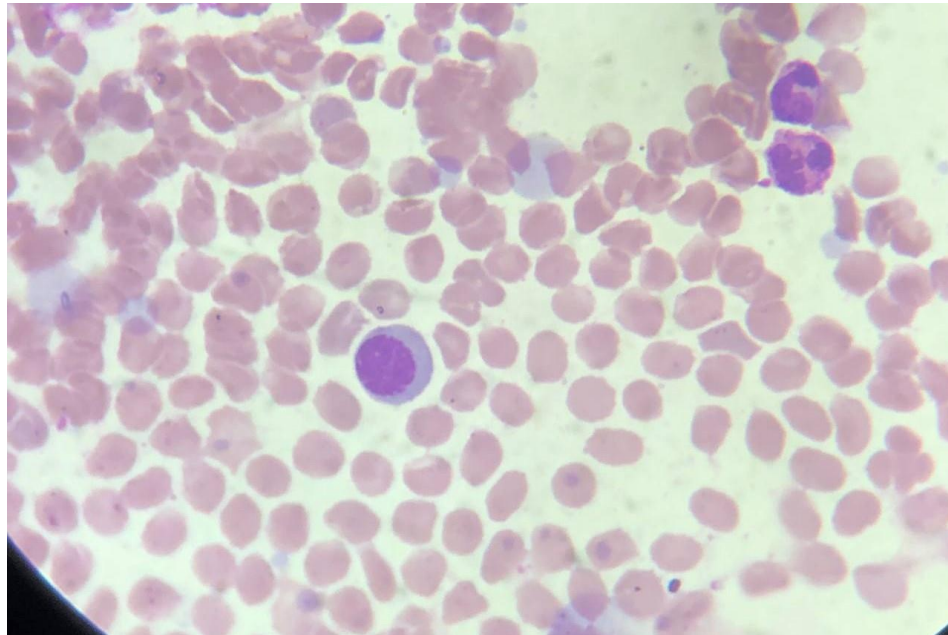
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## 4. Discussion

Vitamin B12 not a fatsoluble vitamin that's essential for nerve conduction, mental functioning, DNA

synthesis, and red blood cell formation. The recommended daily amount of vitamin B12 for most adults is 2.4. It is readily available in day to day nutritious food.



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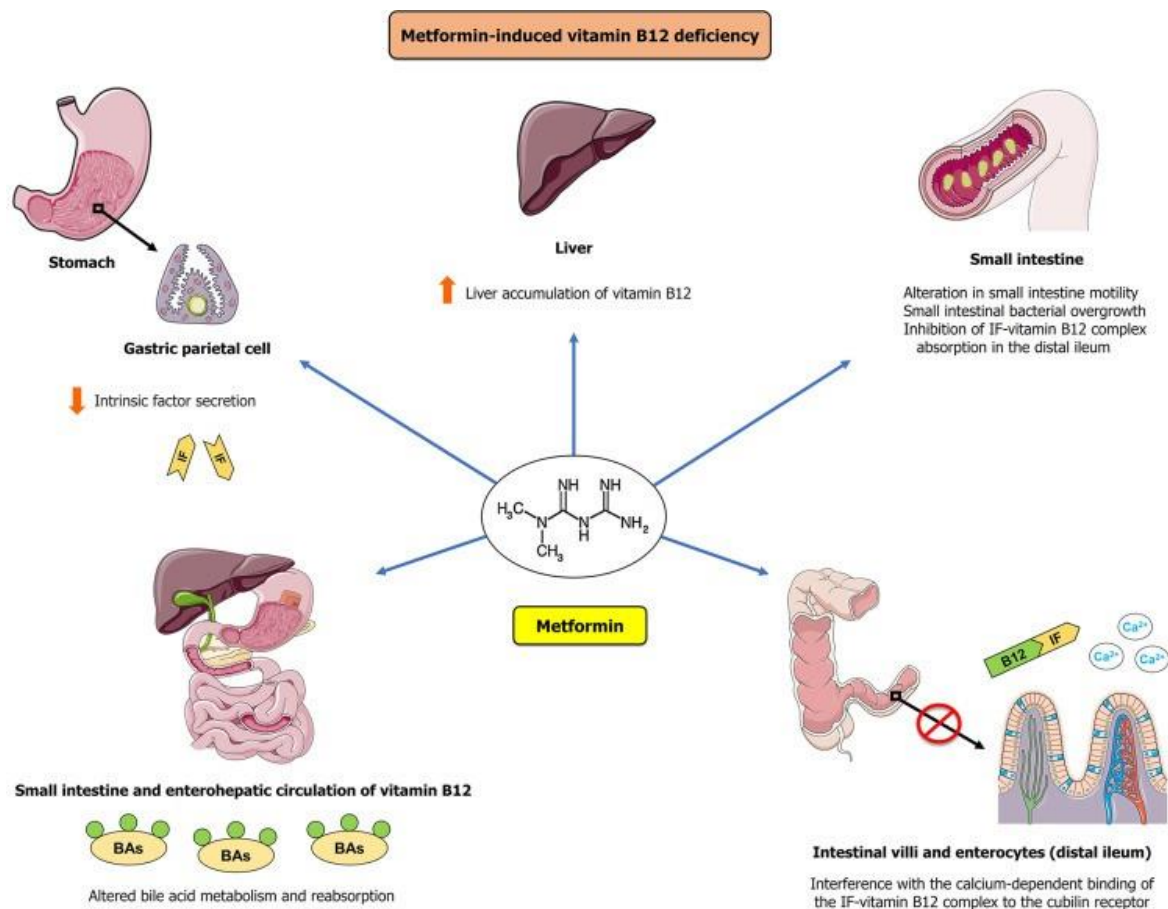
Metformin is a oral hypoglycemic drug used to lower high blood sugar levels in patients with type 2 diabetes. Metformin works by lowering the amount of glucose absorbed from intestines, decreasing how much glucose is made in the liver and improving insulin sensitivity.<sup>2</sup>

A number of studies have found an association between long-term use of metformin and depleted vitamin B12 levels. Among the most significant of these, for example, was a secondary analysis from the Diabetes Prevention Program (DPP)/DDPOutcomes Study (DDPOS), one of the largest and lengthiest studies of metformin use ever conducted.<sup>2</sup> The most common side effect of metformin is gastro intestine alirritation, including diarrhoea , cramps, nausea, vomiting, and increased bloating ; metformin is more commonly associated with gastrointestinal adverse effects than most other

antidiabetic medications.<sup>3</sup>The most serious potential adverse effect of metformin is lactic acidosis ; this complication is rare, and the vast majority of these cases seem to be related to conditions such as impairment of kidnays, liver , rather than to the metformin itself. Metformin is not approved for use in those with severe kidney disease but may still be used at lower doses in those with kidney problems.<sup>4</sup>

Low levels of vitamin B12 can cause serious and sometimes permanent neurological damage, as well as bone marrow production issues with subsequent anemia.<sup>3</sup>This is why levels of this nutrient must be monitored in anyone taking metformin.

The Image below shows how metformin therapy and its relationship with vitb12 deficiency.



Regular intake of metformin gives necessity for yearly check of your vitamin B12 status which can alert your healthcare provider to any dips in your levels that may be early signs of a deficiency.<sup>5,6</sup> One way to determine vitamin B12 status is with a test that directly measures levels of B12 in a blood sample. A more sensitive test looking at levels of a metabolite in the blood called methylmalonic acid (MMA) may be able to detect low B12 levels earlier.<sup>7</sup>

## 5. Conclusion

Vitamin B12 deficiency is found to be seen in patients taking long term and increased dosage of Metformin

So many studies have recently investigated that metformin, also worsening peripheral neuropathy. This study concludes the necessity of vitamin B12 monitoring in such patients and prophylactic B12

supplementation to prevent the known complications.

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