



Metformin use and Vitamin B12 Deficiency



K Mulla^{1,2}, K Bradbury¹

1. Nottingham University Hospitals NHS Trust, 2. Barts Health NHS Trust

Aim: To determine whether serum Vitamin B12 levels are measured in patients with Type II Diabetes Mellitus who are on Metformin therapy

Introduction

Incidence of Type II Diabetes Mellitus (T2DM) is rising; majority of T2DM is managed in primary care. NICE recommends starting Metformin as a first-line therapy¹. Studies have linked Metformin use with Vitamin B12 deficiency and suggest that regular monitoring of levels is warranted². The pathogenesis is not fully understood. Literature suggests that the risk of developing B12 deficiency is greatly influenced by high doses and long duration of therapy^{2,3}.

Guidelines:

- No official NICE guidelines or QOF indicators regarding the monitoring of Vitamin B12 levels in patients on Metformin
- British Society of Haematology (BSH)⁴ recommend that Vitamin B12 levels are checked, when there is a strong clinical suspicion of deficiency in patients on Metformin therapy

Audit Methodology

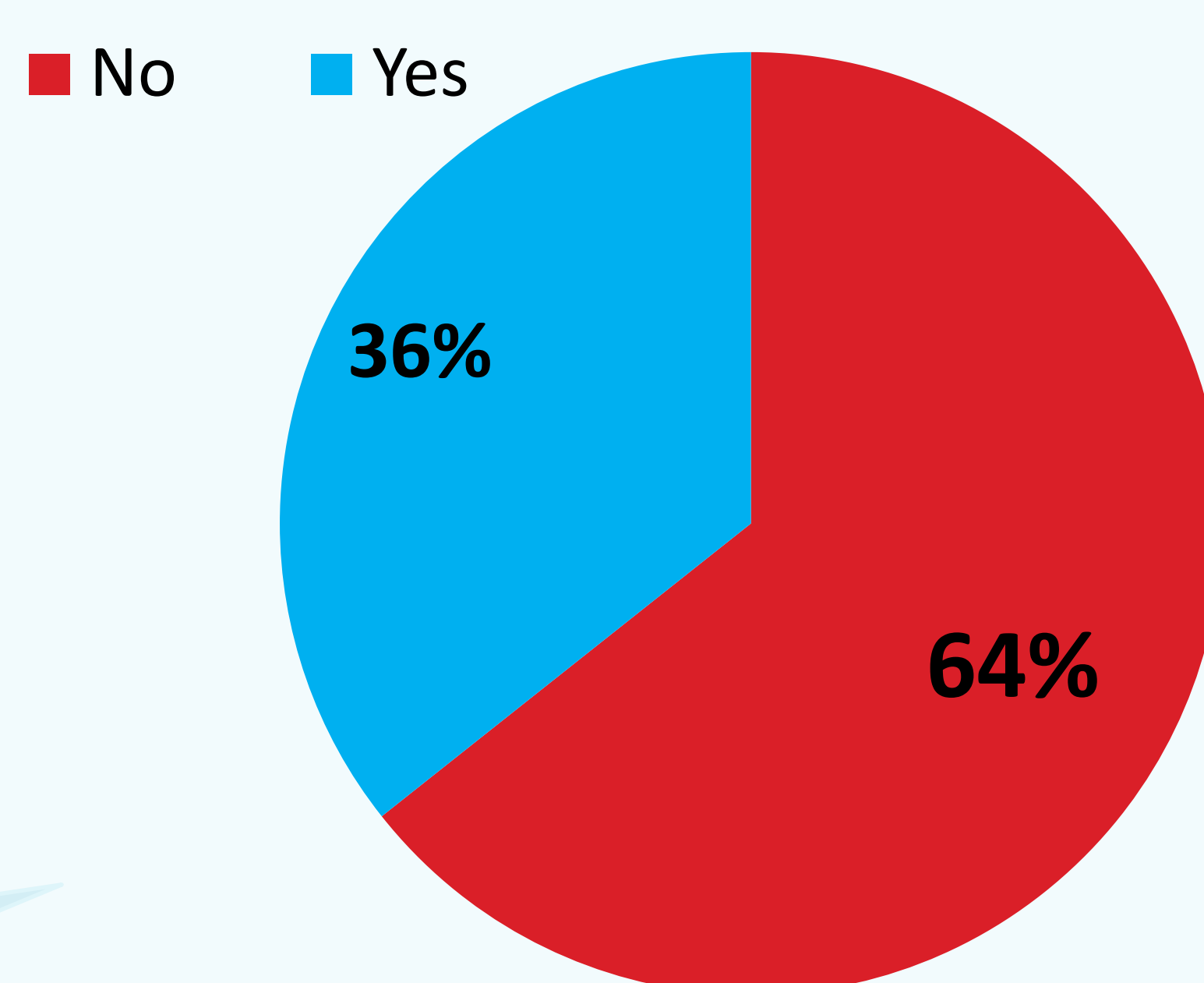
- Review records of 157 females with T2DM on Metformin
- Determine their age, dose of Metformin and duration of intake
- Determine whether their Vitamin B12 level has been checked or not
- Invite Patients for blood test if they have not had their Vitamin B12 checked
- If Vitamin B12 deficient, invite for replacement regime

Inclusion: Patients registered at Hucknall Road Medical Centre in Nottingham- whom have a known diagnosis of T2DM and have been established on Metformin therapy. Project included – all females whom are taking Metformin 500mg tablets or 500mg Modified release tablets. N = 157

Phase 1 Results:

- Average age = 63.4 years
- Most common dose of Metformin = 2000mg a day
- Average duration of Metformin use = 6.4 years
- 10 out 157 patients already had Vitamin B12 deficiency and given replacement injections (6.4%)
- 6 out of 10 patients were on the highest dose of Metformin and on average had been taking the medication for 6.6 years

How many patients have had their Vitamin B12 level checked?



Post Phase 1:

- Letters + blood forms sent to patients- to invite them for a blood test (FBC, Vitamin B12 and intrinsic factor)
- Those patients whom had their annual check due in the next month – had amendments made to include above tests
- If found to be deficient – patients were called to have their folate tested
- If Folate level was normal then patients were recommended to attend a nurse- led appointment for Vitamin B12 injections

Local Haematology consultant advice:

- Review NICE guidelines on Vitamin B12 deficiency
- Vitamin B12 deficiency is not an haematology issue- handled in the community with NICE guidance
- No recommendations on duration of therapy yet
- If cause is still present, it would make sense to continue replacement
- Up to GP surgery to decide the most practical management

NICE Guidelines:

- If Vitamin B12 is low then check for Intrinsic factor antibodies⁵
- If these are negative, then the cause is not pernicious anaemia- most likely Metformin in this case.
- Seek urgent haematology advice if pt has neurological symptoms or is pregnant or if haematological malignancy suspected
- For people with no neurological involvement:
 1. Initially administer hydroxocobalamin 1 mg IM – 3 times a week for the first 2 weeks.
 2. Maintenance dose- administer hydroxocobalamin 1 mg IM every 3 months for life

Phase 2 Results:

Compliance to blood test= 72.2%

5 patients found to be Vitamin B12 deficient

3 out of 5 patients were anaemic too

Phase 1+2: 15 out of 157 were deficient = **9.6%**

Table 1: shows details of patients with deficiency

Age (years)	Dose of Metformin	Duration of Treatment (years)	Vitamin B12 level	Folate
33	2000mg	6	169	Normal
69	3000mg	12	180	n/a
70	2000mg	5	179	Normal
64	1000mg	3	181	Normal
55	2000mg	16	147	n/a

Conclusion and Recommendation:

- Clear association of Metformin induced Vitamin B12 deficiency
- Vitamin B12 deficiency is a clinically important and treatable condition
- Vitamin B12 deficiency is associated with various systemic complications, such as neuropathy, which can be misinterpreted as Diabetic neuropathy
- The cost of checking yearly Vitamin B12 deficiency is fairly low
- Addition to the yearly recall- therefore no extra burden on the patient or appointment availability
- Patients are likely to remain on Metformin therefore oral vitamin B12 replacement should be considered for long term
- NHS- way forward is screening and prevention

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3. Ko, SH et al. Association of Vitamin B12 deficiency and metformin use in patients with type 2 diabetes. Journal of Korean Medical Science [online]. 2014; 29(7): 965-972.
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