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OLDER ADULT PSYCHIATRIC INPATIENTS WITH NON-COGNITIVE DISORDERS SHOULD BE SCREENED FOR VITAMIN B12 DEFICIENCY

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Abstract

Objective—Vitamin B12 (B12) deficiency is most prevalent among older adults. Practice guidelines recommend screening older adults with symptoms of cognitive disorder for B12 deficiency. However, guidelines for non-cognitive psychiatric disorders typically do not mention screening older adults for B12 deficiency. The purpose of this study was to determine whether routine screening of older adult psychiatric inpatients for B12 deficiency, regardless of cognitive symptoms, is clinically justified.

Design—We conducted a retrospective chart-review study of consecutive inpatient admissions.

Setting—Older Adult Acute Psychiatric Inpatient Unit at the University of Maryland Medical Center from 10/2007-4/2010.

Participants—Acute psychiatric inpatients aged ≥ 50 years who met inclusion criteria (N=374).

Measurements—Mean (SD) B12 levels and percentages of probable (<180pg/mL) and possible (180–350pg/mL) B12 deficiency as well as characteristics of patients with probable and possible B12 deficiency compared to patients with optimal B12 levels.

Results—Mean (SD) B12 levels and percentages of probable and possible B12 deficiency, respectively, for cognitive disorder patients [468 (284) pg/mL, 7.8 % (n=5) and 29.7% (n=19)] and for non-cognitive disorder patients [481(268) pg/mL, 4.8 % (n=15) and 33.2% (n=103)] were not significantly different (t=0.339, df=372, P=0.735; $\chi^2=1.084$, df=2, P=0.582, respectively).

Conclusion—Considering the potential benefits and low costs of screening and treatment, we conclude that it is justified to routinely screen older adult psychiatric inpatients for B12 deficiency whether or not cognitive disorder symptoms are present.

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Keywords

Vitamin B12 deficiency; cobalamin deficiency; psychiatric inpatients; geriatric

Introduction

Vitamin B12 (B12) deficiency is a common problem in older adults. Depending on criteria and setting 3–40% of older adults are estimated to have B12 deficiency, with the highest rates in institutional settings (1–3). Older adults are more prone to deficiency due to food-B12 malabsorption. Causes of malabsorption include: gastrointestinal (GI) pathology (e.g. atrophic gastritis, *H. pylori* infection), pernicious anemia (PA), and medication effects. Commonly prescribed medications including proton pump inhibitors (PPI) and histamine 2 receptor antagonists (H2 antagonists), which increase gastric pH, and the oral anti-diabetic drug, metformin (4) can reduce B12 absorption.

Up to 50% of persons with B12 deficiency have incident neuropsychiatric symptoms which often precede hematological manifestations (5). The active forms of cobalamin (methylcobalamin and adenosylcobalamin) serve as cofactors for enzymes in the cytoplasm and mitochondria. When these metabolic pathways are disrupted by cobalamin deficiency, increased levels of homocysteine (Hcy) and methylmalonic acid (MMA) result. Elevated levels of Hcy are known to be neurotoxic and vasculotoxic, while elevated levels of MMA can cause abnormal fatty acid synthesis affecting the neuronal membrane leading to neuropsychiatric symptoms and possible nervous system structural damage (6–8).

Screening for B12 deficiency in patients with symptoms of cognitive disorders, most often older patients, is common practice. This is reflected in practice guidelines such as The American Psychiatric Association (APA) Practice Guidelines on Alzheimer's Disease and Other Dementias (9). However, our review of the current APA guidelines for the psychiatric evaluation of adults with bipolar disorder, delirium, major depressive disorder and schizophrenia, make no specific mention of screening for serum B12 levels, except when evaluating cognitive symptoms in the context of depression. We undertook this chart review study of vitamin B12 status in patients admitted to the Older Adult Acute Psychiatric Inpatient Unit at the University of Maryland Medical Center in order to determine whether routine screening of all admitted patients, not just patients admitted for acute or chronic cognitive disorders (i.e. Dementia, Delirium, Cognitive Disorder NOS), revealed significant numbers of patients who presented with non-cognitive complaints whose serum B12 levels suggested B12 deficiency.

A growing body of case report and epidemiologic literature has demonstrated an association of B12 deficiency with not only cognitive impairment, but also mood and psychotic symptoms (1, 8, 10–14) and treatment outcomes (15–17). However, these findings have yet to be translated into changes in practice guidelines. One reason for this is that the clinical utility of screening patients with non-cognitive disorders in various clinical settings, including acute inpatient units, is unclear. This is due to a lack of recent studies using more sensitive cutoff values that have also analyzed B12 levels by diagnosis.

In reviewing the literature on B12 levels in psychiatric patients, we found numerous studies performed over the past 50 years (18–27), which used various serum B12 cutoff values (100–223pg/mL) to define low B12 status yielding great variation in the rates of low serum B12 levels (0.4–20%). However, there was no study that focused on older adult psychiatric inpatients and the variation in B12 status by cognitive disorder and non-cognitive disorder diagnoses. Furthermore, none of the studies used more sensitive B12 cutoff levels recommended for screening of deficiency prior to the onset of irreversible signs and symptoms (2). Studies in the elderly have recommended not assuming an adequate B12 status unless the screening serum B12 level is ≥ 350 pg/mL (2, 3). We therefore wanted to know how many patients on our unit could be considered to be at risk for deficiency by using this more sensitive cutoff (<350 pg/mL) to define possible B12 deficiency.

Methods

In this retrospective, chart review study, approved by the University of Maryland Institutional Review Board (IRB) we examined the medical records of consecutive admissions to our Older Adult Acute Psychiatric Inpatient Unit at the University of Maryland Medical Center (UMMC) from October 2007 to April 2010. Out of 433 patients, 374 met the following inclusion criteria: (1) age ≥ 50 years and (2) available serum B12 level on admission as per the standard admission order set. 48 individuals were excluded due to lack of a serum B12 level on admission, and 11 were excluded for age <50 years.

Patients were grouped into two psychiatric disorder categories according to their major Axis I disorder requiring inpatient psychiatric admission for acute exacerbation of symptoms: Axis I diagnosis of cognitive disorder (dementia, delirium, cognitive disorder NOS) or non-cognitive disorder (all other patients) in order to compare B12 status. All diagnoses were made by attending geriatric psychiatrists certified by the American Board of Psychiatry and Neurology. Patients were further categorized in a clinically meaningful way as having probable (B12 serum level <180 pg/mL) and possible (B12 serum level 180–349 pg/mL) B12 deficiency or having optimal B12 status (B12 serum level ≥ 350 pg/mL). The probable and possible B12 deficiency groups were compared to patients with optimal B12 status on the following factors: age; gender; race; psychiatric diagnostic category; presence of gastric disease including gastroesophageal reflux disease (GERD) and peptic ulcer disease (PUD); drug interactions that can interfere with B12 absorption including use of PPIs, H₂ antagonists and metformin; nutritional status assessed by albumin level and body mass index (BMI); and the hematologic indices hematocrit (HCT) and mean corpuscular volume (MCV).

Groups were compared on categorical variables by chi square (χ^2) tests. For analysis of continuous variables, we used Student's t test, one way analysis of variance (ANOVA) and Pearson's r. All tests were two-tailed. Statistical significance was set as $P \leq 0.05$, and analyses were performed with the aid of SPSS 12.0 (SPSS Inc., Chicago, IL).

Results

Cognitive and non-cognitive disorder groups did not differ significantly in their mean B12 levels ($t=0.339$, $df=372$, $P=0.735$) nor did they differ in percentages of patients with probable and possible B12 deficiency ($\chi^2=1.084$, $df=2$, $P=0.582$) as shown in Table 1. The relationship of B12 level to age was assessed to determine whether age should be used as a covariate in these analyses, and B12 level was found to not correlate significantly with age ($r=-0.066$, $p=0.202$). The diagnostic composition of both cognitive and non-cognitive disorder groups is described in Table 2. Characteristics of the total inpatient sample and the sample categorized by serum B12 level are shown in Table 3. Groups did not differ significantly on variables with the exception that the group of 20 patients with probable B12 deficiency differed significantly from other patients in having a higher rate of peptic ulcer disease ($\chi^2=92.3$, $df=2$, $P<0.001$).

Discussion

We undertook this chart review study primarily to answer an important clinical and economic question: Is there value in screening all admissions to an older adult acute psychiatric unit for B12 deficiency regardless of presenting symptoms and diagnosis? We also intended to gain a better understanding of the frequency and factors associated with possible and probable B12 deficiency in this population.

Our findings have led us to conclude that our current practice of screening all admissions, regardless of presenting symptoms or diagnosis, is clinically justified. We reached this conclusion, based on the following findings: (1) approximately 38% of patients had relatively low B12 levels in the probable or possible B12 deficiency ranges, placing them at risk for B12 deficiency-related clinical manifestations (2) the prevalence of probable and possible B12 deficiency did not vary significantly according to the presence of cognitive disorder, suggesting that older adults with non-cognitive disorders have a similar risk for deficiency as those with cognitive disorders, and (3) we would have missed about 75% of patients with probable B12 deficiency and 80% of patients with possible B12 deficiency if we had only screened patients with cognitive disorders. Given the inexpensive and readily available treatment for B12 deficiency, we therefore recommend screening all psychiatric inpatients age 50 years and older for B12 deficiency. Consideration should be given to including B12 deficiency screening in practice guidelines for mood and psychotic disorders with mention of the higher risk in older patients.

The possible B12 deficiency rates we found are consistent with available prevalence rates that have been documented in the elderly, but are higher than those previously reported in psychiatric patients, as our serum B12 cutoff value for possible deficiency is higher than previous values used to define B12 deficiency. It has been well established that current hospital laboratory parameters for normal range serum B12 levels are not sufficiently sensitive to diagnose deficiency (28), delaying early prevention of deficiency related disease. In the elderly, it has been recommended to use cutoff values of $<350\text{pg/mL}$ to raise suspicion for deficiency (2) that would lead to further work up or treatment. Our findings suggest that a significant amount of our older adult psychiatric inpatients could be at risk for

B12 deficiency with potential for worsening neuropsychiatric symptoms, including treatment resistance or irreversible structural damage.

As observed in this study, the presence of PUD in this population should raise awareness for B12 deficiency. Possible explanations for this finding are: (1) *Helicobacter pylori* is an important etiologic agent in PUD that has been associated with B12 deficiency (29, 30) and (2) treatments for PUD including H2 antagonists and PPIs can interfere with Cobalamin absorption. We did not find an association of medication use or demographic, hematologic, and nutritional indices with B12 deficiency.

As a retrospective chart review, this study had several limitations. Complete data could not be obtained from all consecutive admissions and no data was available on the use of multivitamin supplements in this cohort. The small number of individuals with probable B12 deficiency and the relatively small percentage of patients with cognitive disorders limited the power of our analyses. In a much larger sample, the slightly higher percentage of cognitive disorder patients with probable B12 deficiency may have achieved statistical significance. Additional laboratory studies including methylmalonic acid and homocysteine levels were not available in most patients to more definitively assess B12 deficiency. This study had several strengths, however: the inclusion of indices of nutritional status such as serum albumin and BMI, and extending the analysis beyond the typical low normal cutoff of 180 pg/mL to assess the number of patients at risk for B12 deficiency. More research, particularly prospective studies observing the outcomes of B12 supplementation over time, is required to better understand the costs and benefits of screening for and treating B12 deficiency in older psychiatric patients.

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References

1. Dharmarajan TS, Adiga GU, Norkus EP. Vitamin B12 deficiency Recognizing subtle symptoms in older adults. *Geriatrics*. 2003; 58:30–4. 37–8. [PubMed: 12650116]
2. Lindenbaum J, Rosenberg IH, Wilson PW, Stabler SP, Allen RH. Prevalence of cobalamin deficiency in the Framingham elderly population. *Am J Clin Nutr*. 1994; 60:2–11. [PubMed: 8017332]
3. Pennypacker LC, Allen RH, Kelly JP, Matthews LM, Grigsby J, Kaye K, Lindenbaum J, Stabler SP. High prevalence of cobalamin deficiency in elderly outpatients. *J Am Geriatr Soc*. 1992; 0:1197–204. [PubMed: 1447433]
4. Andres E, Federici L, Affenberger S, Vidal-Alaball J, Loukili NH, Zimmer J, Kaltenbach G. B12 deficiency: a look beyond pernicious anemia. *J Fam Pract*. 2007; 56:537–42. [PubMed: 17605945]
5. Goebels N, Soyka M. Dementia associated with vitamin B(12) deficiency: presentation of two cases and review of the literature. *J Neuropsychiatry Clin Neurosci*. 2000; 12:389–94. [PubMed: 10956574]
6. Hutto BR. Folate and cobalamin in psychiatric illness. *Compr Psychiatry*. 1997; 38:305–14. [PubMed: 9406735]
7. Obeid R, McCaddon A, Herrmann W. The role of hyperhomocysteinemia and B-vitamin deficiency in neurological and psychiatric diseases. *Clin Chem Lab Med*. 2007; 45:1590–606. [PubMed: 18067446]

8. Lachner C, Steinle NI, Regenold WT. The neuropsychiatry of vitamin B12 deficiency in elderly patients. *J Neuropsychiatry Clin Neurosci.* 2012; 24:5–15. [PubMed: 22450609]
9. American Psychiatric Association. Practice Guidelines for the Treatment of Psychiatric Disorders. 2006 Compendium.
10. Tiemeier H, van Tuijl HR, Hofman A, Meijer J, Kiliaan AJ, Breteler MM. Vitamin B12, folate, and homocysteine in depression: the Rotterdam Study. *Am J Psychiatry.* 2002; 159:2099–101. [PubMed: 12450964]
11. Penninx BW, Guralnik JM, Ferrucci L, Fried LP, Allen RH, Stabler SP. Vitamin B(12) deficiency and depression in physically disabled older women: epidemiologic evidence from the Women's Health and Aging Study. *Am J Psychiatry.* 2000; 157:715–21. [PubMed: 10784463]
12. Ng TP, Feng L, Niti M, Kua EH, Yap KB. Folate, vitamin B12, homocysteine, and depressive symptoms in a population sample of older Chinese adults. *J Am Geriatr Soc.* 2009; 57:871–6. [PubMed: 19484842]
13. Kim JM, Stewart R, Kim SW, Yang SJ, Shin IS, Yoon JS. Predictive value of folate, vitamin B12 and homocysteine levels in late-life depression. *Br J Psychiatry.* 2008; 192:268–74. [PubMed: 18378986]
14. Hector M, Burton JR. What are the psychiatric manifestations of vitamin B12 deficiency? *J Am Geriatr Soc.* 1988; 36:1105–12. [PubMed: 3057051]
15. Masalha R, Chudakov B, Muhamad M, Rudoy I, Volkov I, Wirguin I. Cobalamin-responsive psychosis as the sole manifestation of vitamin B12 deficiency. *Isr Med Assoc J.* 2001; 3:701–3. [PubMed: 11574992]
16. Hintikka J, Tolmunen T, Tanskanen A, Viinamäki H. High vitamin B12 level and good treatment outcome may be associated in major depressive disorder. *BMC Psychiatry.* 2003; 3:17. [PubMed: 14641930]
17. Kalita J, Agarwal R, Chandra S, Misra UK. A study of neurobehavioral, clinical psychometric, and P3 changes in vitamin B12 deficiency neurological syndrome. *Nutr Neurosci.* 16:39–46. [PubMed: 22781060]
18. Carney MW. Serum vitamin B12 values in 374 psychiatric patients. *Behav Neuropsychiatry.* 1969; 1:19–22. [PubMed: 5377816]
19. Henderson JG, Dawson AA. Serum vitamin-B12 levels in psychiatric patients on long-term psychotropic drug therapy. *Br J Psychiatry.* 1970; 116:439–42. [PubMed: 5441804]
20. Isaksson A, Myrstener A, Ottosson JO. Screening for vitamin B 12 deficiency in psychiatric patients. *Acta Psychiatr Scand Suppl.* 1971; 221:133–42. [PubMed: 5286325]
21. Carney MW, Sheffield BF. Serum folic acid and B12 in 272 psychiatric inpatients. *Psychol Med.* 1978; 8:139–44. [PubMed: 635065]
22. Elsborg L, Hansen T, Rafaelsen OJ. Vitamin B12 concentrations in psychiatric patients. *Acta Psychiatr Scand.* 1979; 59:145–52. [PubMed: 420034]
23. Bell IR, Edman JS, Marby DW, Satlin A, Dreier T, Liptzin B, Cole JO. Vitamin B12 and folate status in acute geropsychiatric inpatients: affective and cognitive characteristics of a vitamin nondeficient population. *Biol Psychiatry.* 1990; 27:125–37. [PubMed: 2294976]
24. Brett AS, Roberts MS. Screening for vitamin B12 deficiency in psychiatric patients. *J Gen Intern Med.* 1994; 9:522–4. [PubMed: 7996297]
25. Silver H. Vitamin B12 levels are low in hospitalized psychiatric patients. *Isr J Psychiatry Relat Sci.* 2000; 37:41–5. [PubMed: 10857271]
26. Murphy F, Srivastava PC, Varadi S, Elwis A. Screening of psychiatric patients for hypovitaminosis B12. *Br Med J.* 1969; 3:559–60. [PubMed: 5803687]
27. Lerner V, Kanevsky M, Dwolatzky T, Rouach T, Kamin R, Miodownik C. Vitamin B12 and folate serum levels in newly admitted psychiatric patients. *Clin Nutr.* 2006; 25:60–7. [PubMed: 16216392]
28. Willis CD, Elshaug AG, Milverton JL, Watt AM, Metz MP, Hiller JE. Diagnostic performance of serum cobalamin tests: a systematic review and meta-analysis. *Pathology.* 2011; 43:472–81. [PubMed: 21716160]

29. Kaptan K, Beyan C, Ural AU, Cetin T, Avcu F, Gulsen M, Finci R, Yalcin A. Helicobacter pylori— is it a novel causative agent in Vitamin B12 deficiency? Arch Intern Med. 2000; 160:1349–53. [PubMed: 10809040]
30. Sarari AS, Farraj MA, Hamoudi W, Essawi TA. Helicobacter pylori, a causative agent of vitamin B12 deficiency. J Infect Dev Ctries. 2008; 2:346–9. [PubMed: 19745500]

Table 1

Serum vitamin B12 level distribution in cognitive and non-cognitive disorders

	B12 level (pg/mL)	% by deficiency risk category		
	Mean (SD)	<180	180–349	350
All Psychiatric Disorders	479 (270)	5.3% (20)	32.6% (122)	62.0% (232)
Cognitive Disorder	468 (284)	7.8% (5)	29.7% (19)	62.5% (40)
Non-Cognitive Disorder	481 (268)	4.8% (15)	33.2% (103)	61.9% (192)

Table 2

Diagnostic composition of cognitive and non-cognitive disorder groups

Diagnostic Disorder Category	Diagnosis	N	%
Cognitive Disorders (N=64)	Dementia	53	82.8%
	Delirium	7	10.9%
	Cognitive Disorder NOS	4	6.3%
Non-cognitive Disorders (N=310)	Schizophrenia	57	18.4%
	Schizoaffective Disorder	39	12.6%
	Psychosis NOS	23	7.4%
	Bipolar Disorder	50	16.1%
	Major Depressive Disorder	52	16.8%
	Depressive Disorder NOS	43	13.9%
	Mood Disorder NOS	18	5.8%
	Other Disorders ^a	28	9.0%

^a Adjustment, Substance Related, Dysthymia, Delusional, Anxiety, Secondary to General Medical Condition, and Personality Disorders.

Table 3

Characteristics of the total inpatient sample and the sample categorized by serum vitamin B12 level

Variable ^a	Serum vitamin B12 level (pg/mL)				P
	Total ^b	<180	180–349	≥350	
N	374	20	122	232	
Age (years)	63.5 (10.5)	64.9 (8.8)	64.5 (11.0)	62.8 (10.3)	0.299
Gender					0.433
% male (n)	48.1% (180)	60.0% (12)	50.0% (61)	46.1% (107)	
Race ^c					0.485
White	49.4% (185)	40.0% (8)	51.6% (63)	49.1% (114)	
Black	48.7% (182)	60.0% (12)	45.1% (55)	49.6% (115)	
Other	1.9% (7)	0.0% (0)	3.3% (4)	1.3% (3)	
PUD	3.2% (12)	40.0% (8)	1.6% (2)	0.86% (2)	<0.001
GERD	19.5% (73)	20.0% (4)	19.7% (24)	19.4% (45)	0.997
PPI/H2B	23.3% (87)	35.0% (7)	18.9% (23)	24.6% (57)	0.213
Metformin	9.1% (34)	5.0% (1)	12.3% (15)	7.8% (18)	0.298
Albumin (g/dL)	3.6 (1.1)	3.6 (0.4)	3.6 (0.4)	3.6 (1.3)	0.922
BMI (kg/m ²)	28.2 (11.6)	28.5 (12.3)	28.6 (8.8)	28.0 (12.8)	0.880
HCT (%)	38.8 (6.4)	39.7 (5.1)	39.5 (4.9)	38.4 (7.1)	0.253
MCV (fL)	88.2 (12.3)	88.2 (4.7)	90.2 (6.1)	87.2 (14.6)	0.180

^aFor continuous variables, values are shown as the mean and standard deviation (SD);

^bPercentages are based on using first row N values as denominators;

^cIn this analysis the “Other” category was excluded given the small sample size.; Abbreviations: PUD=Peptic ulcer disease; GERD=Gastroesophageal reflux disease; PPI=Proton Pump Inhibitor; H2B=Histamine Receptor-2 Antagonist; BMI=Body Mass Index; HCT=Hematocrit; MCV=Mean Corpuscular Volume.