

Vitamin B₁₂ deficiency

Prevalence among South Asians at a Toronto clinic

Anil K. Gupta, MD, CCFP Alkarim Damji, MD, CCFP Aparna Uppaluri, MHSC

ABSTRACT

OBJECTIVE To estimate the prevalence of vitamin B₁₂ deficiency in adult South Asian patients.

DESIGN Retrospective chart review.

SETTING Family practice clinic in Toronto, Ont.

PARTICIPANTS Records of 988 South Asian patients.

INTERVENTION Of 1000 randomly selected records, we found 988 charts. From charts with at least one documented B₁₂ level, we extracted data on age, mean corpuscular volume (MCV), hemoglobin and ferritin levels, and diet (if available). Descriptive and analytic statistics were calculated.

MAIN OUTCOME MEASURES Levels of serum B₁₂ and factors associated with low levels of B₁₂.

RESULTS B₁₂ results were documented in 49% of charts; 46% of results showed deficiency. Patients older than 65 and vegetarians were more likely to be B₁₂ deficient. Low serum B₁₂ levels were positively correlated with low hemoglobin and ferritin levels and poorly correlated with low MCV levels.

CONCLUSION Many more South Asian patients than patients in the general population have vitamin B₁₂ deficiency. A vegetarian diet seems a strong risk factor. A single low result, however, might not indicate true B₁₂ deficiency.

RÉSUMÉ

OBJECTIF Estimer la prévalence de la déficience en vitamine B₁₂ chez les patients adultes d'origine sud asiatique.

TYPE D'ÉTUDE Étude rétrospective sur dossiers.

CONTEXTE Établissement de médecine familiale à Toronto, Ont.

PARTICIPANTS Dossiers de 988 patients d'origine sud-asiatique.

INTERVENTION Sur 1000 dossiers sélectionnés au hasard, 988 ont été retrouvés. De ceux qui comportaient au moins une mesure de B₁₂, les données suivantes ont été extraites: âge, volume globulaire moyen (VGM), niveaux d'hémoglobine et de ferritine et régime alimentaire (si disponible). Les statistiques descriptives et analytiques ont été calculées.

PRINCIPAUX PARAMÈTRES MESURÉS Niveaux sériques de B₁₂ et facteurs associés aux bas niveaux.

RÉSULTATS Des résultats de B₁₂ apparaissaient dans 49% des dossiers et 46% d'entre eux indiquaient une déficience. Les sujets de plus de 65 ans et les végétariens étaient plus susceptibles d'être déficients. Il y avait une corrélation directe entre les niveaux de B₁₂ et ceux de l'hémoglobine et de la ferritine; la corrélation avec les niveaux de VGM était faible.

CONCLUSION La déficience en vitamine B₁₂ est beaucoup plus fréquente chez les patients d'origine sud-asiatique que dans la population générale. Une alimentation végétarienne semble constituer un important facteur de risque. Un seul résultat bas n'indique pas nécessairement une déficience réelle.

This article has been peer reviewed.

Cet article a fait l'objet d'une évaluation externe.

Can Fam Physician 2004;50:743-747.

Vitamin B₁₂ deficiency can have neurologic and hematologic sequelae and can lead to hyperhomocysteinemia.¹ Symptoms of B₁₂ deficiency include fatigue, weakness, anorexia, paresthesias, numbness, and dizziness. Initial presentation is often vague.¹⁻⁴

Prevalence of B₁₂ deficiency in the general population has not been well established because a universally accepted normal B₁₂ level has not been defined.^{5,6} Prevalence in the general population varies from 3% to 5%,^{7,8} and from 5% to 20%^{2,9} among people older than 65.

The main causes of B₁₂ deficiency include lack of intrinsic factor and other intestinal factors (eg, malabsorption), rare genetic disorders, and inadequate intake.^{1,5,10} Absorption problems (due to lack of intrinsic or intestinal factors) are thought to be the most common cause of B₁₂ deficiency.^{1,6}

Inadequate intake of B₁₂ through diet is believed to be a rare cause of B₁₂ deficiency, although people who follow a vegan diet are considered at elevated risk.^{1,2,5,6,10} Since the main sources of B₁₂ are eggs and dairy products,^{1,2,5} as well as meat and poultry, there has been less concern about B₁₂ deficiency among vegetarians who consume some animal-based products.^{1,2,5,6,10}

Some evidence suggests South Asians, lacto-vegetarians, and in particular South Asians who are lactovegetarians are at greater risk of B₁₂ deficiency. One study found that about 38% of people in western India followed a lactovegetarian diet and that 47% of the study population (60% of vegetarian and 39% of nonvegetarian people) were B₁₂ deficient.¹¹ Another study found that South Asian men in the United Kingdom had lower mean B₁₂ levels than European controls (270 pmol/L vs 357 pmol/L).¹² In Asia, Indians had lower B₁₂ levels than Chinese or Malays.¹³

Recent estimates indicate that 750 000 South Asians reside in Canada¹⁴; India is now the

second-largest source country for immigrants to Canada. At our urban clinic, more than 50% of patients are of South Asian origin (mainly from India and Pakistan). Clinicians in the practice noticed many patients with neurologic, hematologic, or vague symptoms and signs, and these led to B₁₂ testing. After finding that a sizable proportion of these patients were B₁₂ deficient, we initiated widespread testing among our adult patients and found more abnormal B₁₂ levels.

As a result of these clinical and laboratory findings, we did a literature review using the key words “South Asian,” “vitamin B₁₂,” “cyanocobalamin,” and “vegetarians.” We found no studies examining B₁₂ levels in South Asians living in North America. We decided to conduct a retrospective chart review to estimate the prevalence and characteristics of B₁₂ deficiency in our large South Asian patient population.

METHODS

Participants

In our four-doctor clinic in urban Toronto, about 7000 of our total 13 000 patients are of South Asian origin. We defined South Asian as being from India or Pakistan. From a master list of all adult patients, our administrator selected the South Asian patients based on her 10 years' experience at the clinic and her familiarity with South Asian names. We chose 1000 names by selecting every seventh name from the complete list. We found 988 of their 1000 charts.

Chart review

Data collection. We collected all nonnominal information on a simple data-collection form. From charts that had at least one documented B₁₂ level, we collected data on B₁₂ level; age; sex; mean corpuscular volume (MCV) and ferritin and hemoglobin (Hb) levels. Information on religious background was unavailable.

If a documented B₁₂ level was below our chosen cutoff, that level was used in our analysis. We also attempted to determine whether patients were vegetarian or nonvegetarian. The term vegetarian includes vegans, lactovegetarians, and

Dr Gupta practised at the Rexdale Community Health Centre at the time of the study; **Dr Damji** practises at the North Kipling Health Centre; and **Ms Uppaluri** works in the Department of Medicine at the University of Toronto in Ontario.

lacto-ovo vegetarians. We defined nonvegetarians as anyone who even occasionally consumed meat or fish. St Joseph's Health Centre Research Ethics Board approved the study.

Laboratory tests. Three different tests from Abbott Laboratories (IMx, AxSYM, and Architect, all micro-particle intrinsic factor assays) had been used to measure B₁₂ levels from 1993 to 2001. All three had similar normal and deficient ranges and were very closely correlated with each other as shown by subsequent testing in the laboratory (personal communication from Dr P.F. Stuart, Medical Director of Canadian Medical Laboratories, November 21, 2002).

Cutoff levels for B₁₂ deficiency. There is little consensus on an appropriate cutoff for determining normal and abnormal B₁₂ levels. In a recent Ontario-wide study of 692 consecutively ordered B₁₂ tests, the fifth percentile for vitamin B₁₂ levels was 134.6 pmol/L.⁷ In the National Health and Nutrition Examination Survey III (NHANES III), 3% of 11 851 people who were assessed for B₁₂ levels had levels <148 pmol/L and were considered B₁₂ deficient.⁸ Laboratory values for B₁₂ in our patients' charts spanned several years, and the cutoff used to define deficiency decreased over time (range 180 pmol/L to 132 pmol/L). Our laboratory used ≤132 pmol/L as the cutoff during our data collection period. We elected to use this level because we believed it to be most conservative.

Calculating prevalence of deficiency. Of the charts selected, 49% (482/988) contained B₁₂ measurements. Because people whose B₁₂ levels had been measured might be more likely to be deficient (because suspicion of B₁₂ deficiency leads to testing), estimating prevalence using this denominator (482) could be artificially inflated. Therefore, we also estimated prevalence of B₁₂ deficiency using all 988 charts found.

We noted that most patients who did not have B₁₂ levels measured attended the clinic only once or twice, so they would have had less opportunity for testing. The mean age of patients with B₁₂ levels measured (42 years) was similar to the mean age

of those not measured (41 years). We think those measured and those not measured are likely to be similar populations. Based on these assumptions, we believe that the higher estimate of B₁₂ deficiency is closer to the truth. Therefore, further analysis was completed using data extracted from the charts of patients with documented B₁₂ levels.

Data analysis

Descriptive statistics were obtained for all variables. Spearman correlation coefficients were used to examine the correlation between B₁₂ levels and other hematologic variables. Odds ratios (ORs) and confidence intervals (CIs) were calculated to examine the relationship between age, sex, and vegetarian diet and the presence or absence of B₁₂ deficiency. Calculations were done using SPSS software, version 9.0 for Windows.

RESULTS

Average age of subjects was 42 years (range 18 to 84). There were 210 men (44%) and 272 women. Dietary data were recorded in 40% (195/482) of charts: 172 patients were documented vegetarian; 23 were documented nonvegetarian.

Prevalence of deficiency

Of the 482 people with documented B₁₂ levels, 222 (46%) had at least one deficient result (≤132 pmol/L). Our more conservative estimate based on all 988 charts indicated that 22% (222/988) had at least one deficient result. About 32% (154/482) of the study population was older than 65; 82% of this group were B₁₂ deficient (32% of those <65 were deficient). Risk appeared to be similar for men and women (OR 1.14, 95% CI 0.78 to 1.67) (**Table 1**).

Table 1. Vitamin B₁₂ levels by sex

SEX	B ₁₂ ≤132 N (%)	B ₁₂ >132 N (%)	TOTAL N (%)
Male	99 (21)	111 (23)	210 (44)
Female	123 (26)	149 (31)	272 (56)
TOTAL	222 (46)	260 (54)	482 (100)

Relationship with diet

Vegetarianism was found to be a substantial risk factor for B₁₂ deficiency (OR 2.14, CI 1.65 to 2.77) (Table 2).

Table 2. Vitamin B₁₂ levels by sex and diet

SEX AND DIET	B ₁₂ ≤132 N (%)	B ₁₂ >132 N (%)
MALE		
• Vegetarian	51 (11)	19 (4)
• Nonvegetarian	5 (1)	4 (1)
• Unknown	43 (9)	111 (18)
FEMALE		
• Vegetarian	63 (13)	39 (8)
• Nonvegetarian	14 (3)	0 (0)
• Unknown	46 (10)	110 (23)
TOTAL	222 (46)	260 (54)

Relationship with hematologic factors

Deficient B₁₂ levels were poorly correlated with high MCV levels (*P* = .02) and positively correlated with low ferritin (*P* = .83) and low Hb (*P* = .67) levels.

DISCUSSION

Our retrospective study of a random sample of South Asian patients' charts showed a very high prevalence of B₁₂ deficiency (22% to 46%) compared with estimated rates in the general population (3% to 5%).^{7,8}

Consistent with previous studies, rates of B₁₂ deficiency in our study were similar in men and women, and risk of deficiency was higher among elderly people.^{1,2,6,9} Our study population, however, was younger than populations in some previous studies,^{2,6,9} and we found an unusually high rate of deficiency in people younger than 65 years (32%).

We found that B₁₂ deficiency was positively correlated with iron deficiency and low Hb levels and poorly correlated with increased MCV levels. This is noteworthy because increased MCV levels are typically observed in conjunction with deficient B₁₂ levels. We think that this was not observed in our study, in part, because the often coexisting iron deficiency could decrease MCV levels.

A recent Indian study showed that 60% of vegetarians and 39% of nonvegetarians were B₁₂ deficient.

A more detailed dietary analysis indicated, however, that even nonvegetarians ate meat only occasionally.¹¹ We found high rates of B₁₂ deficiency, even among patients labeled nonvegetarian. Some data in our charts and general knowledge of our population led us to believe that even nonvegetarians ate meat only occasionally.

Limitations

Our study has some important limitations. First, our data provide an estimate of the proportion of the population that is B₁₂ deficient at any time over several years, rather than the number of people who are B₁₂ deficient at any one time. Also, our comparison prevalence rates of 3% to 5% for the general population are point prevalence rates rather than period prevalence rates.

Second, dietary information was not consistently available, and we cannot be sure of the validity of dietary information in the charts. Third, we defined South Asians by our administrator's knowledge of our patient population, and this might not always have been accurate. Fourth, our study was based on serum B₁₂ results, which alone, without biochemical markers such as methylmalonic acid or homocysteine (Hcy), might not be accurate measures of B₁₂ deficiency.

Finally, our findings might not be generalizable to South Asians outside our specific urban setting. On the other hand, our findings were consistent with those of previous researchers, and the magnitude of the prevalence of B₁₂ deficiency in our population strengthens the argument that B₁₂ deficiency is more prevalent in South Asian populations.

Even if our findings are valid, we must consider their clinical significance. We believe that B₁₂ deficiency is not just a laboratory finding but a clinically relevant issue. We have observed that symptoms of B₁₂ deficiency often appear in our population, but are sometimes nonspecific and vague. Symptoms usually appear to respond to treatment.

Studies have shown that B₁₂ levels are inversely correlated with Hcy levels,¹⁵ and researchers have observed an association between elevated Hcy levels and increased risk of cardiovascular

disease.^{3,4,15} South Asians are known to be at higher risk of heart disease and elevated Hcy levels than other populations.^{11,12,14} It is possible that B₁₂ deficiency has a role in South Asians' risk of heart disease. To further explore B₁₂ deficiency, we suggest a point prevalence study be conducted. This would include detailed dietary history, symptoms, more specific markers of B₁₂ deficiency, such as Hcy and methylmalonic acid, and response to treatment.

Conclusion

Results of our retrospective chart review are consistent with the few other studies that found B₁₂ deficiency more prevalent among South Asians. Rates were similar among men and women, and although elderly people are at highest risk, young South Asians also have greatly elevated rates of B₁₂ deficiency. One possible explanation for these observations is that South Asians eat few or no animal products. We believe that this merits further investigation. ❁

Acknowledgment

We thank Drs Karen Jones, Karen Tu, and Rajnee Jolly, and Ms Patricia Baltazar for contributing to the final revision of the article.

Contributors

Dr Gupta was involved in conception of the study, gathering and interpreting the data, and preparing the article for publication. **Dr Damji** was involved in conception of the study and preparing the article for publication. **Ms Uppaluri** developed the data-gathering form and was involved in conception of the study and preparing the article for publication.

Competing interests

None declared

Correspondence to: Dr Anil Gupta, 1625 Albion Rd, Suite 101, Toronto, ON M9V 5H8; telephone (647) 435-9016; fax (647) 435-9018; e-mail patriciabaltazar@hotmail.com

EDITOR'S KEY POINTS

- This is a study of vitamin B₁₂ deficiency among adult South Asians in Canada. Most of the more than 750 000 South Asians in Canada live in Toronto, Ont, and Vancouver, BC.
- In this Toronto practice, where more than half the patients are South Asians, half had had B₁₂ blood tests, and half of these showed laboratory-defined B₁₂ deficiency.
- This high prevalence of B₁₂ deficiency (22% to 46%), contrasts with a general prevalence in the rest of the community of between 3% and 5%.
- A vegetarian diet and being older than 65 were substantial risk factors for B₁₂ deficiency.

POINTS DE REPÈRE DU RÉDACTEUR

- Cette étude évaluait la prévalence de la déficience en vitamine B₁₂ chez les adultes d'origine sud-asiatique vivant au Canada. Au Canada, la plupart des 750 000 Sud-Asiatiques résident à Toronto, Ont. et à Vancouver, BC.
- Dans cette clinique médicale de Toronto, plus de la moitié des patients proviennent de l'Asie du Sud. Plus de la moitié d'entre eux avaient eu une mesure de la B₁₂ sérique révélant une déficience en B₁₂ dans 50% des cas.
- Une telle proportion de déficience en B₁₂ (22-46%) contraste avec la prévalence observée dans le reste de la communauté (3-5%).
- Un régime végétarien et le fait d'avoir plus de 65 ans constituent des facteurs de risque importants pour une déficience en B₁₂.

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