

Holotranscobalamin versus Total Vitamin B12 as Indicators of Vitamin B12 deficiency in Thyrogastric Syndrome

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Introduction

The autoimmune association of Hashimoto thyroiditis and atrophic body gastritis (ABG) is known as thyrogastric syndrome which occurs in at least 14% of autoimmune thyroid disease (ATD). ABG is characterized by the loss of HCl and intrinsic factor (IF) production and is often underdiagnosed. It is important to make an early diagnosis because patients with ABG have greater risk for developing gastric cancer and ABG is responsible for anemia. Holotranscobalamin (HoloTC) is the biologically active form of vitamin B12 (cobalamin) and represents only around 20% of total vitamin B12. HoloTC is believed to be an earlier detection marker than total vitamin B12 to diagnose cobalamin deficiency which is especially frequent when gastritis manifestations are present.

In this study, we want to compare two markers to determine the vitamin B12 status of our population: total vitamin B12 (Roche) and holotranscobalamin (Abbott).

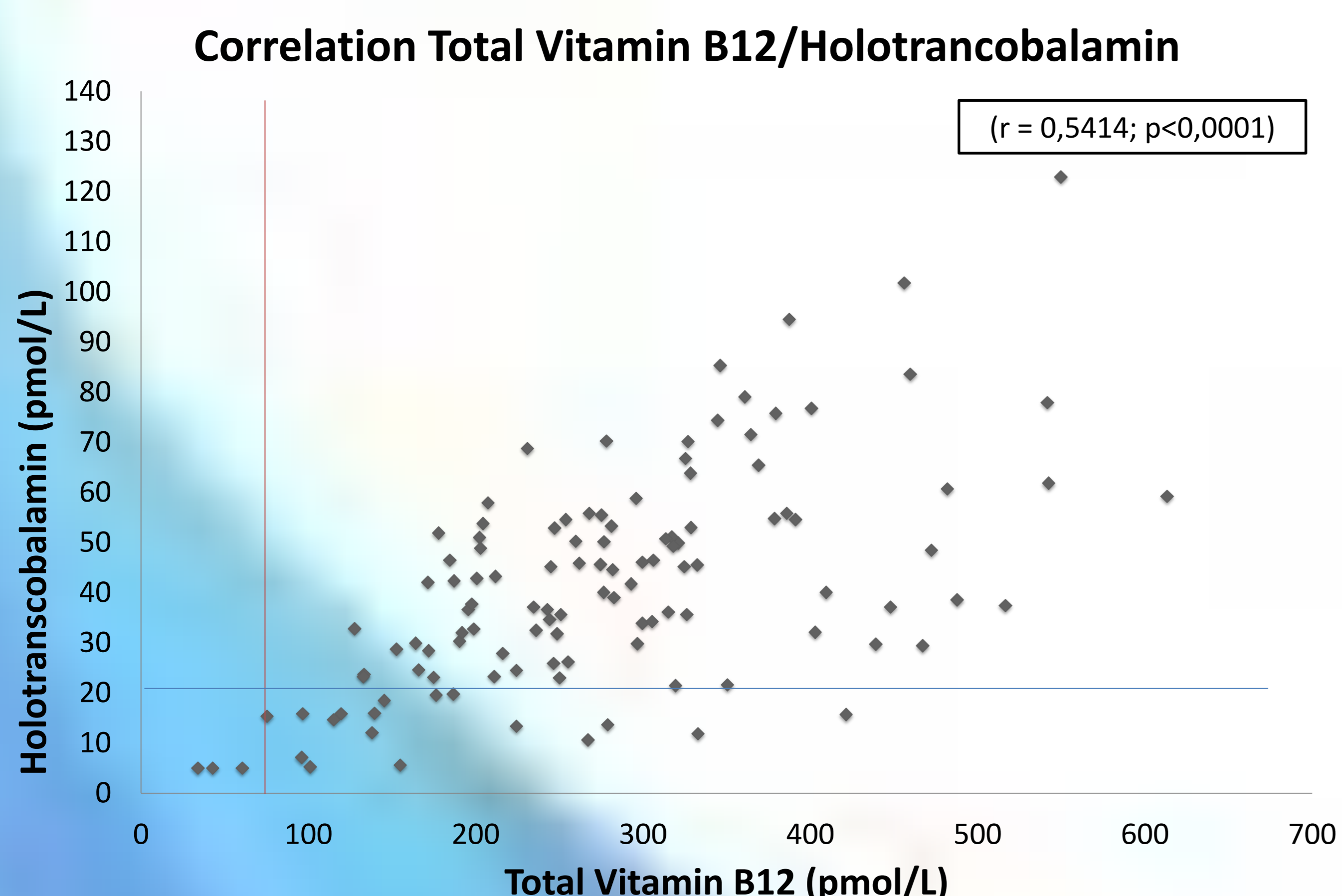
Methods

A total of 118 patients have been separated in 3 groups: "controls" (n=35), "autoimmune thyroiditis" (n=60) and "thyrogastric syndrome" (n=23). Major criteria for thyrogastric syndrome were evidence of ATD as well as cobalamin deficiency and/or ABG in gastroscopy/biopsy and/or hypergastrinemia and/or parietal cell autoantibodies (PCA)/intrinsic factor antibodies (IFA) (neither taking gastric acid antisecretory drugs nor Metformin). We excluded patients with *H.Pylori* infection as well as patients with estimated glomerular filtration rate (eGFR) calculated using MDRD equation <30ml/min/1.73m² because holotranscobalamin concentrations may be affected by renal function. Most patients underwent HoloTC, total vitamin B12, TSH, FT4, FT3, ATPO, ATG, TBII, PCA, IFA and gastrin determinations to determine their auto-immune status. All patients supplemented with vitamin B12 (per os or IM) were excluded of the study.

Serum total vitamin B12 was measured using the Cobas 6000 vitamin B12 kit while serum holotranscobalamin was measured using the Architect i2000 active B12 kit.

Results

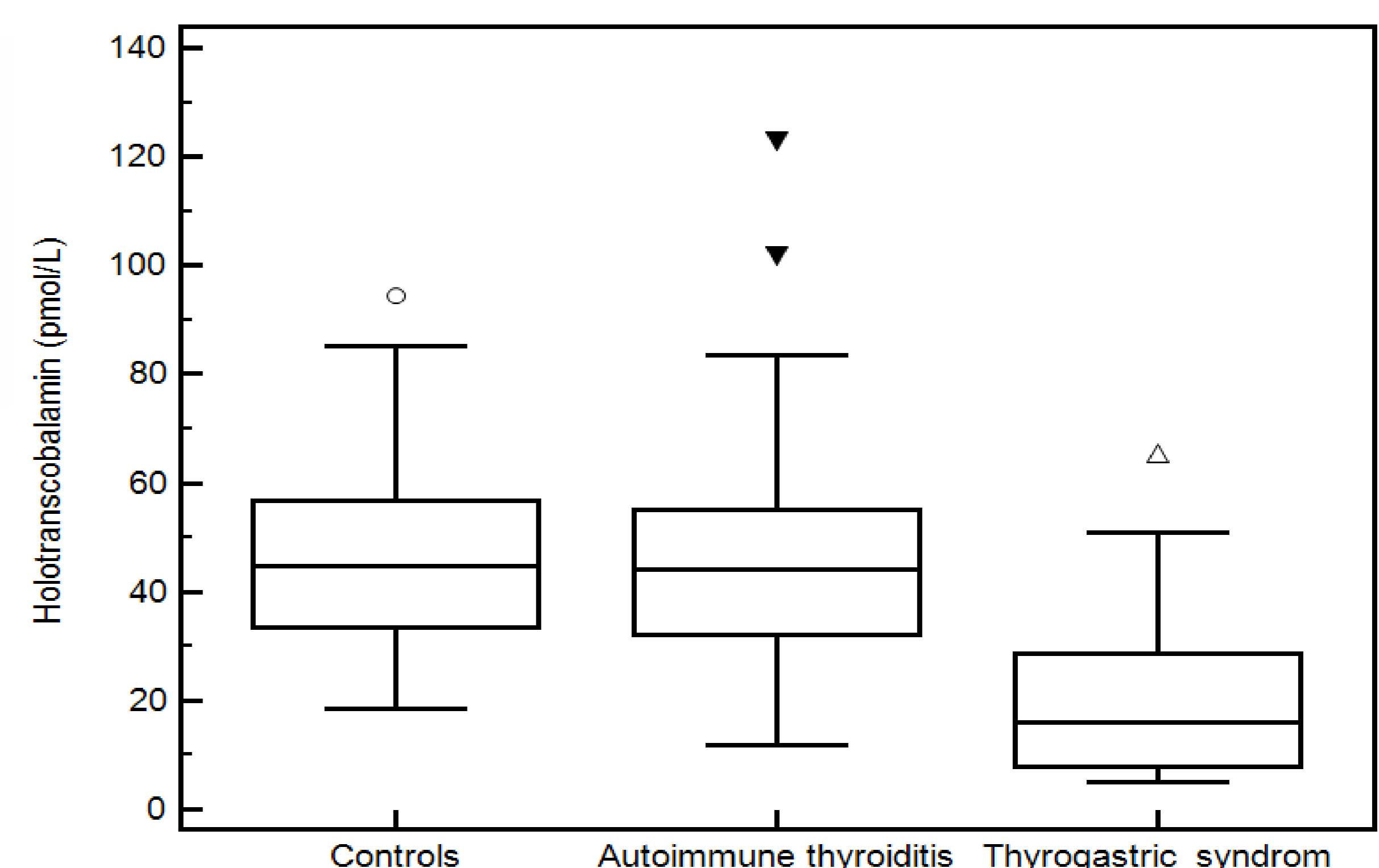
We determined the correlation between holotranscobalamin and total vitamin B12. HoloTC was significantly but not strongly associated with total vitamin B12 ($r = 0,5414$; $p < 0,0001$).



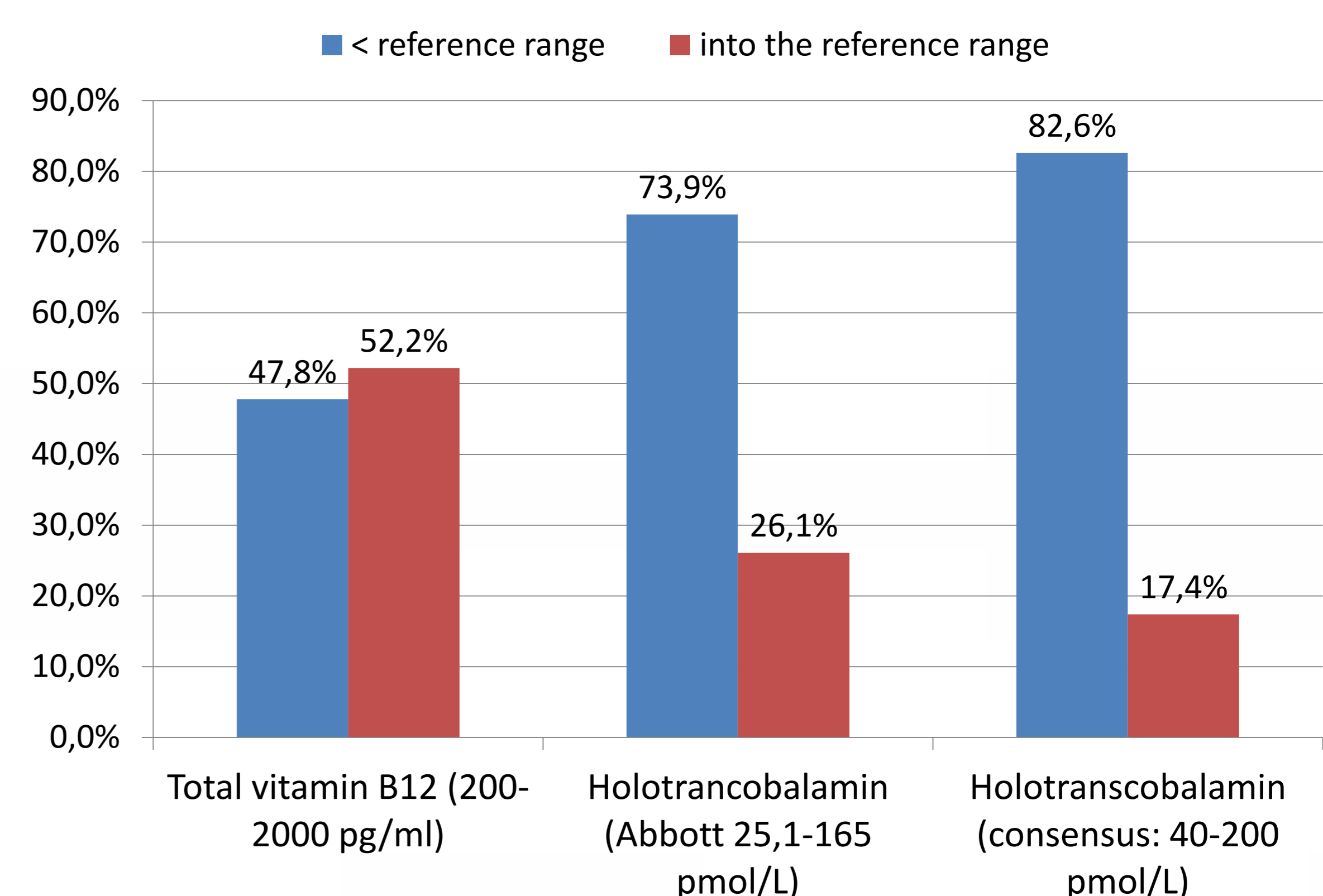
Reference range

Total Vitamin B12 : 147,6-1476 pmol/L
Holotranscobalamin : 25,1 to 165 pmol/L

The vitamin B12 concentration (both total and holotranscobalamin) was significantly lower in "thyrogastric syndrome" group ($p < 0,0001$) that confirms there is vitamin B12 malabsorption during gastritis.



However, more patients were deficient using holotranscobalamin (73,9%) than with total vitamin B12 (47,8%) in the "thyrogastric syndrome" group.



Among the 23 patients affected by thyrogastric syndrome, holotranscobalamin was low in 17 patients (73,9%) even though total vitamin B12 was low in 11 patients (47,8%). Although three quarter of the group had low holotranscobalamin, some of these had normal total vitamin B12 concentrations. Conversely, all patients whose total vitamin B12 concentration was low had also low holotranscobalamin.

The current consensus for holotranscobalamin seems to be that a reference interval of 40-200 pmol/L is appropriate. In these conditions, 19 patients (82,6%) were low in holotranscobalamin.

This suggests that serum holotranscobalamin is a more sensitive marker than total vitamin B12 to diagnose vitamin B12 deficiency. This also suggests that patients with low holotranscobalamin but with normal total vitamin B12 might have an early stage of vitamin B12 deficiency. A total of 6 patients (26%) affected by thyrogastric syndrome were <40 years old.

Conclusion

Holotranscobalamin is as suitable as total vitamin B12 for diagnosis of cobalamin deficiency and tends to be lower than total vitamin B12 in thyrogastric patient. As a result, these patients would be more quickly supplemented if their vitamin B12 status is determined by HoloTC. Using holotranscobalamin as a diagnostic marker would allow early therapy before neurological irreversible damage occurs. The initial symptoms of cobalamin deficiency are insidious and could easily be overlooked, especially as the serum concentration of total vitamin B12 can lie within the reference range. Thyrogastric syndrome can be present even in young patients (<40 years).