



Estimation Of Vitamin B12 Level In Patients With Sjögren's Syndrome Attending Tertiary Care Centre: A Cross- Sectional Study

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Type of Publication: Original Research Paper

Conflicts of Interest: Nil

Abstract

A cross-sectional study involving estimation of Vitamin B12 levels in 31 sjögren's syndrome patients showed 58.1 % patients with Vitamin B12 deficiency. Hence a strong association is found to be seen between Vitamin B12 deficiency and sjögren's syndrome. This justifies screening and treating Vitamin B12 deficiency in sjögren's syndrome patients.

Keywords: NIL

Introduction

An autoimmune disease is a condition in which the body's immune system considers its own healthy tissues as foreign and attacks them. Sjögren's syndrome is the second most common chronic autoimmune rheumatic disease with high morbidity [1]. It is a lymphoproliferative disease with autoimmune features characterized by mononuclear cell infiltration of exocrine glands, especially the lacrimal and salivary glands. These lymphoid infiltrations lead to dryness of the eyes (keratoconjunctivitis sicca), dryness of the mouth (xerostomia), and frequently, dryness of other surfaces connected to exocrine glands [2].

Haematological Disorders have been found to be common in patients with Sjögren's syndrome in around 40% [3]. Haemolytic anaemia, thrombocytopenia, neutropenia, and various hematologic abnormalities have been observed. It is seen predominantly in women compared to men at a ratio of 5:1 and is most common during the third and fourth decades of life. In particular, women of reproductive age group are a high-risk population for

anaemia and micronutrient deficiencies including vitamin B12 [4].

Vitamin B12 or cobalamin deficiency affects approximately 1.5% of the general population and is observed at a higher incidence with advancing age. Various conditions are known to increase the incidence of vitamin B12 deficiency, including a vegan diet, pernicious anaemia, FSA-food-cobalamin malabsorption, drug-induced proton pump inhibitors or metformin therapy, and sometimes it can also be idiopathic [5,6]. Chronic atrophic gastritis is the most common form of gastrointestinal involvement in Sjögren's syndrome [7]. Early diagnosis and treatment of B12 deficiencies makes it possible to correct haematological and mucosal consequences and avoid irreversible neurological complications of the B12 deficiency to be avoided [8].

A possible association between Sjögren's syndrome and vitamin B12 deficiency has been questioned because both conditions shared mucosal, neurological features, and chronic fatigue [9]. This study rationalizes the importance of screening for vitamin B12 deficiency in patients already diagnosed with

Sjögren's syndrome. This is a cross-sectional study that took place in a tertiary care centre and expected to reveal a link between vitamin B12 deficiency and patients with Sjögren's syndrome.

Materials And Methodology:

Study Type And Study Design:

This is a cross-sectional study conducted at the Institute of Rheumatology, Rajiv Gandhi Government General Hospital, a tertiary care centre over a period of 2 months.

Study Population:

The cohort was randomly selected from outpatients on a daily basis.

Inclusion Criteria:

1. Both sexes were included.
2. Age: 20 years and above.
3. This cohort included patients who had already been diagnosed with primary and secondary sjögren's syndrome.
4. Sjögren's syndrome was defined according to the ACR/EULAR 2016 criteria [10].
5. The study population includes already diagnosed patients with Sjögren's syndrome. Patients who have undergone any of the following tests:

Lip biopsy from minor salivary glands, focal score ≥ 1 foci/4 mm², (defined as the number of lymphocytic foci containing more than 50 lymphocytes adjacent to normal-appearing mucosal acini, per 4 mm² of glandular tissue)

Schirmer wetting test < 5mm/ 5 minute

ANA (Anti-nuclear antibody): About 70% of patients with Sjögren's syndrome have elevated antibodies that react against normal components of the cell nucleus.

SS-A (or Ro) and SS-B (or La): 70% of patients are positive for SS-A and 40% are positive for SS-B.

RF (rheumatoid factor): 60-70% of patients have a positive RF.

Exclusion Criteria:

Patients with pernicious anaemia, congenital deficiency of vitamin B12 and other secondary causes of Vitamin B12 deficiency like diabetic patients under metformin treatment are excluded.

Sample Size:

1. Chennai population as of 2011 census is 70 lakhs
2. Prevalence of sjögren's syndrome as per key article [11] is 2.
3. Sample size for a confidence interval of 95% is estimated to be 31.

Sample Size for Frequency in a Population

Population size(for finite population correction factor or fpc)(N): 7000000
 Hypothesized % frequency of outcome factor in the population (p):2%+/-5
 Confidence limits as % of 100(absolute +/- %)(d): 5%
 Design effect (for cluster surveys-DEFF): 1

Sample Size(n) for Various Confidence Levels

ConfidenceLevel(%)	Sample Size
95%	31
80%	13
90%	22
97%	37
99%	53
99.9%	85
99.99%	119

Equation

Sample size $n = [DEFF * Np(1-p)] / [(d^2 / Z^2_{1-\alpha/2} * (N-1) + p * (1-p))]$

Results from OpenEpi, Version 3, open source calculator--SSPropor
 Print from the browser with ctrl-P
 or select text to copy and paste to other programs.

Sample Collection:

1. An informed consent form is discussed with the patient explaining the research methods.
2. Demographic data such as name, age, gender, OP number, type of sjögren's syndrome, any other systemic disorders were collected.
3. The patient was made comfortable after explaining the procedure and research method.
4. Blood samples were collected from each participant using standardized protocols at Rheumatology Laboratory, Institute of Rheumatology, Rajiv Gandhi Government General Hospital.
5. Venous blood (1.5 ml) was collected in red -top vacutainers which was then centrifuged to separate serum from cells and was placed in separate aliquot under -20 degree Celsius in a portable freezer unit until given to the lab for further procedure.
6. The samples were sent to the laboratory for serum vitamin B12 estimation. Serum plasma vitamin B12 was determined by competitive chemiluminescence immunoassay. Laboratory results were correlate with the reference scale as in Table 1

Table 1 Reference scale for Vitamin B12 levels [10]

Vitamin B12 level	Severity
Less than 200 pg/MI	Clinically significant deficiency
200-300 pg/mL	Borderline
300-1000 pg/mL	Normal

Results:

During the two-month study period, serum vitamin B12 levels were assessed in 31 patients with Sjogren's syndrome, including both primary and secondary Sjogren's syndrome, excluding patients with congenital vitamin B12 deficiency and pernicious anaemia. The characteristics of the study are discussed below.

Table 2 Gender distribution

Gender	N	%
Female	29	93.5
Male	2	6.5
Total	31	100.0

This study involved 31 patients among them, 29 were females and 2 males as seen in Table2

Table 3 Distribution of population based of type of disorder

Type	Frequency	Percent (%)
Primary	4	12.9
Secondary	27	87.1

Table 3 shows that among 31 patients, 4 /31 (12.9%) were diagnosed with primary sjögren's syndrome and 27/31 (87.1%) were diagnosed with secondary sjögren's syndrome.

Table 4 Descriptive data of age and Vitamin B12 level

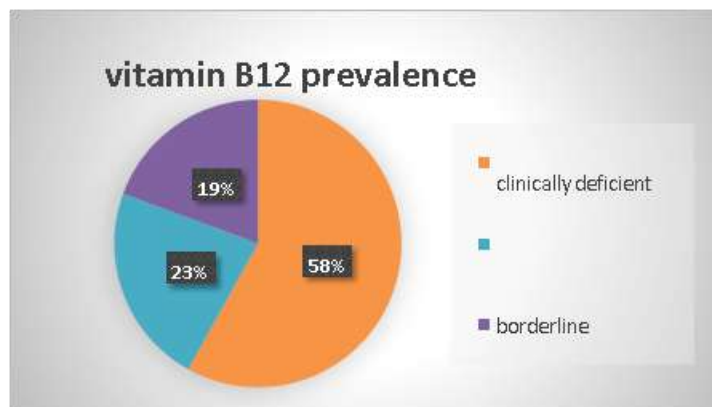
Descriptive Statistics	N	Mean	Std. Deviation
Age (yr)	31	42.03	10.313
Vitamin B12 level (in pg/ml)	31	246.65	210.420

Table 4 shows the descriptive data with a mean age of 42 ± 10.3 and mean vitamin B12 as 246.65 ± 210.42

Observations:

From the above the results, among the 31 sjögren's syndrome patients it is seen that 18 /31 (58.1%) of patients were found the having clinically deficient serum vitamin B12 level, that is their serum vitamin B12 levels were below 200 pg/ml. 7/31 (22.6%) of patients had serum vitamin B12 levels between 200 and 300 pg/ml which is considered to be borderline range and 6/31 (19.4%) of patients had serum vitamin B12 levels above 300 pg/ml as seen in Table 4. The chart 1 demonstrates the prevalence of Vitamin B12 deficiency among the selected population.

Chart 1 Vitamin B12 prevalence



Discussion:

The association between sjögren's syndrome and Vitamin B12 deficiency as suggested in previous case series and case control studies [3,5,6,9]. This study demonstrates a stronger association between sjögren's syndrome and Vitamin B12 deficiency in comparison with a standardised reference scale [10].

According to Urbanski G et al, in their cross-sectional case-control study evaluating the association between primary Sjögren's syndrome and B12 deficiency. Vitamin B12 deficiency was observed in 9/21 (42.9%) patients with primary Sjögren's syndrome and in 12/105 control patients (11.4%, $p < 0.0001$), suggesting a possible correlation between both [9]. From our results and observation 58.1% of sjögren's syndrome patients had Vitamin B12 deficiency, when compared to a similar case control study which

revealed that 42.9% sjögren's syndrome patients were vitamin B12 deficient [9] which highlights the interest of screening B12 deficiency in sjögren's syndrome patients. Study also reveals that 22.6% of patients are under borderline, in such patients it is recommended to consider supplemental testing with plasma methyl malonic acid (MMA) or plasma homocysteine levels to determine biochemical cobalamin deficiency but indeterminate levels. Homocysteine levels are more sensitive but MMA is more specific. The other potential causes of B12 deficiency: elderly people, chronic use of metformin or antacids, Helicobacter pylori infection, veganism, and fundic gastric or ileum resection, Methotrexate drug intake [14,15,16]. This study can be considered to provide insight that correction of vitamin B12 deficiency may provide symptomatic relief in already diagnosed patients with Sjögren's syndrome.

Conclusion:

1. The results show significant association between vitamin B12 deficiency and Sjögren's syndrome.
2. The results of this study give us an idea about the treatment plan of patients with sjögren's syndrome.
3. This study would be sufficient to justify screening and treatment with vitamin B12 in patients with Sjögren's syndrome.

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