



## VITAMIN B12 DEFICIENCY; VITAMIN B12 DEFICIENCY IN PATIENTS WITH HYPOTHYROIDISM

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**ABSTRACT... Objectives:** To determine the frequency of vitamin B12 deficiency in patients with hypothyroidism. **Study Design:** Cross sectional descriptive study. **Period:** 12-05-2016 to 11-11-2016. **Setting:** Liaquat University Hospital Jamshoro / Hyderabad. **Patients and Methods:** All the patients of known hypothyroid patients for  $\geq 01$  month duration, 20-50 years of age, either gender were explored for serum vitamin B12 level. The SPSS was used to manipulate the data in relation to mean  $\pm$ SD, frequencies and percentages and through chi-square test to get the p-values and its level of significance ( $\leq 0.05$ ). **Results:** Total 145 patients with hypothyroidism were evaluated for B12 deficiency, of which 97 (66.8%) were males and 48 (33.1%) were females respectively. Ninety patients (62%) were from urban areas while 55 (37.9%) was rural population. The mean  $\pm$ SD for age of overall population was  $41.83 \pm 8.93$  years while the mean age  $\pm$ SD for vitamin B12 deficient and non deficient was  $39.96 \pm 7.82$  and  $40.74 \pm 8.54$  years respectively. The vitamin B12 deficiency was observed in one hundred and five patients (72%), of which 69 (65.7%) males and 36 (34.3%) females. The mean  $\pm$  SD for duration of infection in overall population was  $5.32 \pm 1.53$  months while it was  $5.81 \pm 1.43$  in vitamin B12 deficient individuals. **Conclusion:** The vitamin B12 deficiency is more pronounced in hypothyroid patients. In present series vitamin B12 deficiency was observed in 105 (72%) individuals with male predominance 69 (65.7%).

**Key words:** Hypothyroidism, Vitamin B12, Thyroid.

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### INTRODUCTION:

The thyroid gland monitor the metabolism of body, development and growth, body environment maintenance by two important hormones tri-iodo thyronine (T3) and thyroxine (T4).<sup>1,2</sup> Hypothyroidism resulting from deficiency of thyroid hormones and is more prevalent among females results in insufficiency of thyroid gland.<sup>3</sup> The worldwide reported prevalence of hypothyroidism is 2-5% including USA 5% while in Pakistan it is 4.1% whereas in India it is 25%.<sup>4-8</sup>

Vitamin B12 (B12) has the complex structure among all of vitamins containing an atom of cobalt produced by anaerobic pathogen within the gastrointestinal tract of animals resulted in its occurrence as animal sources.<sup>9-13</sup> The vitamin B12 deficiency is observed in hypothyroidism; the study conducted in Turkey reported deficiency as 38.5%<sup>14</sup> while the study by Jabbar A, et al reported

40% prevalence for vitamin B12 deficiency in hypothyroid patients.<sup>15</sup>

Literature regarding the finding of vitamin B12 deficiency in Asian hypothyroid patients has been scarce. This study was conducted in a tertiary care teaching hospital describe the frequency of vitamin B12 deficiency in hypothyroid patients. The study supportive for primary care physicians should consider screening for B12 deficiency in hypothyroid patients as early screening can reduce various life threatening complication due to vitamin B12 deficiency.

### Patients and Methods

The cross sectional study duration was six months and was planned at tertiary care teaching hospital. The inclusion criteria of the study were known hypothyroid patients for  $\geq 01$  month duration, of 20-50 years of age either gender presented

at Liaquat University Hospital Hyderabad while the exclusion criteria were known / diagnosed cases for anaemic patients (haemolytic anaemia, malignancy as myeloproliferative disorders, aplastic anaemia, leukaemia and lymphomas, multiple myeloma, chronic pulmonary, liver and kidney disease), the patients had history and evidence of using immunosuppressive, chemotherapeutic or antithyroid drugs / thyroxine or already on antipsychotics or antiarrhythmic drugs (lithium and amiodarone), pregnant and lactation females, vegetarian population (had history of only vegetarian diet) and alcoholic subjects (on the basis of relevant history taken and had history of alcoholism for more than 01 years), patients had history of gut resection or small bowel surgery and subjects with malabsorption syndrome. The hypothyroidism was labeled when TSH > 4mcU/mL, free T<sub>4</sub> < 0.7ng/dl and free T<sub>3</sub> < 2.3 pg/ml while the vitamin b12 deficiency was considered when serum vitamin B12 concentration of <150 pg/ml.

This study was conducted on the subjects had history of hypothyroidism (diagnosed / known cases) for more than one month duration admitted in medical ward. A written consent was taken from all patients for participation in the study. All the hypothyroid patients were explored for vitamin B12 deficiency and ethical consideration was also maintained and pre-design proforma was used to collect the data whereas to analyze data, the SPSS version 17 was used to manipulate the mean  $\pm$ SD, frequencies and percentages and p-values by Chi-square test with level of significance as  $\leq 0.05$ .

## RESULTS

Total 145 patients with hypothyroidism were evaluated for B12 deficiency, of which 97 (66.8%) were males and 48 (33.1%) were females respectively. Ninety patients (62%) were from urban areas while 55 (37.9%) was rural population. The mean  $\pm$ SD for age of overall population was 41.83 $\pm$ 8.93 years while the mean age  $\pm$ SD for vitamin B12 deficient and non deficient was 39.96 $\pm$ 7.82 and 40.74 $\pm$ 8.54 years respectively. The mean  $\pm$  SD for duration of infection in overall population was 5.32 $\pm$ 1.53 months while it was

5.81 $\pm$ 1.43 and 4.72 $\pm$ 1.64 months in vitamin B12 deficient and non deficient individuals. The mean  $\pm$  SD of vitamin B12 level in deficient and non deficient population was 137.52 $\pm$ 7.32 and 279.83 $\pm$ 9.84 respectively. The distribution of age o gender, duration of infection and vitamin B12 deficiency is shown in Table-I to III. The gender distribution in relation to duration and vitamin B12 deficiency is presented in Table-IV and V whereas the duration to vitamin B12 deficiency is mentioned in Table-VI respectively.

|           |       | Gender |        | Total  |
|-----------|-------|--------|--------|--------|
|           |       | Male   | Female |        |
| Age (yrs) | 20-29 | 25     | 14     | 39     |
|           |       | 25.8%  | 29.2%  | 26.9%  |
|           | 30-39 | 46     | 11     | 57     |
|           |       | 47.4%  | 22.9%  | 39.3%  |
|           | 40-50 | 26     | 23     | 49     |
|           |       | 26.8%  | 47.9%  | 33.8%  |
| Total     | 97    | 48     | 145    |        |
|           |       | 100.0% | 100.0% | 100.0% |

**Table-I. The age and gender**  
\*p-value 0.01 (significant)

|           |       | Disease Duration (Months) |        |        | Total  |
|-----------|-------|---------------------------|--------|--------|--------|
|           |       | 1-2                       | 2-3    | > 3    |        |
| Age (yrs) | 20-29 | 18                        | 5      | 16     | 39     |
|           |       | 52.9%                     | 12.8%  | 22.2%  | 26.9%  |
|           | 30-39 | 5                         | 20     | 32     | 57     |
|           |       | 14.7%                     | 51.3%  | 44.4%  | 39.3%  |
|           | 40-50 | 11                        | 14     | 24     | 49     |
|           |       | 32.4%                     | 35.9%  | 33.3%  | 33.8%  |
| Total     | 34    | 39                        | 72     | 145    |        |
|           |       | 100.0%                    | 100.0% | 100.0% | 100.0% |

**Table-II. The age and disease duration**  
\*p-value = 0.001; statistically significant

|           |       | Vitamin B12 Deficiency |        | Total  |
|-----------|-------|------------------------|--------|--------|
|           |       | Yes                    | No     |        |
| Age (yrs) | 20-29 | 34                     | 5      | 39     |
|           |       | 32.4%                  | 12.5%  | 26.9%  |
|           | 30-39 | 35                     | 22     | 57     |
|           |       | 33.3%                  | 55.0%  | 39.3%  |
|           | 40-50 | 36                     | 13     | 49     |
|           |       | 34.3%                  | 32.5%  | 33.8%  |
| Total     | 105   | 40                     | 145    |        |
|           |       | 100.0%                 | 100.0% | 100.0% |

**Table-III. The distribution for age and vitamin B12 deficiency**  
\*p-value = 0.02; statistically significant

|        |        | Disease Duration (Months) |        |        | Total  |
|--------|--------|---------------------------|--------|--------|--------|
|        |        | 1-2                       | 2-3    | > 3    |        |
| Gender | Male   | 11                        | 28     | 58     | 97     |
|        |        | 32.4%                     | 71.8%  | 80.6%  | 66.9%  |
| Gender | Female | 23                        | 11     | 14     | 48     |
|        |        | 67.6%                     | 28.2%  | 19.4%  | 33.1%  |
| Total  |        | 34                        | 39     | 72     | 145    |
|        |        | 100.0%                    | 100.0% | 100.0% | 100.0% |

**Table-IV. The gender and duration of disease**  
\*p-value <0.01; statistically significant

|        |        | Vitaminb12 deficiency |        | Total  |
|--------|--------|-----------------------|--------|--------|
|        |        | Yes                   | No     |        |
| Gender | Male   | 69                    | 28     | 97     |
|        |        | 65.7%                 | 70.0%  | 66.9%  |
| Gender | Female | 36                    | 12     | 48     |
|        |        | 34.3%                 | 30.0%  | 33.1%  |
| Total  |        | 105                   | 40     | 145    |
|        |        | 100.0%                | 100.0% | 100.0% |

**Table-V. The distribution for gender and Vitamin B12 deficiency**  
\*p-value = 0.62; statistically non significant

|                   |       | Vitamin B12 Deficiency |        | Total  |
|-------------------|-------|------------------------|--------|--------|
|                   |       | Yes                    | No     |        |
| Duration (months) | 1-2   | 30                     | 4      | 34     |
|                   |       | 28.6%                  | 10.0%  | 23.4%  |
|                   | 2-3   | 27                     | 12     | 39     |
| 25.7%             |       | 30.0%                  | 26.9%  |        |
| > 3               | 48    | 24                     | 72     |        |
|                   | 45.7% | 60.0%                  | 49.7%  |        |
| Total             |       | 105                    | 40     | 145    |
|                   |       | 100.0%                 | 100.0% | 100.0% |

**Table-VI. The distribution of duration of disease and vitamin b12 deficiency**  
\*p-value = 0.05; statistically significant

## DISCUSSION

Hypothyroidism is a common life threatening disorder and a common reported cause was iodine deficiency worldwide while other causes include former thyroid surgery, congenital disorders, use of drugs that impaired thyroid hormone secretion like amiodarone and lithium, hypothalamic, pituitary and autoimmune disorders.<sup>16</sup> The link among hypothyroidism and vitamin B12 deficiency and its variability in accordance with dietary habits is not explored in detail.<sup>17-19</sup>

The reported prevalence for B12 deficiency was 15-25% in specific population especially in the elderly population.<sup>20</sup> Present study observed the prevalence of B12 deficiency in hypothyroid patients and found 105 (72%) of 145 patients to have low B12 levels while the prevalence detected in males 97 (66.9%) and in females 48 (33.1%) respectively.

The pernicious anaemia was linked to hypothyroid due to auto-immune etiopathology.<sup>21</sup> The anti-diabetic medication metformin and proton pump inhibitors (PPI's) leads to malabsorption due to its action on mucosa of ileum and membrane receptors while Helicobacter pylori, gastric hypochlorhydria due to PPI's and H<sub>2</sub> blockers also play an important role in vitamin B12 deficiency.<sup>22-24</sup> In present series the factors that impaired vitamin B12 level were excluded from the study and the intrinsic factor and gastric parietal cell antibody assays were not included as not relevant to the study group, hence the specific cause for existence of B12 deficiency in hypothyroid population was difficult to determine.

Hypothyroid and B12 deficient population often have unique clinical features and previously reported that many patients on adequate thyroxine therapy had persistence of symptoms and identified as vitamin B12 deficient population.<sup>25</sup> After initiating vitamin B12 therapy the symptoms improved within 3-6 months in hypothyroid population having low serum vitamin B-12 levels.<sup>26</sup>

The metabolism of methyl-melonyl acid (MMA) and homocystine involves cobolamin leads to raised level of these biomarkers in vitamin B12 deficient population.<sup>27</sup> In our study, the homocystine and MMA level was not studied but this is an space of increasing interest presently. The literature reported the association between raised homocystine level and hypothyroidism that improves by making the patient as euthyroid case.<sup>28</sup>

In the study at India, Turkey and Pakistan the reported prevalence for vitamin B12 deficiency in hypothyroidism individuals was 10, 18.6 and

40.5 respectively.<sup>18,29,30</sup>

Orzechowska-Pawilojc A, et al found that both the hypothyroid and hyperthyroid state in women is associated with lower concentration of vitamin B12 when compared to a healthy control group.<sup>31,32</sup> In current series the males population was predominant as far as vitamin B12 deficiency is concerned with statistically non significant ( $p=0.62$ ).

It seems that the literature regarding the role of vitamins in patients with thyroid disorders revealed that it requires further advance multidisciplinary studies. With that in mind, a physician caring for patients with thyroid disorders should realize that supplementation of vitamins probably does not prevent thyroid disorders, but can decrease symptoms in patients with hypothyroidism.<sup>33,34</sup> Atrophic gastritis often coexists with autoimmune thyroid disease and periodic evaluation of vitamin B12 levels seems justified in this patient population.<sup>35,36</sup>

The present study observed vitamin B12 deficiency in hypothyroid subjects, therefore vitamin B12 level should be screened periodically and thereafter in hypothyroid patients. The clinical workup should be explored in detail and the treatment options should be planned as early therapy can prevent the long term complications of vitamin B12 deficiency and larger advanced studies should conduct to further evaluate this association.

## CONCLUSION

Vitamin B12 deficiency or insufficiency appears to be quite common among population in our country implicating thyroid disorders (hypothyroidism) as an etiological factor for B12 deficiency. In present study vitamin B12 deficiency was observed in 105 (72%) patients with male predominance 69 (65.7%). Therefore the medical authorities should advise the early screening (for vitamin B12) of patients with hypothyroidism and preventive and effective measures should be taken against the clinical consequences of vitamin B12 deficiency and its complications in hypothyroid population.

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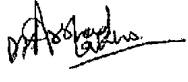

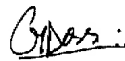


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*We cannot solve our problems with the same thinking we used when we created them.*

– Albert Einstein –

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**AUTHORSHIP AND CONTRIBUTION DECLARATION**

| Sr. # | Author-s Full Name     | Contribution to the paper   | Author=s Signature  |
|-------|------------------------|---|---|
| 1     | Arshad Sattar Lakho    | Contribution to conception and design, acquisition of data, analysis and interpretation of data.  |  |
| 2     | Aqeel Ahmed Channa     | Drafting the article and shares its expert reserach opinion and experience in finalizing the manuscript.                                    |  |
| 3     | Abdul Ghaffar Dars     | Contributed in conception and interpretationof data and give his expert view for manuscript designing.                                      |  |
| 4     | Syed Zulfiqar Ali Shah | Collection and acquisition of data, analysis and interpretation of data and make it suitable for final revision and a corresponding author. |  |
| 5     | Muhammad Iqbal         | Analysis and interpretation of data contributed in conception and shares its expert research opinion.                                       |  |