Journal of Dental Sciences 20 (2025) 2076–2083

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Original Article

# Anemia, hematinic deficiencies, hyperhomocysteinemia, and gastric parietal cell antibody positivity in oral lichen planus patients with normocytosis

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Received 28 July 2025
Available online 16 August 2025

**KEYWORDS**
Oral lichen planus;
Anemia;
Vitamin B12 deficiency;
Hyperhomocysteinemia;
Normocytosis

**Abstract** *Background/purpose:* Normocytosis is defined as having the mean corpuscular volume (MCV) between 80 fL and 99.9 fL. This study evaluated whether the 474 oral lichen planus (OLP) patients with normocytosis (so-called normocytosis/OLP patients) had significantly higher frequencies of anemia, hematinic deficiencies, hyperhomocysteinemia, and serum gastric parietal cell antibody (GPCA) positivity than 588 healthy control subjects or 588 OLP patients.
*Materials and methods:* Complete blood count, serum iron, vitamin B12, folic acid, homocysteine, and GPCA levels in 588 OLP patients, 474 normocytosis/OLP patients, and 588 healthy control subjects were measured and compared.
*Results:* We found that 14.3 %, 12.7 %, 4.0 %, 1.5 %, 16.0 %, and 19.8 % of the 474 normocytosis/

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https://doi.org/10.1016/j.jds.2025.08.003

OLP patients had blood hemoglobin (Hb) and serum iron, vitamin B12, and folic acid deficiencies, hyperhomocysteinemia, and serum GPCA positivity, respectively. Furthermore, the 474 normocytosis/OLP patients had significantly higher frequencies of blood Hb and serum iron, vitamin B12, and folic acid deficiencies, hyperhomocysteinemia, and serum GPCA positivity than 588 healthy control subjects (all *P*-values $<0.05$). On the contrary, the 474 normocytosis/OLP patients had significantly lower frequencies of blood Hb and serum vitamin B12 deficiencies and hyperhomocysteinemia than the overall 588 OLP patients (all *P*-values $<0.05$). *Conclusion:* We conclude that there are significantly higher frequencies of anemia, serum iron, vitamin B12, and folic acid deficiencies, hyperhomocysteinemia, and serum GPCA positivity in normocytosis/OLP patients than in healthy control subjects. On the contrary, normocytosis/OLP patients do have significantly lower frequencies of blood Hb and vitamin B12 deficiencies and hyperhomocysteinemia than overall OLP patients.


## Introduction

Normocytosis of erythrocyte is defined as having the mean corpuscular volume (MCV) between 80 fL and 99.9 fL.[1–6] Patients with both normocytosis and some specific anemia diseases (such as anemia of chronic disease or inflammation, aplastic anemia, posthemorrhagic anemia, and cytokine-induced anemia) or anemia-causing conditions (including hemolysis, hypersplenism, pregnancy, fluid overload, and a mixture of conditions producing both microcytic and macrocytic anemias) may have normocytic anemia (NA).[1–6]

Our previous studies showed that 68 (46.0 %) of 148 anemic oral lichen planus (OLP) patients, 95 (54.3 %) of 175 anemic burning mouth syndrome (BMS) patients, 117 (57.9 %) of 202 anemic atrophic glossitis patients, and 56 (52.3 %) of 107 anemic recurrent aphthous stomatitis patients had NA, suggesting that NA is the most common type of anemia in these four types of oral mucosal disease patients.[7–10] Moreover, some of these oral mucosal disease patients with NA may have simultaneous deficiencies of iron, vitamin B12, and/or folic acid.[7–10] It is also well known that severe iron deficiency can cause microcytic anemia[11,12] and severe vitamin B12/folic acid deficiency can lead to macrocytic anemia.[13–20] Therefore, specific anemia-causing conditions like concomitant deficiencies of iron plus vitamin B12 and/or folic acid may result in NA.[14]

Our previous study found blood hemoglobin (Hb) and serum iron, vitamin B12, and folic acid deficiencies, hyperhomocysteinemia, and serum gastric parietal cell antibody (GPCA) positivity in 25.2 %, 16.8 %, 10.2 %, 1.2 %, 21.1 %, and 23.6 % of 588 OLP patients, respectively.[7] In this study, the blood examination data of 474 OLP patients with normocytosis (so-called normocytosis/OLP patients), 588 OLP patients, and 588 healthy control subjects were retrieved from our previous study and compared between 474 normocytosis/OLP patients and 588 healthy control subjects or 588 OLP patients.[7] We tried to assess whether the 474 normocytosis/OLP patients had significantly higher frequencies of anemia, serum iron, vitamin B12, and folic acid deficiencies, hyperhomocysteinemia, and serum GPCA positivity than 588 healthy control subjects or 588 OLP patients.

## Materials and methods

### Subjects

This study included 474 normocytosis/OLP patients (95 men and 379 women, age range 20–88 years, mean age 56.1 ± 14.2 years) retrieved from our previously-reported 588 OLP patients (110 men and 478 women, age range 20–88 years, mean 55.8 ± 14.1 years).[7] Furthermore, the blood examination data of 588 OLP patients and 588 healthy control subjects (110 men and 478 women, age range 20–89 years, mean 56.0 ± 14.1 years) were also retrieved from the same previous study for comparison.[7] All OLP patients and healthy control subjects were consecutively seen, diagnosed, and treated at the Department of Dentistry, National Taiwan University Hospital (NTUH) from July 2007 to June 2023. The 588 OLP patients were selected based on the following clinical criteria: (i) the presence of characteristic clinical features, such as radiating grayish-white Wickham striae, papules, plaques, either individually or in combination, and erosion or ulceration on the oral mucosa; (ii) a bilateral and symmetric distribution of OLP lesions on the oral mucosa.[7,21–28] For 25 patients with an uncertain clinical diagnosis of OLP, an incisional biopsy of the typical oral mucosal lesion was performed. The histopathological diagnosis of OLP was confirmed using the criteria described previously.[7,21–28] However, OLP patients with the following conditions or diseases including a history of betel quid chewing, heavy alcohol use, autoimmune diseases (such as systemic lupus erythematosus, rheumatoid arthritis, pemphigus vulgaris, etc.), inflammatory diseases, malignancy, recent surgery, or systemic conditions like liver, kidney, coronary artery, or stroke diseases were excluded from this study.[7,21–28] The healthy control subjects were individuals without any oral mucosal or systemic illnesses and with no more than dental caries or very mild periodontal disease. None of the OLP patients had received

medication for OLP for at least three months before participating in the study.

Blood samples were drawn from 588 OLP patients (including 474 normocytosis/OLP patients) and 588 healthy control subjects to measure complete blood count, serum iron, vitamin B12, folic acid, and homocysteine levels, and serum GPCA positivity. All OLP patients (including 474 normocytosis/OLP patients) and healthy control subjects provided informed consent before participating in the study. The study was reviewed and approved by the Institutional Review Board at the NTUH (202402086RINC).

### Determination of blood hemoglobin and serum iron, vitamin B12, folic acid, and homocysteine levels

The complete blood count and serum iron, vitamin B12, folic acid, and homocysteine levels were measured using routine tests conducted in the Department of Laboratory Medicine at the NTUH.[5–15,16–26,27–37,38–48]

## Determination of serum gastric parietal cell antibody level

The serum GPCA level was measured using the indirect immunofluorescence technique, with the rat stomach serving as the substrate, as previously described.[5–15,16–26,27–37,38–48] Sera were considered positive if they exhibited fluorescence at a dilution of 1:10 or more.

### Statistical analysis

Comparisons of the mean corpuscular volume (MCV) and mean blood levels of Hb, iron, vitamin B12, folic acid, and homocysteine between 474 normocytosis/OLP patients and 588 healthy control subjects or 588 OLP patients were performed by Student's *t*-test. The differences in frequencies of blood Hb and serum iron, vitamin B12, and folic acid deficiencies, hyperhomocysteinemia, and serum GPCA positivity between 474 normocytosis/OLP patients and 588 healthy control subjects or 588 OLP patients were compared by chi-square test. The result was considered to be significant if the *P*-value was less than 0.05.

## Results

The MCV and mean blood levels of Hb, iron, vitamin B12, folic acid, and homocysteine in 474 normocytosis/OLP patients, 588 OLP patients, and 588 healthy control subjects are shown in Table 1. Because men usually had higher blood levels of Hb and iron than women, these two mean levels were calculated separately for men and women. We found that the 474 normocytosis/OLP patients had significantly lower mean blood Hb (for men and women), serum iron (for women only), vitamin B12, and folic acid levels as well as a significantly higher mean serum homocysteine level than 588 healthy control subjects (all *P*-values $<0.05$, Table 1). In addition, the 474 normocytosis/OLP patients had a significantly higher MCV and a significantly higher mean blood Hb level (for women only) than 588 OLP patients (both *P*-values $<0.001$, Table 1).

According to the World Health Organization (WHO) criteria, normocytosis of erythrocyte was defined as having an MCV between 80 fL and 99.9 fL,[1–6] and men with Hb $<$ 13 g/dL and women with Hb $<$ 12 g/dL were defined as having Hb deficiency or anemia.[49] Furthermore, patients with the serum iron level $<60$ μg/dL,[50] the serum vitamin B12 level $<200$ pg/mL,[51] or the folic acid level $<4$ ng/mL[52] were defined as having serum iron, vitamin B12 or folic acid deficiency, respectively. In addition, patients with the serum homocysteine level $>12.0$ μM (which was the mean serum homocysteine level of healthy control subjects plus two standard deviations) were defined as having hyperhomocysteinemia. By the above-mentioned strict WHO

**Table 1** Comparisons of mean corpuscular volume (MCV) and mean blood levels of hemoglobin (Hb), iron, vitamin B12, folic acid, and homocysteine between 474 oral lichen planus (OLP) patients with normocytosis (normocytosis/OLP patients, MCV between 80 fL and 99.9 fL) and 588 healthy control subjects or 588 OLP patients.

| Group | MCV (fL) | Hb (g/dL) | | Iron (μg/dL) | | Vitamin B12 (pg/mL) | Folic acid (ng/mL) | Homocysteine (μM) |
|---|---|---|---|---|---|---|---|---|
| | | Men | Women | Men | Women | | | |
| Normocytosis/OLP patients (n = 474) | 90.2 ± 3.5 | 14.8 ± 1.4 (n = 95) | 13.1 ± 1.1 (n = 379) | 100.7 ± 35.1 (n = 95) | 86.4 ± 28.5 (n = 379) | 600.6 ± 245.4 | 12.7 ± 6.3 | 8.9 ± 3.2 |
| [a]*P*-value | 0.377 | 0.011 | <0.001 | 0.511 | <0.001 | <0.001 | <0.001 | <0.001 |
| [b]*P*-value | <0.001 | 0.327 | <0.001 | 0.751 | 0.077 | 0.076 | >0.999 | 0.059 |
| [c]OLP patients (n = 588) | 88.4 ± 8.5 | 14.6 ± 1.5 (n = 110) | 12.7 ± 1.3 (n = 478) | 99.1 ± 36.8 (n = 110) | 82.8 ± 30.3 (n = 478) | 572.9 ± 258.8 | 12.7 ± 6.2 | 9.3 ± 3.6 |
| [c]Healthy control subjects (n = 588) | 90.4 ± 3.8 | 15.2 ± 0.8 (n = 110) | 13.5 ± 0.8 (n = 478) | 103.6 ± 27.9 (n = 110) | 96.7 ± 27.4 (n = 478) | 682.6 ± 231.7 | 14.7 ± 5.8 | 8.2 ± 1.9 |

[a] Comparisons of means of parameters between 474 normocytosis/OLP patients and 588 healthy control subjects by Student's *t*-test.
[b] Comparisons of means of parameters between 474 normocytosis/OLP patients and 588 OLP patients by Student's *t*-test.
[c] The blood examination data of 588 OLP patients and 588 healthy control subjects were retrieved from our previous study.[7].

**Table 2** Comparisons of frequencies of blood hemoglobin, iron, vitamin B12, and folic acid deficiencies, hyperhomocysteinemia, and serum gastric parietal cell antibody (GPCA) positivity between 474 oral lichen planus (OLP) patients with normocytosis (normocytosis/OLP patients, MCV between 80 fL and 99.9 fL) and 588 healthy control subjects or 588 OLP patients.

| Group | Patient number (%) | | | | | |
|---|---|---|---|---|---|---|
| | Hemoglobin deficiency (Men <13 g/dL, women <12 g/dL) | Iron deficiency (<60 μg/dL) | Vitamin B12 deficiency (<200 pg/mL) | Folic acid deficiency (<4 ng/mL) | Hyperhomocysteinemia (>12.0 μM) | GPCA positivity |
| Normocytosis/OLP patients (n = 474) | 68 (14.3) | 60 (12.7) | 19 (4.0) | 7 (1.5) | 76 (16.0) | 94 (19.8) |
| [a]*P*-value | <0.001 | <0.001 | <0.001 | 0.010 | <0.001 | <0.001 |
| [b]*P*-value | <0.001 | 0.070 | <0.001 | 0.892 | 0.044 | 0.157 |
| [c]OLP patients (n = 588) | 148 (25.2) | 99 (16.8) | 60 (10.2) | 7 (1.2) | 124 (21.1) | 139 (23.6) |
| [c]Healthy control subjects (n = 588) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 10 (1.7) | 10 (1.7) |

[a] Comparisons of frequencies of parameters between 474 normocytosis/OLP patients and 588 healthy control subjects by chi-square test.
[b] Comparisons of frequencies of parameters between 474 normocytosis/OLP patients and 588 OLP patients by chi-square test.
[c] The blood examination data of 588 OLP patients and 588 healthy control subjects were retrieved from our previous study.[7]

definitions, 14.3 %, 12.7 %, 4.0 %, 1.5 %, 16.0 %, and 19.8 % of 474 normocytosis/OLP patients were diagnosed as having blood Hb and serum iron, vitamin B12, and folic acid deficiencies, hyperhomocysteinemia, and serum GPCA positivity, respectively. Furthermore, the 474 normocytosis/OLP patients had significantly higher frequencies of blood Hb and serum iron, vitamin B12, and folic acid deficiencies, hyperhomocysteinemia, and serum GPCA positivity than 588 healthy control subjects (all *P*-values <0.05, Table 2). On the contrary, the 474 normocytosis/OLP patients had significantly lower frequencies of blood Hb and serum vitamin B12 deficiencies and herperhomocysteinemia than the overall 588 OLP patients (all *P*-values <0.05, Table 2).

In this study, OLP patients with NA were defined as having anemia and normocytosis (MCV between 80 fL and 99.9 fL).[1–6] By this definition, 68 (14.3 %) of 474 normocytosis/OLP patients had NA. Of these 68 NA/OLP patients, 30 (44.1 %), 12 (17.7 %), 2 (2.9 %), and 12 (17.7 %) had serum iron, vitamin B12, and folic acid deficiencies and serum GPCA positivity, respectively.[7]

## Discussion

There were two major findings in this study. First, the **474 normocytosis/OLP patients showed significantly lower mean levels of blood Hb, serum iron (for women only), vitamin B12, and folic acid**, as well as **significantly higher mean serum homocysteine level** compared to 588 healthy control subjects. Moreover, **14.3 %, 12.7 %, 4.0 %, and 1.5 %** of the 474 normocytosis/OLP patients had blood Hb and serum iron, vitamin B12, and folic acid deficiencies, respectively. In addition, **16.0 % and 19.8 % of** the **474 normocytosis/OLP patients had hyperhomocysteinemia** and **serum GPCA positivity**, respectively. Second, when compared to the full cohort of 588 OLP patients, the normocytosis/OLP subgroup showed significantly **higher MCV** and **higher mean Hb level** among women, but had significantly **lower frequencies of anemia, serum vitamin B12 deficiency, and hyperhomocysteinemia**. These findings suggest that the **normocytosis/OLP patients** may represent a relatively distinct hematologic subgroup within the broader OLP patient population.

Our previous study and this study found that 68 (14.3 %) of the 474 normocytosis/OLP patients had NA.[7] Of these 68 NA/OLP patients, 30 (44.1 %) had serum iron deficiency, 12 (17.7 %) had serum vitamin B12 deficiency, 2 (2.9 %) had serum folic acid deficiency, and 12 (17.7 %) had serum GPCA positivity.[7] Thus, from the nutritional point of view, the iron and/or vitamin B12 deficiencies (34 (50 %) of 68 NA/OLP patients) were the two major contributing factors and the folic acid deficiency (2 of 68 NA/OLP patients) was a very minor contributing factor causing anemia in these 68 NA/OLP patients. A more detailed analysis showed that of the 68 NA/OLP patients, 8 had concomitant deficiencies of iron and vitamin B12, one had concomitant deficiencies of iron and folic acid, one had concomitant deficiencies of vitamin B12 and folic acid, 21 had iron deficiency only, three had vitamin B12 deficiency only, and 34 had none of iron, vitamin B12, and folic acid deficiencies by the strict WHO definitions of iron, vitamin B12, and folic acid deficiencies.[7] These findings indicate concomitant hematinic deficiencies of iron plus either vitamin B12 or folic acid are found in only 9 (13.2 %) of our 68 NA/OLP patients.

The pathogenesis of NA is multifactorial and is associated with disorders such as chronic diseases, inflammatory diseases, infections, bone marrow hypoplasia, decreased production of erythropoietin or a poor response to erythropoietin, hemolytic blood diseases, mild but persistent blood loss from gastrointestinal tract, and cytokine-induced suppression of erythropoiesis.[1–6] Therefore, further studies are needed to explore the exact mechanisms that result in

formation of NA in our 68 NA/OLP patients, especially for those 34 NA/OLP patients without hematinic deficiencies of iron, vitamin B12, and folic acid.

This study demonstrated that 60 (12.7 %) of the 474 normocytosis/OLP patients had serum iron deficiency. Iron deficiency can be attributed to chronic blood loss associated with excessive menstrual flow or gastrointestinal diseases (such as peptic ulcer, diverticulosis or malignancies), hypochlorhydria, a decrease intake of iron during old-age stage, and a reduced absorption of iron in patients with gastrectomy or celiac sprue.[11] Of the 60 normocytosis/OLP patients with serum iron deficiency, 40 (66.7 %) were older than 50 years of age and 19 (31.7 %) had serum GPCA positivity. Patients with serum GPCA positivity may have destruction of gastric parietal cells, resulting in hypochlorhydria and poor absorption of iron.[53] We suggest that some of our 60 normocytosis/OLP patients with iron deficiency may also have atrophic gastritis or *Helicobacter pylori* infection or take antacids or drugs that decrease gastric acid production (such as $H_2$-receptor antagonists) or transport (such as proton pump inhibitors). The atrophic gastritis, *Helicobacter pylori* infection, or administration of antacids or drugs that decrease gastric acid production or transport all can lead to malabsorption of iron and subsequently resulting in iron deficiency.[54] However, other underlying causes that lead to iron deficiency in our 60 normocytosis/OLP patients with iron deficiency may need further studies.[11,49]

Furthermore, 19 (4.0 %) of the 474 normocytosis/OLP patients had vitamin B12 deficiency. Of the 19 normocytosis/OLP patients with vitamin B12 deficiency, 7 (36.8 %) had serum GPCA positivity, suggesting that at least one-third of the 19 normocytosis/OLP patients with vitamin B12 deficiency, the vitamin B12 deficiency can be attributed to the GPCA-induced lack of intrinsic factors.[55–58] Thus, the other 12 normocytosis/OLP patients with vitamin B12 deficiency might be due to insufficient intake of vitamin B12, food-bound vitamin B12 malabsorption, ileal malabsorption of vitamin B12, and biologic competition (including bacterial overgrowth and tapeworm infestation) or defective transport of vitamin B12 (such as transcobalamin II deficiency).[15]

The present study also found that 7 (1.5 %) of the 474 normocytosis/OLP patients had folic acid deficiency. Folic acid deficiency is reported to be associated with poor nutritional intake, malabsorption, hepatobiliary dysfunction, increased folate catabolism, and medication (e.g., methotrexate, 5-flurouracil, and phenytoin).[13] Our previous study demonstrated that cigarette smoking can decrease the serum folic acid level in 87 oral precancer patients with smoking habit, especially in 26 heavy smokers (consuming $>$20 cigarettes per day).[45] The folic acid deficiency in oral precancer patients with smoking habit may be due to consumption of a relatively large amount of folic acid for repair of smoke carcinogens-induced DNA damages in oral epithelial cells.[45] However, further investigations are needed to explore the real etiologies of folic acid deficiency in our 7 normocytosis/OLP patients with folic acid deficiency.

In this study, 76 (16.0 %) of the 474 normocytosis/OLP patients had hyperhomocysteinemia. Of these 76 normocytosis/OLP patients with hyperhomocysteinemia, 17 had vitamin B12 deficiency, three (one had concomitant vitamin B12 deficiency) had folic acid deficiency, and 39 (7 also had vitamin B12 deficiency) had serum GPCA positivity. Therefore, in only 19 normocytosis/OLP patients with hyperhomocysteinemia, the hyperhomocysteinemia could be resulted from vitamin B12 and/or folic acid deficiency.[7–9] Deficiencies of vitamin B6, folic acid, and vitamin B12 can lead to high serum homocysteine levels (hyperhomocysteinemia).[59] However, in our hospital routine blood examination does not include the measurement of serum vitamin B6 level; thus, we did not know whether our normocytosis/OLP patients had vitamin B6 deficiency or not. Furthermore, chronic consumption of alcohol may also result in increased serum homocysteine levels.[60,61] In addition, our previous study also discovered that cigarette smoking may raise the mean serum homocysteine level in 87 oral precancer patients with cigarette smoking habit.[45] Further survey of the oral habits in our 474 normocytosis/OLP patients is necessary to understand the proportions of our 474 normocytosis/OLP patients having alcohol drinking and cigarette smoking habits, respectively. In addition, the main cause of hyperhomocysteinemia has been reported to be a dysfunction of enzymes and cofactors associated with the process of homocysteine biosynthesis.[62] Other causes may include excessive methionine intake, certain diseases (chronic renal failure, hypothyroidism, pernicious or sickle cell anemia, and malignant tumors in the breast, ovary, and pancreas) and side effects of some drugs (cholestyramine, metformin, methotrexate, nicotinic acid, and fibric acid derivatives).[62] However, further studies are needed to explore the real mechanisms resulting in hyperhomocysteinemia in our 76 normocytosis/OLP patients with hyperhomocysteinemia.

This study had several important clinical implications. First, clinicians should be cautious in assuming normal hematologic status in OLP patients solely based on normocytic red blood cell indices. Our data clearly demonstrated that a substantial proportion of our normocytosis/OLP patients harbored significant clinical abnormalities, including anemia and nutritional deficiencies. Routine blood tests including complete blood count and serum levels of iron, vitamin B12, folate, and homocysteine should be considered in the management of OLP patients, particularly those with persistent or recalcitrant symptoms. Second, the identification of serum GPCA positivity in nearly 20 % of 474 normocytosis/OLP patients suggests that **autoimmune screening** may be warranted, especially in those with unexplained hematologic or gastrointestinal symptoms. Early detection of autoimmune gastritis can lead to timely vitamin B12 replacement and surveillance for associated risks such as gastric neoplasia.[53,54] Third, from a pathophysiological standpoint, our findings support the hypothesis that OLP may not be a purely localized oral disease but may reflect or interact with broader systemic immune or nutritional imbalances.

Although this study had a relatively large sample size and our normocytosis/OLP patients and OLP patients were well-characterized cohorts, this study still had several limitations. First, it was a retrospective analysis based on previously collected data, which might limit the ability to control for confounding factors such as dietary intake, menstrual status, medication use, and coexisting mild

systemic illnesses. Second, we did not evaluate functional markers such as ferritin, transferrin saturation, or methylmalonic acid, which might have provided more precise information on iron and B12 status.[49—52] Third, although OLP patients with major systemic or autoimmune diseases were excluded, the presence of **subclinical or undiagnosed systemic conditions** could not be fully ruled out. Finally, the cross-sectional nature of the data precluded determination of causal relationships or temporal evolution of anemia and nutrient deficiencies in our normocytosis/OLP patients and OLP patients.

This study demonstrates that a considerable proportion of our normocytosis/OLP patients had hematologic abnormalities, including NA, iron and vitamin B12 deficiencies, hyperhomocysteinemia, and serum GPCA positivity. These findings highlight the importance of comprehensive hematologic and serologic screening in OLP patients, even when red blood cell indices appear normal. The observed associations also suggest potential underlying inflammatory and autoimmune mechanisms linking OLP to systemic alterations. Finally, we conclude that the 474 normocytosis/OLP patients had significantly higher frequencies of blood Hb and serum iron, vitamin B12, and folic acid deficiencies, hyperhomocysteinemia, and serum GPCA positivity than 588 healthy control subjects. On the contrary, the 474 normocytosis/OLP patients had significantly lower frequencies of anemia, serum vitamin B12 deficiency, and hyperhomocysteinemia than the overall 588 OLP patients.

## Declaration of competing interest

The authors have no conflicts of interest relevant to this article.

## Acknowledgments

None.

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