



## Oral and perioral manifestations of iron deficiency anemia in Hiwa Hospital in Sulaimani city

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### Abstract

**Background/objective:** the oral cavity is a mirror for the general health; anemia is one of these disorders that fit this idea. The aim of this study was to show the prevalence of oral and perioral changes in patients with iron deficiency anemia and control people, then compare these changes between them, also to know the frequency of oral and perioral manifestations with the degree of iron deficiency anemia.

**Methods:** This comparative study involved 100 patients who visited Hiwa Hospital Hematology department between May and September 2023. All participants filled a questionnaire form for personal information and data collection, and they were examined clinically for the presence of any oral changes.

**Result:** the sample included 96 females and 4 males, with an age range of 18–67 years; there was no significant correlation between age groups and the prevalence of lesions. Patients with a high incidence of manifestations like paling of lip and oral mucosa (74%), xerostomia (60%), each of glossitis and taste disturbance (36%), and a low incidence of each of an oral ulcer and fissured tongue (18%), each of angular cheilitis and dysphagia (14%), and perioral numbness (6%). There were significant associations between iron deficiency anemia and all manifestations except fissured tongue.

**Conclusion:** the manifestations are more common in patients than in control group. The frequency of oral lesions does not significantly differ with the degree of anemia, except pallor of (vermillion border of lip and oral mucosa) and glossitis.

**Key words:** Hiwa hospital, Iron deficiency anemia, Oral manifestation

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## Introduction

A decrease in the overall quantity of hemoglobin, or red blood cells, in the peripheral circulation is known as anemia. The functional result of anemia is a decrease in the blood's capacity to transport oxygen, which leads to tissue hypoxia.<sup>1</sup> Less than 12 g/dl in women and less than 13 g/dl in males is when it happens.<sup>2</sup> Anemia due to a lack of iron is ubiquitous and typically observed in adolescents who are menstruating as well as newborns.<sup>3</sup> It impacts a predicted 293 million young kids globally, with iron deficiency accounting for over half of these cases.<sup>4</sup> Most of the iron is stored and reprocessed for utilize in heme and non-heme enzymes from aging erythrocytes in the reticuloendothelial system. The average amount of iron absorbed daily by healthy adults is around 1-2 mg. This amount may normally compensate for the daily iron loss due to the shedding of epithelia, which is approximately 1.5–2 mg for females with standard menstrual periods and 1 mg for males.<sup>5-6</sup> Iron is delivered to tissues by circulating transferrin, a transporter that captures iron released into the plasma essentially by enterocytes or reticuloendothelial macrophages.<sup>7</sup> Iron deficiency anemia is brought on by insufficient iron in the red blood cells, which results in insufficient hemoglobin synthesis and the development of microcytic hypochromic red blood cells, which are usually caused by inadequate iron consumption, inadequate absorption, chronic blood loss or a combination of these.<sup>8-9</sup> Menstrual cycles, pregnancy, vegetarians, excessive intake of antacids and proton pump inhibitors, peptic ulcerations, gastrectomy, persistent bleeding from colonic cancer, uterine malignancy, and parasite disease are examples of conditions that might cause impaired absorption or blood loss. The foremost common cause in females of reproductive period is heavy menstrual bleeding, whereas in men and ladies after the

menopause stage, gastrointestinal disorders are primary reasons.<sup>10-11</sup> The non-specific systemic signs and symptoms of anemia include light mucous membranes, rapid breathing, increased jugular venous force, orthostatic hypotension, an increase in heart rate, fatigue, dizziness, shortness of breath, murmurs, and the occurrence or exacerbating of ischemic heart disease features.<sup>12</sup> While oral manifestations involve faded mucosa of the oral cavity, glossitis, especially atrophic type, glossodynia, angular cheilitis, erythematous mucositis, oral candidiasis, recurrent oral ulcers, and a burning feeling in the mouth.<sup>13</sup> The laboratory finding in diagnosis of iron deficiency anemia include complete blood count which can be helpful in determining the mean corpuscular volume (MCV), and mean corpuscular hemoglobin concentration (MCHC), serum ferritin and serum iron indices.<sup>14</sup> The aim of this study was to show the prevalence of oral and perioral changes in patients with iron deficiency anemia and control people, then compare these changes between them, also to know the frequency of oral and perioral manifestations with the degree of iron deficiency anemia.

## Patients and methods

A comparative study conducted between May 2023 and September 2023, consisting of a total of 100 people of both sexes including 4 men and 96 women with an age range of 18-70, attended Hiwa Hospital Hematology department in Sulaimani Governorate, in which 50 of them were diagnosed with iron deficiency anemia with different severity according to hemoglobin levels as mild (Hb.10g/dl - normal range), moderate (8.0-9.9g/dl), severe (5-7.9g/dl), and life-debilitating (Hb<5 g/dl), while the other 50 were randomly selected who attending hematology department in Hiwa Hospital for checking up, after investigation they were found to be without IDA anemia and other excluded conditions. Women with





hemoglobin levels <12 gr/dl, serum ferritin < 15 µg/L was considered to have IDA, whereas men<13 gr/dl of hemoglobin and < 15 µg/L of serum ferritin were regarded to have it. Those with coexistent folate or vitamin B12 deficiency (after confirmation by serum folate and serum vitamin B12 investigation), thalassemia minor, anemia of chronic disease (after total blood count), diabetic patients (after blood glucose test or sometimes Hb1c), liver disease (after liver function tests GPT, GOT, ALP, ACP) and kidney disease (serum urea and serum creatinine), cancer patients, drugs causing oral and perioral reactions like ( antihypertensives, antidiabetics, antipsychotics) , pregnancy and local factors like traumatic ,chemical and physical factors were excluded. The participants were already diagnosed by a Hematologist as having iron deficiency anemia or not based on their clinical history, examination, and laboratory investigations( complete blood count include RBC count and packed cell volume(low) hemoglobin level (decreased), mean corpuscular volume(MCV) (decreased) ,mean corpuscular hemoglobin (MCH) (decreased),red cell distribution width(RDW %) (high), serum ferritin (decreased) and total iron binding capacity (TIBC) (increased).After agreeing and signing of consent form by the participant, a comprehensive history was taken including

asking about oral symptoms (dry mouth, taste disturbance, burning sensation of tongue and other intra oral areas and dysphagia) , perioral symptoms (burning sensation and numbness of lips and cheeks) then clinical examination in which looking for any changes in structure, color, consistency of oral mucosa, site and number of lesions. Oral signs (palling of oral mucosa including all intra oral structures, oral ulcers, glossitis, fissure tongues, any abnormality in buccal mucosa, vestibules, floor of mouth, gingiva, hard and soft palate). Perioral signs (pallor of skin surrounding lips and over cheeks, angular cheilitis). The SPSS program for Windows was used to data analysis. Variables were categorical and Chi square test used to identify significant changes. A p-value of equal to or less than 0.05 was regarded as crucial statistically. The study protocol was approved by the ethical committee of Kurdistan Higher Council of Medical of Specialties. Consent was obtained from all the participants before starting.

**Results**

The descriptive statistics of hematological investigations for both test and control group, using (t-test) to identify significant changes. There were significant differences between groups regarding all hematological investigations; the p value was < 0.05, Table (1).

**Table (1):** Descriptive statistics for hematological findings

Lab. tests	Patients with IDA (n=50)		Controls (n=50)		P value
	Mean±SD	Range	Mean±SD	Range	
Hb. (gr/dl): Male	9.5±0.3(n=3)	(9.2-9.8)	12.50 (n=1)	(12.5)	< 0.001
Hb. (gr/dl): Female	9.4±1.5(n=47)	(6.5-11.6)	12.6±0.64(n=49)	(12-14.4)	< 0.001
Ferritin (ng/mL)	6.26±3.1	(1.8-14.6)	49.76±24.4	(21.6-125)	< 0.001
TIBC (µg/dL)	401±65.6	(211-530)	312±33.4	(233-388)	< 0.001
RBC (×10 <sup>12</sup> /L)	4.08±0.4	(3.0-5.2)	4.74±0.5	(3.82-6.13)	< 0.001
MCV (fl)	70.5±9.2	(53-86.6)	81.6±6.1	(71-91.4)	< 0.001
MCH	23.62±3.0	(16.8-28)	27.9±2.4	(24-35.6)	< 0.001
RDW (%)	17.7±3.4	(12-24.5)	13.47±1.3	(6.2-17.5)	< 0.001





Chi-square test was used for age and sex groups, in which the age of the majority of participants in the test and control groups was between 30 and 49 years old, 82% and 76%, respectively. The majority of participants were females in both groups- IDA 94% and control 98%. There were no significant differences between groups regarding age and sex; the p value was > 0.05, Table (2). The oral manifestations among IDA patients and controls, shown a high frequency of burning sensation (38, 76%) in cases versus (1, 2%) of control group, pallor of oral mucosa and vermilion border of lips observed in (37, 74%) cases, versus (3, 6%) of the control group. Dry mouth was observed in (30, 60%) cases, while (11, 22%) of controls. The frequency of other manifestations decreased to a low range in each of angular cheilitis and dysphagia, with (7, 14%) in case and only (1, 2%) for each of them in control. The lowest number of patients have oral and perioral numbness in IDA group (6, 12%),

whereas (2, 4%) of the control group, Table (3).

**Table (2):** Distribution of participants according to age groups and sex

Participants		IDA group	Control group	p-value X <sup>2</sup> test
		No (%)	No (%)	
Age groups	18 - 29 Years	4 (8)	8(16)	0.46
	30 - 49 Years	41(82)	38(76)	
	≥50 Years	5 (10)	4 (8)	
Sex	Female	47(94)	49(98)	0.31
	Male	3 (6)	1 (2)	
Total		50(100)	50(100)	

**Table (3):** distribution of oral and perioral manifestations in case and control group.

Oral sign and symptom	Pallor		Dry mouth		AtrophicG lossitis		Oral ulcer		Taste disturbance		Fissure tongue		Burning sense		Oral numbness		Angular cheilitis, dysphagia	
	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes
No. (%) IDA	13	37	20	30	32	18	41	9	32	18	41	9	38	12	44	6	43	7
	26	74	40	60	64	36	82	18	64	36	82	18	76	24	88	12	86	14
No. (%) Control	47	3	39	11	47	3	48	2	48	2	46	4	49	1	49	1	49	1
	94	6	78	22	94	6	96	4	96	4	92	8	98	2	98	2	98	2
P-value	0.001		0.001		0.002		0.03		0.006		0.13		0.001		0.05		0.03	
Oral sign and symptom	Pallor		Dry mouth		AtrophicG lossitis		Oral ulcer		Taste disturbance		Fissure tongue		Burning sense		Oral numbness		Angular cheilitis, dysphagia	
	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes
No. (%) IDA	13	37	20	30	32	18	41	9	32	18	41	9	38	12	44	6	43	7
	26	74	40	60	64	36	82	18	64	36	82	18	76	24	88	12	86	14
No. (%) Control	47	3	39	11	47	3	48	2	48	2	46	4	49	1	49	1	49	1
	94	6	78	22	94	6	96	4	96	4	92	8	98	2	98	2	98	2
P-value	0.001		0.001		0.002		0.03		0.006		0.13		0.001		0.05		0.03	





IDA %: {burning sensation (76)>pallor (74)>dry mouth (60)>atrophic glossitis (36) =taste disturbance (36)>oral ulcer (18) =fissure tongue (18)>angular cheilitis (14) =dysphagia (14)>numbness (12)}. Control %: {dry mouth (22)>fissure tongue (8)>pallor (6) =atrophic glossitis (6) >taste disturbance (4) =oral ulcer (4) >burning sensation (2) =angular cheilitis (2) =dysphagia (2) = numbness (2)}. All the manifestations are clinically significant and have a  $p \leq 0.05$ , except fissure tongue ( $p = 0.13$ ), which is not clinically significant. Iron deficiency anemic patients were further more grouped according to their hemoglobin levels. Results showed, mild% {dry mouth (65)>pallor (55)>taste disturbance (40)>oral ulcer(20)=fissure tongue(20)=atrophic glossitis(20)>dysphagia(15)=burning,sensation(15)=numbness(15)>angular,cheilitis(10)}. Moderate % {dry mouth (85)>pallor (55)>

atrophic glossitis (35) >taste disturbance (30) =burning sensation (30)>angular cheilitis (20) =dysphagia (20) =numbness (20) =fissure tongue (20)>oral ulcer (15)}. Severe % {pallor (90)>atrophic glossitis (70)> dry mouth (60)>taste disturbance (40)>burning sensation (30)>oral ulcer (20)>fissure tongue (10) =angular cheilitis (10) =dysphagia (10) =numbness (10)}. No one of our participants had life –debilitating anemia. The data shows significant increases in the manifestations of pallor ( $P=0.04$ ) and atrophic glossitis ( $P=0.03$ ) with the severity of IDA, making them clinically significant, the percentage of atrophic glossitis increased from 20 to 35 then to 70 as found in mild, moderate and severe cases respectively. Other manifestations had fluctuated percentages and were not related significantly to the severity of IDA, Table (4).

**Table (4):** Frequency of oral and perioral manifestation according to the stages of IDA

Oral and perioral Manifestation	Total IDA	Present	Mild IDA No. (%)	Moderate IDA No. (%)	Severe IDA No. (%)	p-value
Oral Ulceration	41	No	16(80)	17 (85)	8 (80)	0.9
		Yes	4(20)	3 (15)	2 (20)	
Pallor	13	No	9 (45)	3 (15)	1(10)	0.04
		Yes	11(55)	17 (85)	9 (90)	
Dry mouth	20	No	7 (35)	9 (45)	4 (40)	0.8
		Yes	13(65)	11 (55)	6 (60)	
Atrophic Glossitis	32	No	16 (80)	13 (65)	3 (30)	0.03
		Yes	4 (20)	7 (35)	7 (70)	
Fissured Tongue	41	No	16 (80)	16 (80)	9 (90)	0.8
		Yes	4 (20)	4 (20)	1 (10)	
Burning sensation	38	No	17(85)	14 (70)	7 (70)	0.5
		Yes	3 (15)	6 (30)	3 (30)	
Numbness	42	No	17 (85)	16 (80)	9 (90)	0.3
		Yes	3 (15)	4 (20)	1 (10)	
Dysphagia	43	No	17 (85)	17 (85)	9 (90)	0.9
		Yes	3 (15)	3 (20)	1 (10)	
Taste disturbance	32	No	12 (60)	14 (70)	6 (60)	0.8
		Yes	8 (40)	6 (30)	4 (40)	
Angular cheilitis	43	No	18 (90)	16 (80)	9 (90)	0.6
		Yes	2 (10)	4 (20)	1 (10)	
Total	50 (100)		20 (40)	20 (40)	10 (20)	





## Discussion

The mean Hb concentration in the present study for test group was 9.5 g/dl for males and 9.4g/dl for females, revealing no significant difference between both sexes, this mean Hb concentration was lower than that reported in the study by Wu et al.<sup>15</sup> In which mean Hb level in males was 10.6 g/dl and mean Hb level in females was 10.5 g/dl. This difference between Hb means might be due to different sample size in both studies. The current investigation did not discover a measurably noteworthy correlation between the hemoglobin level and the appearance of oral lesions. This was in contrast with Nayak from India, clamming signs of anemia like pallor in the mouth occurring in patients whose hemoglobin's levels fall below 7 g/dl.<sup>16</sup> In the present study, mild and moderate IDA anemia is frequent, but severe IDA is little with no case of life-threatening anemia; this clearly indicates that anemia in all the examined cases was not as severe as in the study by Lu from Taiwan, who reported that 16% of patients had life-threatening IDA, 40% of patients were severely anemic, and 24% of cases were moderately anemic. The last group was mildly anemic; they constituted 20% of patients.<sup>17</sup> This variety in seriousness can be related to the various causes of iron deficiency anemia in each review. The foremost sign related to the oral and perioral regions of iron deficiency anemia in our research was paleness and it increases with the severity of anemia, Nayak et al. reported that among the 78 patients with IDA, 20.51% showed oral mucosal pallor. These patients' Hb levels ranged from 5 to 7 g/dl in women and 4 to 9 g/dl in men. So, IDA in the Nayak et al study was more severe, but with less oral manifestations. The incidence of atrophic glossitis found in case group was significantly greater than in control group also greater than that of Eman AL sheikh's study from Egypt, in which about 34.4% of the patients had AG.<sup>18</sup>

Differences in the inclusion and exclusion criteria may be the cause of the discrepancy between the results. Although in the IDA patients group the number of cases had fissured tongue greater than control group, there was no critical correlation ( $p= 0.13$ ) between IDA and fissure tongue; this could suggest that the occurrence of IDA is unrelated to fissure tongue. Recurrent aphthous ulcerations (RAU) in cases with IDA approximately five times as much as control group, also more prominent than that in the Taiwanese study by Lu, in which RAU comprised 6% of their study test, this variety may be because of various variables involved in the cause of recurrent aphthous ulceration in inspected people. In the ongoing survey, burning sensations of the mouth is so high in relation to control group that is almost non-existent, but less than that of study done by Shrotriya and Shrotriya, who revealed 65% of patients have burning sensations.<sup>19</sup> This variety may be because of the distinction in the approach used in the study. Albeit angular cheilitis (AC) is a typical appearance of anemia in many examinations (Lu) and has been referenced as a characteristic sore of IDA in an Indian study by Nilofer et al.<sup>20</sup> This was not common in our review, the absence of an extreme rate of AC in the current review may be expected primarily because of the prohibition of sick individuals with chronic illnesses that result in incidental iron deficiency anemia.

## Conclusions

The oral and perioral signs and symptoms in a group of patients at Hiwa Hospital (Hematology department) in Sulaimaniyah City were more in those with iron deficiency anemia than in the controls. The frequency of oral and perioral manifestations was significantly difference with the disease except fissure tongue, but does not significantly different with the degree of anemia, except pallor of (vermillion border of





lip and oral mucosa) and glossitis which increased with the severity of anemia.

### Conflicts of interest

There are no disclosed conflicts of interest by the author.

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