Case report of oral candidiasis in iron deficiency anemia patients from Basrah, Iraq

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Abstract

Iron deficiency (ID) is the most common causes of anemia throughout the world. Iron is one of a variety of nutritional factors has been associated in the pathogenesis of oral candidiasis, it is the most common fungal infection, caused by an overgrowth of opportunistic fungus *Candida spp.* in immunodeficiency hosts. Two patients with oral manifestation such as angular cheilitis and atrophic glossitis were reported to have iron deficiency anemia(IDA). The first case was a 17 years old female, high school student with symptoms of oral thrush and moderate IDA (Hb 8.0 - 9.9 g/dl) suffers from Angular cheilitis and atrophic glossitis with pseudomembranous candidiasis. The second case was 62 years old female, housewife, suffers from life-threatening IDA (Hb < 6.5 g/dl) had symptoms of oral thrush with angular cheilitis and chronic mucocutaneous candidiasis. Morphological and biochemical identification of the yeast isolated from the two cases tongue revealed that it belongs to *C. albicans.* At conclusion, IDA patients are more susceptible to oral candidiasis and *C. albicans* is the most frequent species in the oral cavity of IDA patients as the causative agent of candidiasis.

KEYWORDS: Iron deficiency anemia, Oral candidiasis, *Candida albicans*, Case report

1. Introduction

Iron deficiency anemia (IDA) is the most common cause of anemia throughout the world and accounts for approximately one-half of other anemia cases and it developed when the iron available to the body cannot complete the need of it for the production of red blood cells. It is a global public health problem, as harmful and as compelling the epidemics of infectious diseases [1,2].

Patients with IDA have many systemic symptoms such as fatigue, pallor, weakness, exertional dyspnoea, lightheadedness, palpitations, postural hypotension, tachycardia, and neuropathy. Oral signs and symptoms may include atrophic glossitis, mucosal atrophy, angular cheilitis, anemic stomatitis,

burning sensation of oral mucosa, dysgeusia, lingual varicosities, recurrent aphthous ulcers, and various types of oral candidiasis [3, 4, 5].

Oral candidiasis is the most common fungal infection, caused by an overgrowth of opportunistic fungus *Candida* spp. in immunodeficiency hosts, the patients may suffer from dysgeusia, anorexia, dysphagia, and weight loss, that leading to nutritional deficiency [6, 7, 8].

During our study on prevalence of *Candida* species in IDA patients, we reported 2 cases of IDA with oral candidiasis in Basrah, Iraq.

2. Material and methods

Two iron deficiency anemia patients attending Alsader Teaching Hospital, Basra governorate, Iraq in November and December 2017. Oral swabs were taken from oral cavity by using sterile cotton swabs (AFCO, Jordan) from patients for isolation the causative agents on SDA medium with chloramphenicol, and incubated at 37c for at least 3days.The isolated yeast were identified by and identification of species of Candida by morphological methods that included growth on CHROMagar *Candida* medium, germ tube formation and growth on cornmeal agar with tween 80 to detect chlamydospore formation, and finally biochemical methods by using VITECK2 technique. 2-3 ml of blood were obtained from the basilic vein of each patients using a sterile syringe and collected in Ethylenediaminetetraacetic acid tube (EDTA) to prevent clotting for complete blood count test (CBC) and another tube without anticoagulant factor to obtain serum by centrifugation (3000 rpm/10 minutes) for biochemical parameters. The samples collected in compliance with ethical standards.

The collected blood (Whole blood) were tested in an automated blood count system (SYSMEX XT 2000I blood analyzer), to get the following parameters: Red blood cells (RBC), white blood cells (WBC), hemoglobin (HB), hematocrit (HCT), mean corpuscle (cell) volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC) and red cell distribution width (RDW). The principle of work was based on two methods of analysis the blood samples: direct current detection method and non-cyanide hemoglobin analysis method [9].

The serum iron concentration were measured by enzymatic (colorimetric) method using commercial Kit for iron (RANDOX) (Cat. No. SI 257 England). The principle was according to Ceriotti and Ceriotti [10]. The ferric iron (Fe^{3+}) was separated from its carrier protein transferrin, in an

acid medium and at the same time convert into the ferrous iron (Fe^{+2}). The Fe^{+2} is then combined with the chromogen (a sensitive iron indicator), to supply a blue chromophore that absorbs a proximally at 595 nm.

The TIBC measured by enzymatic (colorimetric) method using commercial kit for TIBC (RANDOX) (Cat. No. TI 1010 England). The principle is according to Ceriotti and Ceriotti [10]. The value of TIBC and the serum iron value is used to calculate the transferrin saturation (TS) (%) for each sample using the following equation: Transferrin saturation (TS) (%) = 100 × (serum iron / TIBC). The serum ferritin was measured using elisa kit from CALBIOTECH (Cat. No. FR248T).

3. Results

Patient 1: A female of 17 years old, high school student had symptoms of oral thrush with angular cheilitis and moderate IDA (Hb 8.0 - 9.9 g/dl). The blood parameters results showed RBC value 4.75 $x10^6$ (µl); Hb 8.9 g/dl; Hct 28.2 %; MCV 69.8 fl; MCH 18.7 pg/cell; MCHC 27.4 g/dl; RDW 22.4%. Biochemical parameters showed Fe 10.5 µg/dl; TIBC 411 µg/dl; TS 2.55 %; serum ferritin 8.4 ng/ml.

The growth of the isolated yeast on CHROMagar *Candida* medium showed light green color colonies, the growth in human serum showed germ tube formation and formed chlamydospore onto cornmeal with tween 80 medium Figure 2. biochemical identifications of the yeast isolated from the patient tongue with VITEK2 test revealed that it belongs to *C. albicans.* Oral macroscopic observation showed Angular cheilitis and atrophic glossitis with pseudomembranous candidiasis Figure 1.

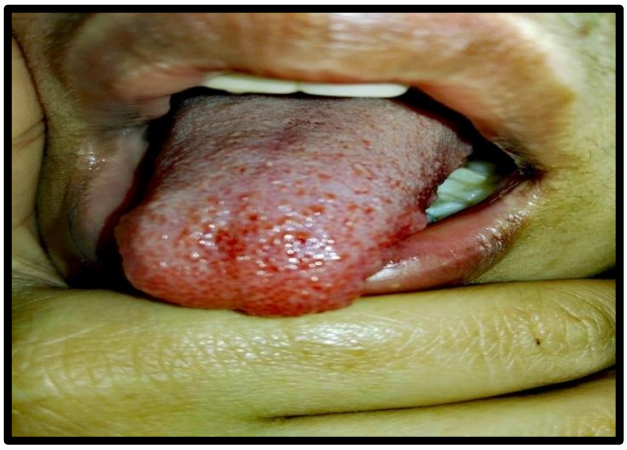

Figure 1: Clinical photograph of IDA patient (1) showing Angular cheilitis and atrophic glossitis with pseudomembranous candidiasis.

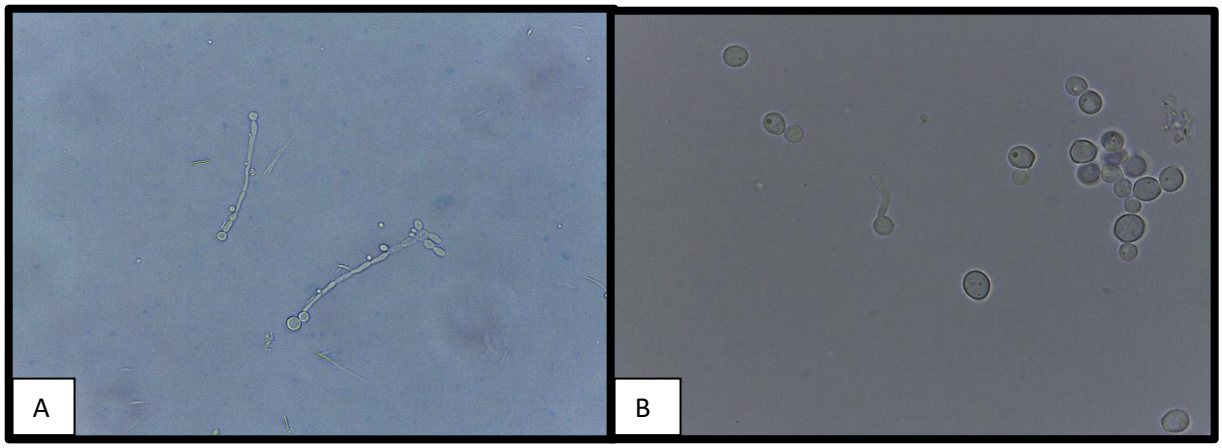

Figure 2: A: Chlamydospores of *C. albicans* in human serum 100X, B: Germ tube formation of *C. albicans* 100X.

Patient 2: A female of 62 years old, housewife, suffers from life-threatening IDA (Hb < 6.5 g/dl) had symptoms of oral thrush with angular cheilitis and chronic mucocutaneous candidiasis. The blood parameters results showed RBC value 4.12 x10^6 (µl); Hb 5.2 g/dl; Hct 18.6 %; MCV 76.3 fl; MCH 22 pg/cell; MCHC 28.3 g/dl; RDW 21.2%. Biochemical parameters showed Fe 25.7 µg/dl ; TIBC 421.3 µg/dl; TS 6.1 %; serum ferritin 9.7 ng/ml.

The growth onto CHROMagar *Candida* medium showed light green color colonies, the germ tube formation test was positive, and the growth onto cornmeal with tween 80 medium showed chlamydospore formation, Figure4. biochemical identifications of the yeast isolated from the patient tongue with VITEK2 test revealed that it belongs to *C. albicans.* Oral macroscopic observation showed Angular cheilitis and chronic mucocutaneous candidiasis Figure 3.

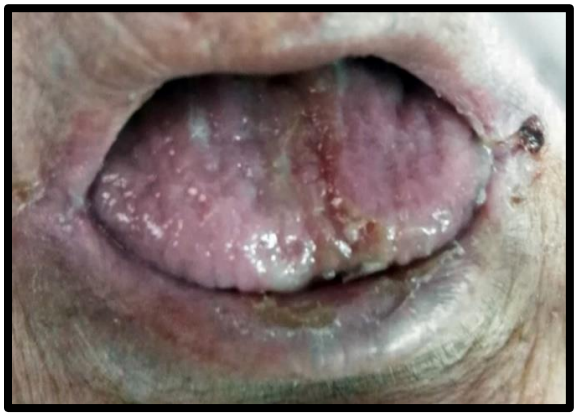

Figure 3: Clinical photograph of IDA patient (2) showing Angular cheilitis and chronic mucocutaneous candidiasis.

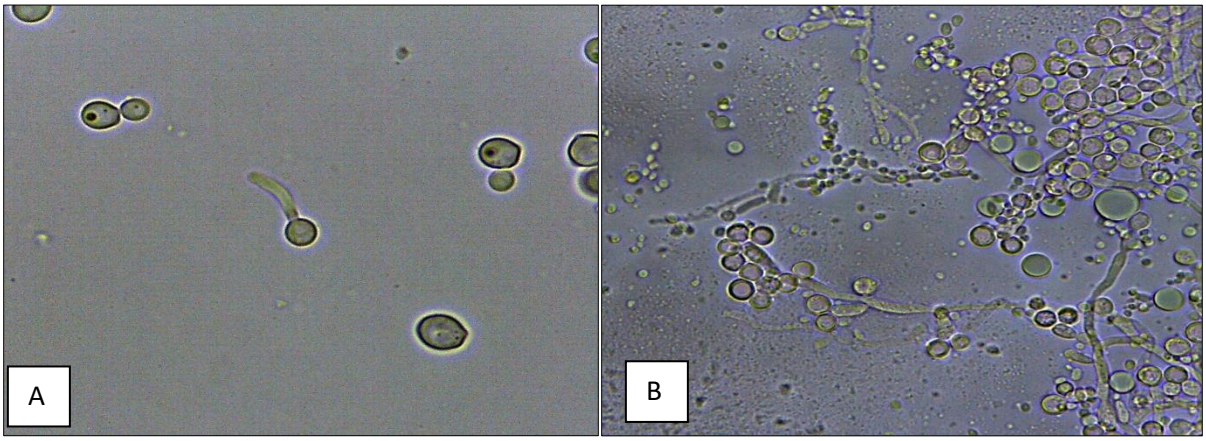

Figure 4:A: Germ tube formation of *C. albicans* in human serum 100X, B: Chlamydospores of *C. albicans* 100X.

4. Discussion

IDA is caused mainly by the lack of iron, and it develops when there is insufficient iron for Hb synthesis. Major causes include blood loss and increasing of iron demand. Females in reproductive age group, menstruation, pregnancy, nutritional deficiency, blood loss, and malabsorption are all known predisposing factors. The diagnosis of IDA depending on clinical history with questions about dietary intake, and the presence of blood in stools, which may be a sign of gastrointestinal bleeding. In women, questions about the uterine bleeding or heavy menstruation [11, 12].

Candida spp. are the most prevalence microorganism in the oral cavity, and can be exist in the mouth of healthy individuals without any effect to the host [13]. The high prevalence of *Candida* spp. in the oral cavity in immune-deficient patients is caused by many virulence factors including morphogenesis, adhesion, biofilm formation, phenotypic switching and secretion of hydrolytic enzymes as well as the ability to adapt the surrounding environment changes [14].

Oral symptoms as outlined by Wu *et al*. [15] chiefly due to atrophic mucosa and *Candida* infections included oral mucosa burning sensation, pain, dry mouth, numbness of oral mucosa, recurrent ulcers, bad taste, and dysfunction of taste. Oral candidiasis associated with internal diseases with immunodeficiency, such as diabetes, thymoma, endocrine disorders, HIV infection, and IDA, that

supported by the study of Fletcher *et al.*, [16] which reported that saliva from IDA patients with mouth lesions contained *Candida* spp. compared with the control group.

Kumar and Choudhry [17]; Naderi *et al.*, [18] displayed that oral candidiasis in IDA patients result of impaired cellular immunity. However, impaired cellular immunity cannot demonstrate the mouth lesions and growth of *Candida spp.* in saliva, because it was equally Discouraged in patients with and without oral lesions. So that, the effects of iron deficient on the oral flora change and the epithelial abnormalities may be important. Many studies have showed a highly significant reduction in the epithelial thickness, specially the thickness of the maturation compartment, and low levels of enzyme in the buccal epithelium of IDA patients [19].

Bhattacharya and Misra, [5] reported that IDA adversely affects the normal defense system of the body as it compromises the body's immune system to act against pathogens. IDA also negatively influences the normal defense systems against infections.

Loiarro *et al*. [20] explained the role of iron dependent co-enzyme nicotinamide adenine dinucleotide phosphatehydrogen oxidase (NADPH Oxidase) and cytochrome b in immunity and explained that the activation of (NADPH Oxidase) enzymes does not occur in the IDA and consequently the formation of free hydroxyl radicals within the leukocyte are affected thus phagocytic capability of neutrophils decreased. Soukka *et al*. [21] found that the human lactoferrin, in iron free state had lethal effect at neutral pH in fungal cell suspension. Many yeast species may have associated with *Candida* to attacked skin under deficiency of immune system [22]. *C. albicans* may use either a high affinity reductive system, a siderophore uptake system or the hemoglobin–iron uptake system for iron acquisition [23].

Rennie *et al*., [19] and Wu *et al*., [15] referred to that IDA leads to reduced Hb levels that carry insufficient oxygen to oral mucosa and thus result in mucosal atrophy. The previous studies indicate that IDA, either acting locally or by systemic mechanisms, could affect the pathogenesis of oral candidiasis, and their finding illustrate a high prevalence of oral candidiasis in IDA patients, which is agreed with our results. . also, It seems that Iiron deficiency anemia determines the balance between and the intensity of The (T helper cells) Th1 and Th2 arms of the immune response and leads to a deviation toward Th2 response which could contribute to recurrence of candidiasis [24].

Conclusions:

IDA patients are more susceptible to oral candidiasis and *C. albicans* is the most frequent species in the oral cavity of IDA patients as the causative agent of candidiasis.

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تقرير حالة داء المبيضات الفموي لدى مرضى فقر الدم الناجم عن عوز الحديد في البصرة، العراق

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المستخلص

نقص الحديد (ID) هو أكثر الأسباب شيوعًا لفقر الدم في جميع أنحاء العالم. الحديد هو أحد العناصر المتنوعة التي ترتبط مع تسبب داء المبيضات الفموي-العدوي الفطرية الأكثر شيوعا، الناتجة عن فرط نمو الفطريات الانتهازية *Candida spp.* في المرضى المصابين بنقص المناعة. اثنين من المرضى المصابين بفقر الدم نقص الحديد المصاحب لاعراض الاصابة الفموية مثل التهاب الشفة الزاوي والتهاب اللسان الضموري تمت الاشارة إليهم في الدراسة الحالية حيث كانت الحالة الأولى لمريضة تبلغ من العمر 17 عامًا، وهي طالبة بالمرحلة الثانوية تعاني من أعراض مرض القلاع الفموي وتعاني من فقر الدم نقص الحديد من النوع المعتدل (Hb 8.0 - 9.9 g / dl) كما انها مصابة بالتهاب الشفة الزاوي والتهاب اللسان الضموري مع داء المبيضات الكاذب. الحالة الثانية كانت ربة منزل تبلغ من العمر 62 سنة، تعاني من فقر الدم نقص الحديد المهدد للحياة (Hb <6.5 g / dl) كانت تعاني من أعراض مرض القلاع الفموي مع التهاب الشفة الزاوي وداء المبيضات المخاطي المزمن. الدراسة المظهرية والكيمو حيوية للخميرة المعزولة من الحالتين اظهرت انها تنتمي إلى *C. albicans* . في الختام، مرضى فقر الدم عوز الحديد هم أكثر عرضة لداء المبيضات الفموي و *C. albicans*هو أكثر الأنواع المنتشرة في تجويف الفم لمرضى فقر الدم عوز الحديد كعامل مسبب لداء المبيضات.