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Original Article

Comparison of Salivary Iron and Total Iron-Binding Capacity Levels Between Patients With Iron Deficiency Anemia and Healthy Individuals

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Abstract

Background: According to the high prevalence of iron (Fe) deficiency anemia, it is highly important to reach simple and cost-effective methods for accurate diagnosis. Considering that saliva, as a diagnostic substance is of great value, the present study aimed to compare the amount of salivary Fe and total iron-binding capacity (TIBC) levels of patients with Fe deficiency anemia and healthy individuals.

Methods: In this descriptive-analytic cross-sectional study, thirty 20-40-year-old women participated in case (patients with anemia) and control (healthy individuals) groups. After collecting the serum and saliva samples of each participant, Fe and TIBC levels were measured in µg/dL. Data were analyzed using SPSS with Kolmogorov-Smirnov, *t* test and Pearson correlation tests at the significant level of 0.05.

Results: The mean age of the participants of the case and control groups was 31.25 and 30.6, respectively. The average amounts of salivary Fe and TIBC of patients with Fe deficiency were 28.60 and 610.00 µg/dL, respectively. Further, the means of salivary Fe and TIBC of the control group were 78.80 and 290.00 µg/dL, respectively. Based on the results, the serum Fe and TIBC of anemic patients were 27.05 and 589.70 µg/dL, whereas the means of the serum Fe and TIBC of the control group were 80.27 and 286.80, respectively. There were significant differences between both salivary and serum values of the Fe and TIBC of case and control groups ($P<0.05$). Furthermore, the relationship between the serum and salivary levels of Fe and TIBC were positive and significant ($P<0.05$).

Conclusions: Based on the results of the present study, significant changes were found in the salivary amount of the Fe and TIBC of patients with Fe deficiency anemia corresponding to the serum levels of Fe and TIBC, thus saliva could be considered as a diagnostic substance for the detection of Fe deficiency anemia.

Keywords: Iron, Anemia, Serum, Total iron-binding capacity

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Introduction

Iron (Fe) is a crucial element in the body that is present in almost all types of cells and is a part of biological molecules, including hemoglobin, myoglobin, and some other vital enzymes. It plays a significant important role in biochemical reactions (1). Fe deficiency as one of the major problems compromises health in the 20th century all around the world, resulting in a wild range of diseases. One of the most common illnesses occurring due to Fe deficiency is anemia, which happens more in females and children (2). Total iron-binding capacity (TIBC) is a diagnostic indicator used to detect many Fe-related diseases, including Fe deficiency anemia. It shows the Fe binding capacity of transferrin which is the most important blood protein that is responsible for taking Fe from the place it is absorbed and delivering it to different types of Fe consuming cells. Transferrin is increased when the Fe stores are depleted, thus TIBC is elevated in patients with Fe deficiency capacity (3). Fe and TIBC of the serum are among the most important elements that are measured

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for the diagnosis of Fe deficiency anemia (4,5).

Saliva is a unique biologic liquid that keeps the oral cavity healthy and reflects the systemic changes of the body. Saliva, as a diagnostic substance has apparent benefits compared to the serum, including the non-invasive method of sample collection, reliable results, and its user-friendly nature. In addition, the evaluation of saliva is a cost-effective method for screening diseases in large populations. Accordingly, analyzing the saliva is extremely useful in detecting hereditary anomalies, autoimmune diseases malignancies, infectious diseases, endocrinopathy, and drug levels in the body (6).

Canatan and Akdeniz evaluated the serum and salivary amount of the Fe and ferritin of patients either having Fe deficiency anemia or thalassemia. They concluded that the levels of the salivary Fe and ferritin of patients with thalassemia were higher compared to healthy individuals; however, these levels were lower in patients with anemia. The above-mentioned changes were in accordance with changes in serum (7). Jagannathan et al introduced salivary ferritin as a predicting marker of Fe deficiency anemia in children as its level was significantly higher in children with anemia in comparison with healthy cases (8).

Based on the importance of Fe in an individual's growth and development, as well as the high prevalence of Fe deficiency anemia, it seems necessary to reach accurate, not expensive, and simple diagnostic and monitoring methods. Saliva sample collection is relatively simple, cost-effective, and at hand, thus the current study was sought to compare the salivary level of Fe and TIBC in patients with Fe deficiency and healthy individuals.

Materials and Methods

This descriptive-analytic cross-sectional study was approved by the Vice-chancellor of the Research and Technology of Hamedan University of Medical Sciences (930126250). Overall, thirty 20-40-year-old females, attending the Hematology Clinic of Be'sat Hospital of Hamadan University of Medical Sciences, participated in this study. The sample size was calculated via the comparison of two means based on the following formula (9).

$$n = \frac{(z_{1-\alpha/2} + z_{1-\beta})^2 * (s_1^2 + s_2^2)}{(\mu_1 - \mu_2)^2} = \frac{8 * (1600 + 73)}{(42.5 - 18.6)^2} = 15$$

Accordingly, 15 participants were considered as the control group, who had no abnormal results in their complete blood cell count with differential and common screening tests used to rule out blood discrepancies, including Fe, ferritin, and TIBC (10) and reported no illnesses in their medical records. All 15 tests were interpreted by a hematologist. Females participating in the present study as the case group were those attended to the hematology clinic with at least two clinical symptoms and signs of anemia (including chronic fatigue, pallor of the mucus membranes, brittle nails, palmar creases, and the like) and diagnosed as patients with Fe deficiency according to the results of their blood evaluating tests by the hematologist. A serum ferritin < 30 µg/dL, Fe level < 50 µg/dL, TIBC > 450 µg/dL, and RBC < 4.2 10^6/µL were used as diagnostic laboratory criteria for Fe deficiency anemia. According to the above-mentioned results, all participants in the case group had at least stage two Fe deficiency anemia (4). The patients of the case group were newly diagnosed and received no treatments.

A history of an illness, consumption of medicine, observation of a special diet (e.g., those who are vegetarians), and the presence of gingival or periodontal diseases were considered as the exclusion criteria. All participants signed the informed constant form before starting sample collection.

Unstimulated salivary sample collection of the study participants was conducted at 9-11 a.m. in order to decrease the circadian effects. Saliva sample collection was performed according to the method presented by Navazesh and Kumar (11). The participants were advised of the rules they should follow before sample collection, including having no meal, drinking nothing, not brushing teeth, and not smoking at least 2 hours before taking the saliva sample. The saliva was collected while the participant was sitting upright for 30 minutes up to 5 mL in a falcon tube and was analyzed to measure salivary TIBC and Fe by a chemistry analyzer machine test (BS-380 Mindray, Shenzhen, China). The serum samples were taken on the same day in order to measure the amount of Fe and TIBC using an automatic analyzer (Celltak F, Tokyo, Japan).

The levels of Fe and TIBC in µg/dL of the serum and saliva of all participants were measured, and data were analyzed by SPSS software, version 16.0 (SPSS Inc., Chicago, IL, USA). The Kolmogorov-Smirnov test was employed to ensure the normal distribution of data. Moreover, a *t* test was used to compare the amount of the Fe and TIBC of the saliva and serum of case to control groups. Additionally, the Pearson correlation test was applied to find if there is a relation between the salivary and serum levels of Fe and TIBC. The value of 0.05 was considered significant for all tests.

Results

Based on the results, the mean age of patients with Fe deficiency anemia was 31.25 years old, and the average age of the control group was 30.60 years old; the difference between the age of the two groups was not significant ($P > 0.05$). Table 1 presents data on the means of the salivary and serum Fe and TIBC of case and control groups.

The results of the Kolmogorov-Smirnov test showed that the amount of the Fe and TIBC of both serum and saliva of two experimental groups had a normal distribution ($P > 0.05$). The comparison of the salivary levels of the Fe and TIBC of patients with Fe deficiency anemia to healthy ones revealed significant differences between experimental groups (Table 1).

There was a significant positive relationship between the

level of serum and saliva Fe either in the case or control group. Based on data in Table 2, the relation between salivary and serum TIBC was also positive and significant in both experimental groups ($P > 0.05$).

Discussion

Anemia is a situation in which either the number of red blood cells or the percentage of hemoglobin decreases due to different situations. Anemia might present as a reduction in any red blood cell indices. No symptom presents in mild cases; however, it can be life-threatening in severe ones. Laboratory tests are still the most reliable methods for early diagnosis and detection of its underlying causes (12). One of the most common types of anemia is Fe deficiency anemia, as a challenge for health care providers, could lead to a wild range of disturbances (13). Therefore, it seems crucial to make an accurate diagnosis and appropriate treatment to prevent its complications (14).

Using saliva as a biologic diagnostic liquid has been wildly accepted because of its potential benefits such as simple, non-invasive, and user-friendly method of sample collection, as well as being a relatively low-cost procedure (15). Fe deficiency anemia in 20-40-year old females is more common due to menstruation, delivery, and breastfeeding in non-industrial countries in particular (4).

The results of the present study revealed that the salivary level of the Fe of patients with Fe deficiency anemia was significantly lower compared to healthy ones. Conversely, the salivary levels of the TIBC of the anemic patients were higher. These results are in accordance with the expected results of the standard blood test used for the diagnosis of Fe deficiency anemia (16).

The results of our study confirm those of Canatan and Akdeniz. They evaluated ferritin in addition to Fe and TIBC and found that salivary ferritin also reduced in patients with Fe deficiency anemia (7). Mishra et al also concluded that the Fe of saliva decreased in patients with anemia (17), but their study was only performed on children.

In line with the present study, Rahim (18) reported that salivary Fe and ferritin could be used as diagnostic indices according to their ease of collection and reliable results even in differentiating between Fe deficiency anemia and thalassemia.

One of the strengths of the current study was to evaluate the relation between the serum and salivary levels of Fe and TIBC. To the best of our knowledge, no study has so far focused on this issue. Based on the current results, the amount of the Fe and TIBC of saliva changed in conformity with the serum level.

Considering the limited sample size of the present study, it is strongly suggested that similar studies use large populations, including a variety of races and nationalities to obtain more reliable results for using saliva as a clinical diagnostic substance. It is highly important to find the normal range of Fe and TIBC in the saliva to detect a threshold for making an accurate diagnosis.

Table 1. Mean ± SD of Saliva and Serum Fe and TIBC of Case and Control Groups

	Control	Case	*P* Value[a]
N	15	15	0.000
Salivary Fe	78.80 ± 27.17	28.60 ± 12.49	0.000
Serum Fe	80.27 ± 32.02	27.05 ± 10.10	0.000
Salivary TIBC	290.00 ± 54.87	610.00 ± 10.21	
Serum TIBC	286.80 ± 56.17	587.70 ± 99.30	0.000

Note. Fe: Iron; TIBC: Total Fe-binding capacity. SD: Standard deviation.
[a]*P* was considered significant at the level of 0.05.

Table 2. Correlation Coefficient (r) and *P* Value of the Pearson Correlation Test

	Saliva Fe-serum Fe	Saliva TIBC-Serum TIBC
Control group (15)	r = 0.984, *P* = 0.000	r = 0.842, *P* = 0.000
Case group (15)	r = 0.916, *P* = 0.000	r = 0.926, *P* = 0.000

Note. Fe: Iron; TIBC: Total Fe-binding capacity.

Conclusions

Based on the results of the present study, the salivary levels of Fe and TIBC had a significant positive relationship with their serum levels, and they were considerably lower in anemic patients. It seems that the evaluation of Fe and TIBC in saliva could be considered as a diagnostic tool for Fe deficiency anemia. Needless to mention that further complementary studies are necessary in this regard.

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Authors' Contribution

Study concept and design: SR; Data acquisition: AE; Data analysis and interpretation: MAS and Mina Jazaeri; Manuscript drafting: MJ; Critical revision of the manuscript for important intellectual content: SR; Statistical analysis: MAS; Administrative, technical, and material support: MH; Study supervision: SR.

Competing Interests

The authors declare that they have no conflict of interests.

Ethical Approval

The present study was approved by the Ethics Committee of the Hamadan University of Medical Sciences. Moreover, all patients expressed their willingness to participate in the study.

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