

# Salivary and Serum Ferritin Levels: Is There a Correlation?

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## Abstract

**Background and Aim:** Blood samples are used for the diagnosis of many diseases. Serum ferritin level is known to be a marker of anemia and iron overload disorders. However, blood collection is an invasive method. Saliva, as a bio-fluid, contains a variety of important components that are successfully used for assessment of body health. The use of saliva samples for ferritin evaluation can be regarded as a simple and noninvasive alternative to serum assessment. The aim of the present study was to evaluate the correlation between salivary and serum ferritin levels.

**Materials and Methods:** In this cross-sectional study, 107 participants who were referred to a medical laboratory in Qazvin, Iran, voluntarily provided unstimulated saliva and blood samples using the standard methods. The levels of ferritin in the serum and saliva samples were determined. The Spearman's rank-order correlation coefficient was used to analyze the data.

**Results:** The results suggested a positive correlation between the salivary and serum ferritin levels ( $P=0.004$ ,  $r=0.27$ ). Gender and age had no significant correlation with salivary and serum ferritin levels ( $P>0.05$ ).

**Conclusion:** Considering the equivalent diagnostic efficacy as serum samples, salivary samples can be used as a noninvasive and simple method to determine the ferritin levels.

**Key Words:** Anemia, Ferritins, Saliva, Serum

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## Introduction

Iron deficiency anemia is one of the most common disorders worldwide [1,2]. There is a notable emphasis in the literature on the prevention and control of iron deficiency during early childhood because evidence suggests that low levels of iron have a negative effect on cognitive performance [3]. Furthermore, iron deficiency causes long-term physical damage because iron plays a role in supporting the nervous system, glial energy metabolism,

neurotransmitter synthesis, and myelination [1,4,5].

Ferritin is an important protein that can store iron for future needs [6]. It consists of approximately 25% iron [7,8]. Since ferritin levels reflect iron storage in the body, it is an important marker for monitoring anemia and iron overload disorders [9]. A common method of ferritin assessment is through drawing a venous blood sample. However, this approach requires laboratory equipment and trained

individuals. Moreover, it is invasive and may not be suitable for children [1].

Saliva is a protective fluid and is secreted from the major and minor salivary glands. For years, there has been hope that saliva could be used to help in diagnosis of various diseases [8,10]. Agrawal et al, [11] and Aghazadeh et al. [12] observed that ferritin can also be found in the saliva, and that ferritin levels in the saliva are sometimes much higher than in the serum.

Salivary ferritin levels can also reveal anemia and iron overload disorders [11,12]. Thus, the use of saliva has come to be regarded as a reliable alternative method of ferritin assessment, one that is less invasive and offers a similar degree of sensitivity as serum [9,13]. In addition, it appears that changes in the salivary ferritin levels occur even before changes in the serum, meaning that saliva can be used as a valuable tool to assess the iron status [3,9,14]. The present study aimed to explore the correlation between the salivary and serum ferritin levels.

### Materials and Methods

This cross-sectional study was approved by the ethical committee of Qazvin University of Medical Sciences (IR.QUMS.REC.1395.3). The participants were 107 volunteers with no obvious systemic disorders and no history of smoking or medication intake, who were referred to a medical laboratory in Qazvin, Iran, for a blood test. Written informed consent was obtained from all participants. A form was used to evaluate the clinical characteristics and medical history of participants.

Venous blood samples were collected in plain tubes with 21-gauge needles. A tourniquet was used to prevent blood stasis. About 7 mL of blood was collected from each participant using an iron-free syringe and iron-free plastic vacuum tubes. Thirty minutes after clot formation at room temperature, the tubes were centrifuged at 3500 rpm for 10 min. Subsequently, the serum was separated and placed in special tubes. Then, it was frozen and stored at -20°C until analysis.

About 5 mL of unstimulated saliva was collected from all participants by the spitting method.

They were instructed to refrain from eating, chewing gums and drinking for at least 60 min before the sample collection. The samples were centrifuged at 3500 rpm for 15 min at 4°C. Then, about 1 mL of the supernatant was separated and placed into microtubes and kept at -20°C until analysis.

Both serum and saliva samples were removed from the storage at the same time and allowed to reach the room temperature. Once the samples were homogenized, they were centrifuged for the second time at 3500 rpm for 5 min. At this time, the levels of ferritin in the serum and saliva samples were determined using Ferritin Immunoradiometric Assay (IRMA) (Ferritin IRMA, Padyab Teb diagnostic) commercial kit, via a one-step noncompetitive method.

The sensitivity of the IRMA kit was 0.16 ng/mL and there was no cross-reactivity with other molecules. The kit is capable of measuring 0-2000 ng/mL of ferritin without the need for dilution.

For hemoglobin and mean corpuscular volume (MCV) analysis, the frozen samples were thawed at 37°C for 5 min before the analysis and then assessed by an automated hemoglobinometer.

Based on the World Health Organization standards, any participant with a hemoglobin level lower than 12 g/dL, an MCV value of lower than the normal range (i.e., 78 FL), and a ferritin value of less than 30 µg/L was considered to have iron deficiency anemia.

The data obtained from the participants were analyzed using SPSS 23 (SPSS Inc., NY, USA). To determine the relationship between the serum and salivary ferritin levels, the Spearman's rank-order correlation coefficient was used.

### Results

The mean age of the participants was 35.2±11.4 years (range 9-67 years). Most of the participants were females (82.2%).

There was no significant correlation between gender and serum and salivary ferritin levels using the Mann-Whitney U test. The Mann-Whitney U test, however, showed a significant relationship between gender and

level of hemoglobin. The hemoglobin levels were higher in males than females ( $P=0.001$ ). The Spearman's correlation coefficient showed no significant relationship between age and hemoglobin with serum and salivary ferritin levels (Table 1). There was a significant positive correlation between serum and salivary ferritin levels ( $P=0.004$ ,  $r=0.27$ , Table 2). There was no significant correlation between the salivary and serum ferritin levels in participants with anemia ( $P=0.154$ ).

**Table 1.** Relationship between age and variables under study

Variables	P value	r
Serum ferritin	0.31	0.098
Salivary ferritin	0.60	-0.051
Hemoglobin	0.57	0.061

**Table 2.** Relationships between the variables under study ( $P < 0.05$ )

Variables	P value	r
Salivary ferritin and serum levels	0.004	0.276
Salivary ferritin and hemoglobin levels	0.53	0.068
Serum ferritin and hemoglobin levels	0.056	0.206

## Discussion

In the present study, we found a significant relationship between the salivary and serum ferritin levels (weakly positive). It was also found that age and gender do not play a significant role as possible factors in this relationship.

Many studies have recommended the use of saliva as a reliable method for ferritin evaluation [1,13,15]. The use of saliva is noninvasive, low-cost and simple, and does not require specific equipment [13].

The results showed no significant differences between the salivary and serum ferritin levels in participants with iron deficiency anemia. These results are consistent with the findings of

Canatan and Akdeniz [15] who also reported a significant relationship between salivary and serum ferritin levels. However, a study by Jagannathan et al. [1] reported that levels of salivary ferritin increased in children with iron deficiency anemia; although much fewer samples were evaluated in their study compared with our study. A study by Kodati [13] reported lower levels of ferritin in serum and saliva of patients with iron deficiency anemia. Rahim [14] reported that salivary ferritin levels significantly increased in patients with thalassemia. The discrepancy between the two studies may be explained by the differences in sample size and, age of patients.

Use of unstimulated saliva has been confirmed because unstimulated saliva is more closely correlated with serum levels of ferritin [1,15,16]. In the present study, we used the spitting method as the most common method of saliva collection [17]. Some studies used cotton swabs (absorption method), but it has been stated that use of methods other than the spitting method would underestimate the values of salivary factors (17,18).

## Conclusion

This study found no significant correlation between the amount of ferritin, and age or gender of patients. There was a significant relationship between the salivary and serum ferritin levels, and this could allow us to use saliva as a reliable and noninvasive method for assessment of ferritin levels.

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