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Evaluation of correlation between Saliva and serum ferritin Level In Patients with Iron deficiency Anemia and comparision group

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Abstract,Introduction: Iron deficiency anemia is one of the common factors that can result from reducing the intake or absorption of iron, or iron loss caused by the bleeding. Measuring the concentration of ferritin, an important parameter to measure the amount of iron reserves in the body. Saliva and other body fluids are significant similarities in some markers. This study designed for evaluation of correlation between saliva and serum ferritinlevel in patients with iron deficiency anemia and comparison group

Materials & methods: In this study, 280 samples of 140 healthy individuals and 140 patients on blood tests problem Anemic they have been determined by sampling saliva, and the amount of ferritin, their saliva wasmeasured and the data obtained by soft reviewed and analyzed using SPSS.

Results: Themeanvalueofsalivaryferritininirondeficientcaseswas111.4µg/dlandthemeanferritinlevelsincontrolsubjectwere94.77µg/dl. Thus the salivary ferritin was found to be significantly higher in iron deficient subjects compared to the controls.

Discussion & Conclusions: Results of this study was to evaluate salivary ferritin iron deficiency anemia as a valuable diagnostic test and seems when blood vessels appears to be difficult in the cases sampling of saliva is a helpful for diagnostics of this diseases.

Key words*:-* *Anemia, Ferritin, saliva, serum*

I. INTRODUCTION

Iron deficiency anemia is caused by iron reduction in the body and this reduction is in the extent to which iron storage becomes completely empty and some degree of tissue iron deficiency appears. Determination ofprevalence of mild iron deficiency without anemia and also more advanced iron deficiency anemia in demographic studies is a common issue. Iron deficiency is a worldwide serious threat to health, killing 841,000 people and causing 35,057,000 social disability per year. This disorder also has a direct effect on cognitive impairment and reduced job performance and, dying from severe anemia have been reported [1]. Evidence suggests that iron deficiency affects cognitive function and leads to physical damage in a long-term period, disorder in energy metabolism of nerve cells and glial cells and the synthesis of neurotransmitters and myelin [2, 3].Glossitis and stomatitis are known as the oral protests of anemia. In a study, prevalence rate of oral protests of iron deficiency anemia for cracks in the corner of the lips (58%), glossitis with varying degrees of atrophy and stringy fungal Papi (42%), pale oral mucosa (33%), oral candidiasis (25%), RAS (8%), mucositis erythematosus (8%) and irritation of the mouth (8%) were reported for a few months to a year [1]. Iron deficiency definitive diagnosis requires evidence that demonstrates iron stores are fully depleted and also iron of tissues is deficient. Optimal diagnostic process involves measuring serum ferritin as an indicator of iron storage, serum transferrin receptor as an index of tissue iron deficiency. Ferritin is the storage form of iron and stores and releases iron in a revision control required for cell proliferation and metabolism [4, 5]. Ferritin appears to reflect the iron storage value in the body and the increase or decrease serum ferritin level is used as an indicator of anemia and iron overload disorders [1].Saliva test is a laboratory test to identify hormonal, immunological, inflammatory and infectious markers. Steroid hormones such as cortisol, genetic markers, such as RNA and proteins such as enzymes and antibodies are released and measurable in saliva [6, 7]. Saliva is a collection consisted of a variety of organic and inorganic components at a level comparable to the serum [8]. Some similarities between amounts of some markers in blood serum with saliva have been referred in numerous studies and also, some of these markers in saliva as a diagnostic and laboratory tests can be measured. For example, measurement of free hormones have not bonded to their receptors has higher diagnostic value than

measuring them in blood serum. In various studies, cortisol, creatinine, phenytoin and retention and osteopenic markers values in saliva have associated with blood serum and has had diagnostic value [8-10]. Anemia characterized by a reduction in hemoglobin and hematocrit in CBC, is the first sign of iron deficiency. In addition, erythropoisis criteria with iron deficiency including; transferrin iron saturation, mean concentration of hemoglobin of corpusculars (MCHC), protoporphyrin zinc (zinc) in erythrocytes, the percentage of Hypochromic red blood cells, or reticulocyte hemoglobin concentration, are required to aid in diagnosis [1].
The results of studies that have been done in the field of saliva and serum ferritin levels are different. Agarwal and colleagues in a study on children with anemia with iron deficiency observed that ferritin level in the saliva of these patients was much higher than the normal level [11].

Jagannathan study hypothesis was that there is no changes in salivary ferritin levels in children with iron deficiency anemia. In this study, saliva ferritin in mild and severe anemia groups and saliva ferritin to serum ferritin ratio was found. This ratio in patients with severe iron deficiency anemia was significantly higher and, in patients with mild iron deficiency anemia was reported a little more [12].

The Duran Canatan's study, iron and ferritin levels in saliva and serum of patients with thalassemia and iron deficiency anemia were compared. For this purpose, 96 patients with iron overload, 30 patients with iron deficiency anemia and 35 healthy children participated in the study as control group. Iron and ferritin levels were measured in serum and saliva of patients. Iron and ferritin levels in serum and saliva of patients with iron overload was higher than the control group and lower than iron deficiency group. In addition, in this study, levels of iron and ferritin of serum and saliva in the studied groups were not significantly different. And significant difference between the amount of ferritin in serum and saliva in these patients were not reported [13].
In some studies it has been reported that changes in ferritin level in saliva occurs even before we have blood changes and hence, it may be considered to be a valuable tool used to monitor iron status [14].
Venous bloodletting is the most common method of checking blood markers in patients with blood disorders however, sampling of venous blood and carrying it has had the risk of contamination, in addition, this relatively invasive and painful procedure may not be appropriate for younger and older patients, and patients with low working and those have difficulty in finding vessels. With regard to the relationship between the amounts of markers in saliva and blood serum and limited and conflicting results of previous studies, this design has conducted identification of a non-invasive method to evaluate the ferritin with sensitivity and the evaluation characteristics of blood ferritin in large numbers of patients compared to previous studies.

II. MATERIAL AND METHODS:

The design and method of this study were approved Tabriz Dental and Periodontal Research Center of the Tabriz University of Medical Sciences' Investigation Committee (TBZMED.REC.1394.619).
In this study, 280 samples of 140 healthy subjects and 140 patients which their anemic problem has been identified in the blood tests, have had saliva sampling and the amount of ferritin has been measured, and achieved data have been surveyed and analyzed by SPSS software.Their saliva samples were taken within 24 hours before sampling at a rate of 2cc, emphasizing the avoidance of food, toothbrushes or cigarettes during the two hours before sampling in the interval of 9-11 am and lack of dental procedure and, was transferred to the laboratory. In order to determine the amount of ferritin in saliva, saliva samples were centrifuged and were frozen at -80 until collecting the samples fully to the desired number. Then, salivary samples were evaluated with salivary Ferritin kit and ferritin concentration was measured in saliva, saliva ferritin level was investigated with ferritin kit (Human Ferritin ELISA Kit, E1702hu) and the results were collected.In patients with iron deficiency anemia based on laboratory results and if they had undetermined serum ferritin level and, in Laboratory cc5 of venous blood were taken from the control group and serum ferritin level was surveyed with ferritin kit (Human Ferritin ELISA Kit, E1702hu) and the results obtained were collected.

III. RESULTS

Objective 1: determining the serum ferritin level in patients with iron deficiency anemia and control group
The average serum ferritin in the control group is 22.47 and in the group with iron deficiency is equal to 16.9 T. test shows a significant difference in both averages ($t = 4.5$, $p < 0.1$). In other words, serum ferritin of the group with iron deficiency is significanly lower than the control group.
Objective 2: Determining the level of saliva ferritin in patients with iron deficiency anemia and control group
The average saliva ferritin level is 94.77 in the control group and in the group with iron deficiency is equal to 111.4. T test shows a significant difference in both averages ($t = 4.6$, $p < 0.1$). In other words, saliva ferritin of the group with iron deficiency is significantly higher than the control group.
Objective3:Determining the correlation between salivary and serum ferritin levels in the two groups
The investigation of the relationship between serum ferritin level and saliva ferritin level indicates that, there is no significant correlation between these two serum ferritin levels in the control group. But in people with iron

deficiency, there is a significant inverse correlation between serum ferritin with saliva ferritin. In other words, by reducing serum ferritin, saliva ferritin increases.

IV. DISCUSSION

Saliva test is a laboratory diagnosis test to identify hormonal, immunological, inflammatory and infective markers. Steroid hormones such as cortisol, genetic markers, such as RNA and proteins such as enzymes and antibodies are released and measurable in saliva [6, 7]. Some similarities between amounts of some markers in blood serum and saliva have been referred in numerous studies and even, some of these markers in saliva as diagnostic and laboratory tests can be measured. In various studies, cortisol, creatinine, phenytoin retention and osteopenic markers values in saliva have associated with blood serum and have had diagnostic value [8-10]. In the present study, the correlation between salivary and serum ferritin levels in patients with iron deficiency anemia and the control group was investigated.

Jagannathan during a study, examined salivary ferritin levels in children with iron deficiency anemia. In this study, saliva ferritin in mild and severe anemia groups and saliva ferritin to serum ferritin ratio was found. This ratio in patients with severe iron deficiency anemia was significantly higher and, in patients with mild iron deficiency anemia was reported a little more [12]. In this study, saliva ferritin in patients with iron deficiency anemia was higher.The Duran Canatan's study, iron and ferritin levels in saliva and serum of patients with thalassemia and iron deficiency anemia were compared. For this purpose, 96 patients with iron overload, 30 patients with iron deficiency anemia and 35 healthy children participated in the study as control group. Iron and ferritin levels were measured in serum and saliva of patients. Iron and serum and saliva ferritin levels of patients with iron overload was higher than the control group and lower than iron deficiency group and, significant difference between the amount of ferritin in serum and saliva in these patients were not reported [13]. Statistical analysis results of this study show that serum ferritin level in anemic cases is less than control group and saliva ferritin level in anemic cases is more than control group.Agarwal and colleagues in a study on children with anemia with iron deficiency observed that ferritin level in the saliva of these patients was much higher than the normal level. In this study, in both groups of control and anemic cases, saliva ferritin is much more than serum ferritin [11].I.Johansson, C.Fragrans in a study examined the relationship between the amount of iron deficiency and salivation. In this study, two sets of rats, including the first series of 42 newborn rats and second series of 20 adult rats (41 days old) with iron deficiency anemia and the control group were selected to check the amount of salivation. Average salivating at the first set of rats in was significantly lower than the control group ($p < 0.001$). And there was no difference between the salivation of the second series of rats and the control group. In accordance with the results of this iron deficiency study, in the secretion of saliva or discharge does not affect the electrolyte [15].Michael Horowitz's study found that saliva ferritin levels significantly increased in obese adults, this study showed that enhanced saliva ferritin levels was associated with increasing FPG, blood pressure, triglycerides, and HOMA-IR and, there is a positive correlation between FPG, FTI, TG, HOMA-IR and saliva ferritin levels in this study [16]. In the present study in anemic cases, there is a significant relationship between salivary and serum ferritin.Venkatapathy's study had been designed to investigate the possibility of replacing saliva instead of blood serum to estimate creatinine in patients with chronic kidney disease. The aim of this study is to identify the relationship between salivary and serum creatinine level and the role of saliva as a non-invasive alternative to serum in chronic kidney patients. The study population consisted of 142 subjects including 37 healthy and 105 CKD patients. Based on the results of this study, the average of serum and saliva creatinine concentration in CKD patients was significantly higher than the control group and a significant positive correlation was found between salivary and serum creatinine amounts in patients with chronic kidney disease [7]. The results of this study shows that saliva ferritin in healthy subjects is significantly less than the anemic cases. Serum ferritin in healthy subjects is significantly higher than the anemic cases.Ankolekar and Karjodkar in a study examined the iron and minerals amounts in serum and saliva of patients taking gutkha. In this study, the group A included patients who have chewed gutkha and have had OSMF, Group B included patients who have chewed gutkha and have not had OSMF and Group C included who did not consume gutkha. According to the results of this study, iron of saliva increases from Group A to B to C [8].A new study also shows that serum ferritin levels in anemic cases is lower than control group and saliva ferritin levels in anemic cases is more than control group.The aim of the PetraSurlin and his colleagues' study were investigation of salivary levels of TNF-α, L-FABP / FABP 1 and RGM-C / HJV and whether they are associated with serum levels. The rats were divided into four groups: C: control group, A: Aripiperazol consumer group, M: mirtazapine group, AM: Aripiperazol consumer mirtazapine groupSignificant changes were registered between the initial and final saliva levels of L-FABP, or between its serum levels in the control group and three treated groups. These findings showed that Aripiporazol and mirtazapine consuming does not make change in saliva or serum L-FABP.Significantly higher value for RGM-C / HJV serum was found in group A, comparison of group M and AM with Group C showed increase in serum level for α - TNF. Positive or strong or very strong correlation, between the salivary and serum levels of TNF-α, L-FABP and RGM-C allows to use saliva instead of blood [17].In this study, there is no meaningful relationship between saliva and serum ferritin in healthy

people. There is a significant relationship between salivary and serum ferritin in anemic subjects.Pellegrini and colleagues' study to determine whether bone alkaline phosphatase concentration and telopeptide C terminal of type I collagen (CTX) in saliva in different conditions: normal, increase and decrease bone remodeling with serum samples is the same? The results indicate that saliva samples in normal conditions are the same as serum samples and in increasing and decreasing condition, bone remodeling changes [18].In contrast, in the recent study, the saliva ferritin levels in anemic cases is higher than serum ferritin levels and saliva ferritin levels in control group is less than serum ferritin.Laidi and colleagues studied the relationship between salivary and serum concentrations of Ca 15-3 in patients with breast cancer and asymptomatic healthy volunteers including 60 women (29 women with breast cancer and 29 healthy women). In this study, a positive correlation was found between serum and saliva to detect the marker [19].In this study, there is no significant relationship between saliva and serum ferritin in healthy people. There is a significant correlation between saliva and serum ferritin in anemic cases.Taye.lasisi's study results show that, there is no correlation between salivary and serum immunoglobulin.In this study, there is no significant relationship between saliva and serum ferritin in healthy people. In anemic cases there is significant relationship between salivary and serum ferritin [20]. Blood collection includes potential risks for people like transient discomfort, bruising, infection in the blood vessel region and anemia in the case of high bloodletting or being vulnerable and has the lowest approval rating for children and people who finding vessel in them is difficult, such as the elderly or patient cases. While unstimulated saliva samples are considered as the gold standard for analysis.

Saliva has the necessary advantages compared with other body fluids and is a convenient and simple diagnostic tool. With sensitive and specific diagnostic future methods such as proteomics, genomics, transgenic, and microfluidics with saliva, considerable potential as a diagnostic tool has been earned. With the advent of more sensitive techniques and standard values and standard techniques, saliva diagnostics will become the chosen technique in the near future.

V. CONCLUSIONS

In accordance to the results of this study, evaluation of salivary ferritin in iron deficiency anemia has been valuable as a diagnostic test and, it seems in cases where the sampling of blood vessels is difficult, sampling of saliva can be helpful in this disease as a diagnostic test. This study has been merely a descriptive study and does not analyze the obtained results. Achieving more accurate results which are generalizable to clinical applications in this area needs further more accurate investigation

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Table & Figure

Table 1: Comparison of serum ferritin levels in the two study groups

Standard deviation	average	Number	Group	
8.03249	22.4793	140	**Control**	serum ferritin
11.98289	16.9071	140	iron deficiency	

Table 2: Comparison of saliva ferritin levels in the two study groups

Standard deviation	average	Number	Group	
28.88910	94.7721	140	**Control**	saliva ferritin
32.17211	111.42	140	iron deficiency	

Table 3: matrix of correlation between salivary and serum ferritin levels in the two groups.

Saliva ferritin			
With iron deficiency	Control		
-.410**	-.043	Correlation coefficient	**serum ferritin**
.000	.617	Significant level	
140	140	number	

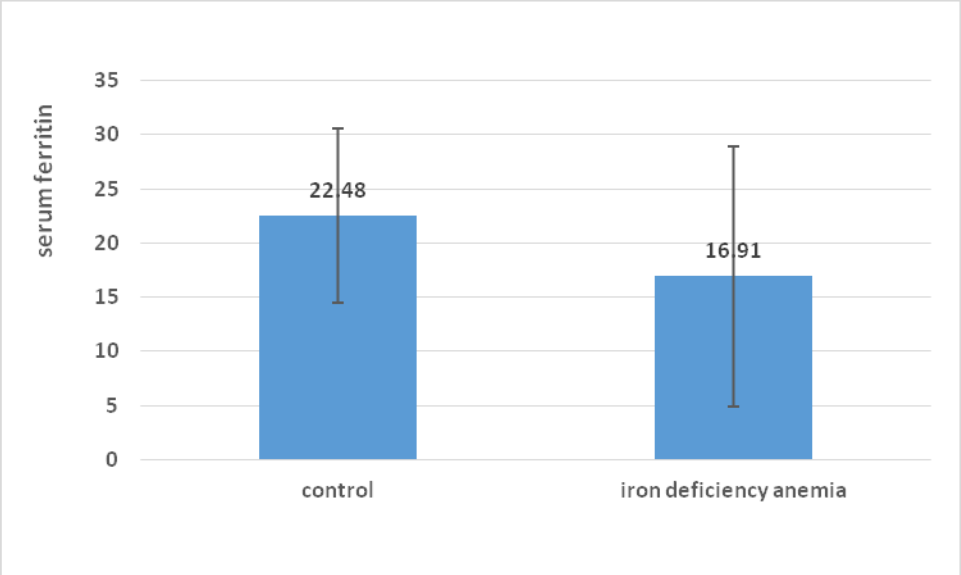

Figure 1 Comparison of serum ferritin levels in the two study groups

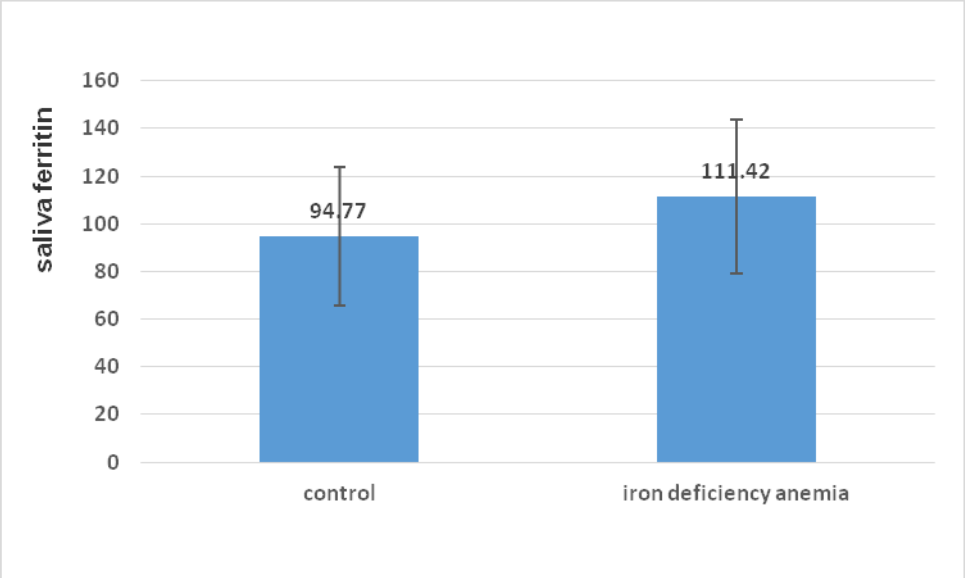

Figure 2: Comparison of saliva ferritin levels in the two study groups