Osmotic fragility in essential hypertension revisited: A correlation with Iron status and lipid profile

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Abstract. Essential hypertension is a major public health associated with increased pressure on the vascular walls and red blood cells (RBCs). In the present work, osmotic fragility (OSF) of RBCs was reexamined in the measure of its correlation with two risk factors; iron status and lipid profile. OSF, iron status parameters, and lipid profile components were measured in eighty-eight patients and compared to the results of thirty controls. The results presented a significant increase in all iron indices of hypertensive patients compared to the normotensive group excluding transferrin concentrations and UIBC decreasing in these patients compared to the healthy group. Serum TGs, total cholesterol, VLDLc, and LDLc increased in patients as compared with control group. There is no significant change in OSF between patients and controls. The iron status parameters and LDLc and TG components were dependent on sex and smoking state. Hemoglobin and PCV were correlated significantly with total cholesterol and LDLc. Transferrin saturation showed a positive correlation with cholesterol, LDLc, and TGs, but negatively correlated with HDLc. No significant correlation between all the measured parameters and OSF in patients with HT. There is a significant correlation between serum ferritin and systolic BP and between Hb and systolic BP. Conclusion. Hypertension as a mechanical challenge for RBCs membrane has no significant effect on the OSF in hypertensive patients. Iron status parameters showed an elevation in HT patients as compared with controls. OSF has no significant correlation with iron status parameters or with lipid profile components in HT patients.

Keywords: Iron, TIBC, ferritin, osmotic fragility, and hypertension.

1. Introduction

In Iraq's overall population, the prevalence rate of hypertension (HT) is 4.15% of Iraqi.1 Among the adult population; the rate reached 40% in 2008. Non-communicable diseases cause about 50% of the total mortality in Iraq. HT is a major contributor to non-communicable diseases, a global epidemic that necessitates greater and coordinated efforts by all concerned parties 2. HT distribution throughout Iraq showed a wide variety depending on the geographical area. In 2014 in the south of Iraq, spatially in Thi-Qar Governorate a household survey conducted showed that the overall prevalence of hypertension was 26.5%. While in the north of Iraq, 54.7% out of 1480 participants were identified as having HT.3 Therefore, examining the factors related to or affecting the HT is still an important field of study. One of these factors is the lipid profile. Hypertension and dyslipidemia are the most important risk factors for the occurrence of cardiovascular disease (CVD).4 Hypertension and dyslipidemia synergistically act to accelerate CVD progression 5, and more than half or one and a half patients with hypertension have
dyslipidemia. Dyslipidemia factors that lead to endothelial dysfunction may cause HT has a strong association with CVD and abnormal lipid metabolism. Not only the traditional lipid biomarkers but also the recent lipid components like Apo A1 and Apo B100 were a target for treatment by new drugs.

Another less studied factor is the effect of mechanical pressure on the Osmotic fragility (OSF) of red blood cells (RBCs). OSF indicates the proportion of the degree of hemolysis that happens when a sample of RBCs is undergone osmotic stress, such as placing it in a hypotonic solution. OSF is influenced by several factors, including integrity and membrane, RBCs sizes, and surface-area-to-volume ratios. The OSF test is common in hematology and is frequently performed to assistance with diagnosing diseases associated with RBCs membrane abnormalities. OSF of RBCs may be considered a screening test for hypertensive patients who will benefit from diuretic therapy. OSF was increased in other diseases that have a bad prognosis, including heart diseases and metabolic syndrome.

The erythrocyte shape, size and OSF were affected by various factors, including conformation status of membranous proteins, membrane fluidity, membrane cytoskeleton proteins and membrane lipid fluidity. It has been proposed by the biochemical studies of erythrocytes and other cells that the abnormalities of cell membrane have a role in the pathogenesis of essential hypertension. However, this concept is neglected during the last decade, and very few studies were carried out in this field. The third parameter to be studied in the HT patients is the iron status. Iron has an important role in maintaining various cellular functions and enzyme reactions, but iron overload is considered a risk factor in the progression of essential HT. Iron plays an important role in maintaining physiological homeostasis in the body; however, elevated iron can lead to free radical generation, resulting in tissue damage. Iron is stored primarily in the ferritin protein. Ferritin is a protein regulating iron homeostasis, which is widely used to evaluate the iron status and is specifically important for identifying iron deficiency.

Hydrogen peroxide (H$_2$O$_2$) and organic compound (hydroperoxides) react with hemoglobin to release iron, which promotes Fenton reaction and DNA degradation. In the Fenton reaction, iron cation (Fe$^{2+}$) catalyzes the formation of reactive hydroxyl radicals. The interaction of the excess iron in HT may cause an increase in Fenton reaction and lipid peroxidation, leading to the formation of oxidized LDL that ultimately leads to the development of foam cells and CVD progression, including HT. It was published that high iron stores (hyperferritinemia) are associated with aortic stiffness and cardiac diastolic impairment. Oxidative stress has been considered as a pathogenic factor associated with essential hypertension. Oxidative stress has a vital role in the development of hypertension. Redox imbalance leads to the activation of several signaling pathways arranged by reactive. In middle-aged Korean men the significant predictor of hypertension is a serum ferritin, but not iron level oxygen species (ROSs) and reactive nitrogen species (RNSs).

In the present study, an attempt has been made to study the effect of HT on the OSF of RBCs, also, to find out the correlation of OSF with other factors affecting HT, including lipid profile and iron status in Iraqi hypertensive patients.

### 2. Experimental section

#### 2.1 Study Group

This study was designed to examine the association between fragility, iron status, and lipid profile on eighty-eight patients with uncomplicated essential-hypertension who have no other systemic diseases with mean age 49±13 years old for the period from May 2018 till June 2019. HT was diagnosed according to the European Society of Hypertension (ESH) and the European Society of Cardiology (ESC) guidelines. Each HT patient had a blood pressure measurement by conventional sphygmomanometry over 95/140 mmHg (seated posture). The arm in the horizontal position after five minutes of quiet sitting. Thirty healthy individuals as a control group was also enrolled in this study for comparing purposes with normal blood pressure and their aged range was between 46±14 years old. The control group was confirmed to be normal by biochemical and hematological examinations. Exclusion criteria included a history of infection, inflammation, cancer, diabetes mellitus, and congestive heart failure. Biochemical, hematological, all clinic-pathological data of the patients were collected from the
clinical files of the patients. Body mass index (BMI) was calculated as weight (kg) divided by the square of height (m²). Informed consent was taken from all the participants before participation in the current study. All procedures were under the established ethical standards. The Ethics Committee of the University of Kufa approved the study protocol (512/2018).

2.2 Blood collection:
Blood samples were collected from individuals in the morning after at least 12 hours of overnight fasting and put in a plain tube for serum separation by centrifugation in order to estimate the iron status parameters and hormone level. Another part of the fresh blood was put in the EDTA tube for estimation of OSF. Total serum cholesterol and TGs were measured by enzymatic colorimetric methods using the kits supplied by Biolabo®, France. HDLc level was measured after precipitation of all other lipoproteins using HDLc phosphotungstic acid precipitant kit supplied by Biolabo®, France.

Very low-density lipoprotein (VLDLc) were estimated using the following formula:

\[ \text{VLDLc} = \frac{\text{TG (mM)}}{2.19} \]

Low-density lipoprotein (LDLc) were estimated using the following formula:

\[ \text{LDLc} = \text{TC (mM)} - \text{VLDLc (mM)} - \text{HDLc (mM)} \]

Different Atherogenic indices were calculated by dividing total cholesterol, TGs, or LDLc by HDLc. Serum levels of iron were estimated using Ferrozine® colorimetric method. total iron Binding Capacity (TIBC) was estimated colorimetrically by the following procedure: An excess of iron is added to the serum iron to saturate the transferrin. The unbound iron is precipitated with basic magnesium carbonate. After centrifugation, the iron in the supernatant was determined. Unsaturated iron-binding capacity (UIBC), the amount of protein (apotransferrin) available to bind iron, can be estimated from the formula:

\[ \text{UIBC} = \text{TIBC} - \text{Serum iron} \]

The quantitative ferritin test is based on a solid phase enzyme-linked immunosorbent assay (ELISA). The assay system utilizes one rabbit anti-ferritin antibody for solid phase (microtiter wells) immobilization and a mouse monoclonal anti-ferritin antibody in the antibody-enzyme horseradish peroxidase (HRP) conjugate solution.

Transferrin saturation percentage (TS%) was calculated from the following equation: \[ \text{TS} \% = \frac{\text{Serum Iron/TIBC}}{100} \]

Transferrin concentration can be calculated using the following formula: \[ \text{Transferrin Conc. (g/L)} = \frac{\text{S. Iron (µmol/L)}}{\text{TS\%}*3.98} \]

The formula is based on the maximal binding of 2 mol Fe³⁺/mol of transferrin and a molecular weight of 79,570 gm/mol for transferrin.

2.3 Statistical analysis:
The student T-test was employed to assess differences in scale variables between diagnostic categories, and analysis of contingency tables (χ²-test) was used to check associations between nominal variables. Associations among variables were computed using Pearson’s product-moment and Spearman’s rank-order correlation coefficients. All tests were 2-tailed, and a p-value of 0.05 was used for statistical significance. All statistical analyses were performed using IBM SPSS windows version 25, 2017.

3. Results and Discussion:
Comparison in the appearances of study groups in (Table 1) indicated that the patient's group had more smokers and employed, but less educated than the control group.

| Iron indices | Patients | Control | p-Value |
|--------------|----------|---------|---------|
| Age          | 49.13±9.33 | 46.49±6.88 | N.S.    |
| Sex (M/F)    | 40/48    | 15/15   | N.S.    |
| Education (Y/N) | 63/25  | 3/27    | 0.003   |
Blood pressure, as estimated, is elevated in patients than healthy groups. No significant difference between groups in age and sex. The major finding in Table 1 is that the number of smokers among HT patients is higher compared to the control group. Previously, smoking was found as one of the main danger reasons for hypertension in addition to alcohol depletion, obesity, dyslipidemia, and dietary types. The multivariate analysis identified age, male, non-employment, and obesity as the statistically significant factors associated with hypertension.

### Table 2. Iron indices and lipid profile components in patients and control group.

| Iron indices | Patients       | Control       | p-Value |
|--------------|----------------|---------------|---------|
| Hb (g/dL)    | 13.44±2.11     | 12.65±1.13    | N.S.    |
| PCV (%)      | 43.31±6.32     | 40.94±3.39    | N.S.    |
| Ferritin (pM)| 383.17         | 166.08        | <0.001  |
| S.Iron (μM)  | 21.67±6.21     | 17.82±4.37    | 0.026   |
| TIBC (μM)    | 51.91±10.96    | 53.17±12.83   | N.S.    |
| TS (%)       | 42.87          | 32.48         | <0.01   |
| Transferrin (mg/L) | 127.00 | 84.21 | 0.008 |
| UIBC (μM)    | 30.07±6.18     | 35.49±9.11    | <0.001  |
| TG (mM)      | 2.50±0.90      | 1.69±0.43     | <0.001  |
In iron indices there is a significant elevated ($p<0.05$) of hypertensive patients in comparison with the normotensive group except transferrin concentrations, UIBC and TIBC which decrease in these patients compared to the healthy group.

In terms of lipid profile, the results in Table 2 showed a significant increase in serum TGs, TC, VLDLc, and LDLc in patients compared with the control group, while there were no significant differences in serum HDLc between patients and the control group.

The results of the lipid profile in Table 2 indicated a dyslipidemia state in HT patients compared with controls. Any disorder in lipid plays a major role in CVD and endothelial dysfunction, which lead to the pathogenesis as atherosclerosis, thrombosis, insulin resistance, and hypertension. Our study exhibited that there were significant elevations in the levels of serum TG, cholesterol, VLDLc, LDLc in patients group with HT as compared with the control group. These findings were concordant with the previous studies. Many types of research have found a positive correlation between blood cholesterol levels and CVD. Thus, a decrease in cholesterol levels can significantly reduce the CVD risk. Atherogenic ratios of HT patients and control groups were used to estimate the risk of CVDs. Some studies demonstrated that the TC/HDLc and the LDLc/HDLc ratios are well indicators of atherosclerosis and CVD than any other lipid marker. Similarly, the TG/HDLc ratio was established to be as major indicator of CVD as the other ratios lipid. Hence, the study of lipid profile in hypertensive patients is an important matter to determine the risk of CVDs in those patients. It is hypothesized that it is the ratio of TG/HDLc in the plasma that determines the esterification rate of cholesterol. Furthermore, increased ratios between TG/HDLc also show that the incidence of atherogenic small dense (LDLc) particles, which could aid as a right marker for coronary atherosclerotic lesions and the presence of myocardial infarction (MI).

3.2 Comparison in OSF between HT patients and controls

There was a slight difference in the results of OSF, but it was insignificant ($p>0.05$). The explanation of this unexpected finding might be due to the smaller sample size enrolled in this study, technical method differences and individual differences within the sample such as age, sex, type of treatment, and disease duration. Another explanation for this non-significant difference between patients and control groups might be the control group has a family history of hypertension. Other studies found that in a 0.6% saline solution the normal cell is swell. Usually, hemolysis occur is normally begins at 0.42%, when the RBCs volume grows to about 145% compared to normal volume. The cells are fully hemolyzed in a 0.35% saline solution. (RBCs) volume at this concentration, before it bursts, (critical hemolytic volume) is about 165% of normal.

OSF in essential hypertensive patients increased more than the healthy groups. These results demonstration in essential hypertension patients the erythrocyte membranes increased lability. RBCs deformability was found decreased in essential hypertension patients versus the normal. A direct correlation was revealed between red cell mechanical resistance (from the time of hemolysis) and the value of arterial pressure in essential hypertension.
patients with essential hypertension might be due to the abnormality of Ca-handling of the cell membranes. This leads to a rise in the intracellular Ca concentration contributing, which contributes to the pathogenesis of essential HT. Increase OSF was diagnosis in essential hypertensive patients and healthy with a family history of hypertension as a compared with no a family history so normotensive controls and hypertension. Thus, the OSF might reflect structural and functional irregularities of cell membranes and maybe one of the genetic biomarkers of the hypertensive susceptibility. Furthermore, abnormalities of the physical properties of the membrane and of multiple transport systems have been implicated in the pathogenesis of increase blood pressure. In hypertensive patients the sodium hydrogen exchanger (Na⁺/H⁺) is increased than healthy either by an increased enhanced external calcium entry or cellular calcium load. An increased sodium hydrogen (Na⁺/H⁺) exchanger might play an important role in the pathogenesis of hypertension, both by catalyze cell growth and vascular tone and possibly by enhancing sodium reabsorption by renal proximal-tubule cells.

As presented in Figure 1, there is no significant change in fragility between patients and controls where (p-value =0.173)

![Figure 1](image_url)

**Figure 1.** Normal osmotic fragility curve with a left shift in hypertensive patients group. The p-value of the comparison=0.173.

### 3.3 Comparison and correlation between female and male HT-patients

Table 3 shows the comparison of iron indices between male and female patients.

| Iron indices | Male Group       | Female Group      | p-value |
|--------------|------------------|-------------------|---------|
| Hb g/dL      | 14.38 ±2.45      | 12.78 ±1.86       | 0.036   |
| PCV %        | 45.21 ± 5.88     | 38.12 ± 4.19      | 0.012   |
| Ferritin pM  | (411.25)         | (178.71)          | <0.001  |
| S.Iron μM    | 18.81± 4.27      | 14.38 ± 5.09      | 0.028   |
| TIBC μM      | 39.67± 7.17      | 56.19 ± 10.76     | 0.037   |
| TS %         | (46.14)          | (25.59)           | 0.008   |
| Transferrin mg/L | 102.43         | 141.19            | <0.001  |
| UIBC μM      | 21.69 ± 3.47     | 42.44 ± 5.71      | 0.017   |
TG (mM) 2.62 ± 0.64  2.01 ± 0.77  0.014
Chol (mM) 6.11 ± 1.43  5.97 ± 1.38  0.076
HDLc (mM) 1.08 ± 0.37  1.03 ± 0.51  0.317
VLDLc (mM) 1.20 ± 0.29  0.92 ± 0.35  0.014
LDLc (mM) 3.83 ± 0.77  4.02 ± 0.52  0.082
TC/HDLc 5.66 ± 3.87  5.80 ± 2.71  0.094
TG/HDLc 2.43 ± 1.73  1.95 ± 1.51  0.111
LDLc/HDLc 3.55 ± 2.08  3.90 ± 1.02  0.214

There is a statistical increase (p<0.05) in both iron status parameters in the male group when compared with the female group except transferrin (Tf), TIBC, and UIBC, which showed a decrease in the male group. TG, VLDLc, and TG/HDLc were lower in the female group than in the male group. At the same time, all other lipid profile parameters have been changed insignificantly. No significant change in fragility between female and male HT-patients.

3.4 Effect of smoking on the parameters
The results of all the measured parameters in smokers and non-smokers patients, in addition to p-values of the comparison between both groups, are represented in Table 4.

| Iron indices | Smokers       | Non-Smokers  | p-Value |
|--------------|---------------|--------------|---------|
| Hb (g/dL)    | 14.27 ± 2.48  | 13.35 ± 1.9  | 0.034   |
| PCV%         | 44.31 ± 8.48  | 43.05 ± 5.68 | 0.031   |
| Ferritin (pM)| 342.14 ± 338.25 | 251.66 ±190.34 | 0.008   |
| S.Iron (μM)  | 21.99 ±13.92  | 18.87 ± 5.78 | 0.002   |
| TIBC (μM)    | 51.91±10.96   | 53.17 ± 12.83 | 0.471   |
| TS%          | 55.94 ± 37.14 | 47.81 ±15.90 | 0.008   |
| Transferrin (g/L)| 108             | 113          | 0.906   |
| UIBC (μM)    | 28.92±30.08   | 21.79 ± 13.26 | 0.001   |
| TG (mM)      | 2.51 ± 0.66   | 2.50 ± 0.95  | 0.075   |
| Chol (mM)    | 6.36 ± 1.30   | 5.92 ±1.34   | 0.755   |
| HDLc (mM)    | 1.09 ± 0.43   | 1.02 ± 0.44  | 0.601   |
| VLDLc (mM)   | 1.15 ± 0.29   | 1.14 ± 0.44  | 0.075   |
| LDLc (mM)    | 5.14 ± 1.50   | 4.79 ± 1.33  | 0.742   |
| TC/HDLc      | 7.15 ± 4.19   | 6.86 ± 3.11  | 0.117   |
All iron status biomarkers were increased (p<0.05) in smoker HT patients in comparison with non-smoker patients except TS% and UIBC, which reduced in smoker patients. However, TIBC showed no significant difference between both smoker and non-smoker HT patients. No significant difference was also observed in lipid profile parameters between smokers and non-smoker HT patients. There was no significant change in fragility between smokers and non-smokers patients.

### 3.5 Correlation between parameters

To obtain an indication of the usefulness of iron indices as a risk factor for CHD, correlation coefficients (r) between iron indices and lipid profile components were calculated. No significant correlation was found between the variables of the lipid profile and serum iron. Hb and PCV were correlated significantly with total cholesterol (r=0.288, p=0.018) and LDLc (r=0.271, p=0.021). UIBC were correlated significantly with total cholesterol (r=0.274, p=0.016) and LDLc (r=0.277, p=0.021). The strongly positive correlation between transferrin saturation with total cholesterol (r=0.323, p=0.004), LDLc (r=0.310, p=0.008), and TGs (r=0.283, p=0.018), but strongly negative correlation with HDLc (r=−0.282, p=0.022). No statistical correlation was found between all the measured parameters and OSF in HT patients. There is a significant correlation between serum ferritin and systolic BP (r=0.317, p=0.014) and between Hb and systolic-BP (r=0.247, p=0.037).

According to the data shown in Table 3, it is expected that the iron status is more consistent in the male in comparison with the female group due to the menstruation state and usual lower Hb in females as to males. As women become older, the CVD incidence increases gradually, largely narrowing the gender gap, and that there is a parallel increase in body iron stores. In the present work, there is no statistically difference between female and male with HT patients in OSF values. In one study, it is found that the OSF appeared to be a little increased in females as compared with that in males. However, our result indicated no correlation between gender and OSF in HT patients.

All iron status biomarkers were increased (p<0.05) in smoker HT patients in comparison with non-smoker patients except TS% and UIBC, which were reduced in smoker patients as seen in Table 4. Free radical (OH\(^{-}\)) produced oxidative damage by aqueous cigarette to increase free radical (hydroxyl radical).

Cigarette smoke and dust synergistically lead to damage in the cells. Cell death induced by cigarette smoke exposure can largely be accounted for an enhancement in oxidative stress. It is undoubted point that smoke is a strong source of oxidative stress. Smoking routine is a danger factor for heart diseases such as peripheral vascular, cerebrovascular diseases and coronary artery. Cigarette Smoking causes atherosclerosis, arrhythmias and endothelial dysfunction, through the joint effects of carbon monoxide, nicotine and aromatic compounds such as polycyclic hydrocarbons. Serum iron and red blood cell hemoglobin levels increased in continuing cigarette smoker patients than nonsmoking patients. These results are in contract with previous studies. As increased hypoxia tissues which result from oxygen inadequate in blood flow through lungs causes in erythrocytosis and following increased production of erythropoietin.

The rise total red blood cell mass and count lead to increases the number of destroyed red blood cell in the normal turnover route, which consequently increases iron overload. Significantly increase in serum ferritin in smoking patients is potentially due to iron rise in smokers’ patients. Other studies have found smoking is associated with an increased level of serum ferritin.

Serum marker of iron homeostasis shown changes between non-smokers and smokers. Relative in serum iron, ferritin concentrations and transferrin saturation to non-smokers and in cigarette smokers were statistically increased. There is a significant decrease in serum TIBC and serum UIBC in smoking and nonsmoking patients (p<0.05). These result according to with Saudi population in which that
The mean lipid profile parameters increased in the smokers group compared to non-smoker group. This difference is statistically insignificant (p>0.05), as seen in Table 3. Those results may be due in part to the significant parallel increase in both groups versus the control group, and the increase in these cases may follow up the same factors that affect lipid profile in hypertension. The other cause could be due to the small number of smokers in comparison with non-smoker individuals. In one research, it found that the cigarettes lead to an increase in the concentration of serum total cholesterol, TGs, LDLc, VLDLc and a fall in the levels of antithromogenic HDLc. There is no significant change in fragility between smokers and non-smokers patients indicating a deficiency of the direct effect of nicotine on the OSF in HT and control groups.

The correlation study indicated that Hb, PCV, and UIBC were correlated significantly with total cholesterol and LDLc. Transferrin saturation was establish to preserve an intensely positive correlation with LDLc, total cholesterol , and TGs, but the correlation with HDLc is a strongly negative. No significant association was detected between all the measured parameters and OSF in HT patients. These results may be cause the role of iron cation in lipid peroxidation, oxidation-reduction reaction and other related biological processes. The general mechanism is that Fe (II) and certain chelates react with lipid hydroperoxides (ROOH) and splitting the O-O bond to produce RO•, which can also abstract H• from polyunsaturated fatty acids and from ROO• radicals that can continue the propagation of lipid peroxidation. It is suggested that the catalytic role of iron in lipid peroxidation may be an important factor in the formation of atherosclerotic lesions. Normal native LDLc can cross the arterial wall without causing damage to the vessel wall. Iron-catalyzed free radical reactions cause oxidation of LDLc, which occurs in endothelial cells, smooth muscle cells, lymphocytes, or macrophages. In our study, there was a significant correlation between the total serum lipids and Fe. Some researchers found that iron deficiency is linked to low serum lipid level, and Fe has been shown as a potential risk factor for hyperlipidemia in humans. However, Suliburska et al. (2011) found no significant correlation between the serum and diet concentration of iron and the serum cholesterol or TGs level. It has been previously found that Hb levels were positively associated with the risk of incident hypertension. Other studies reported that Hb showed a substantial positive association with blood pressure. Iron overload showed augmentation of atherosclerotic lesions formation in hypercholesterolemic rabbits, probably by stimulating LDLc oxidation in the arterial intima or by influencing lipoprotein synthesis in the liver, which could lead to increased susceptibility to oxidation in the intima. Due to the increase of disorders in the structure of erythrocyte cytoskeleton proteins and membrane lipids fluidity increase potentially causes a rise in erythrocyte OSF. RBC membranes from hypertensive patients to increase cholesterol: phospholipid ratio in association with high sodium lithium transport and increased ratios of fatty acid metabolites to the triglycerides precursors compared to those from same age normotensives. Such changes in lipids produce a high membrane microviscosity and decrease in fluidity, which may be responsible for increased permeability to sodium and other alterations in sodium transport. The high polyunsaturated fatty acid content of the red blood cell membrane and the continuous exposure to the high concentration of oxygen and iron in hemoglobin are factors that make RBCs very sensitive to oxidative injury. The biomechanics of erythrocytes, determined by the membrane integrity and cytoskeletal structure, provide critical information on diseases. Such biomechanical properties reflect a sensitivity to any changes in OSF induced by chemical, heating, and glucose treatment. The RBCs membrane fragility indicates a decrease in the membrane flexibility (increased fragility) of hyperlipidemic, resulted from the disturbance of ionic motion through the membrane and/or the change in the molecular properties of the macromolecules that forming the membrane. This change in ionic mobility through the cellular membrane leads to changes in metabolic function and may causes changes in OSF. OSF may be determined as a screening tool for hypertensive patients who will benefit from diuretic therapy. The RBCs size was larger in hypertensive subjects than in normal controls. This could be due to the fact that the mean erythrocytic zeta potential of the healthy group was higher in
hypertensive patients. The previous data recommended that there are several morphological changes in RBCs structure, in addition, to increase OSF value as associated to that of control which possibly be the major cause for CVD progression.

4. Conclusion
The increase in blood pressure in HT patients has no significant effect on OSF values. HT patients have increased levels of iron parameters in comparison with controls. OSF has no correlation with iron status parameters or with lipid profile components. There is a correlation between iron parameters and lipid profile parameters that may exacerbate the arteries wall's damage leading to an increased risk of coronary artery disease. Further studies are required for other biochemical parameters in a larger patients' sample size.

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