Assessment of salivary and serum oxidative stress and antioxidants as plausible parameters in prediction of ischemic stroke among Iraqi Samples

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Citation

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Abstract

Background: Oxidative stress is one of the mechanisms involved in neuronal damage induced by free radicals production in ischemic stroke due to ischemia- reperfusion. Antioxidants, on the other hand, may provide protection from neuronal damage caused by oxidative stress.
Objectives: The present study was designed to measure some oxidative stress marker and antioxidants in serum and saliva of ischemic stroke patients and patients with some stroke related diseases in an attempt to obtain the predictive value for ischemic stroke in stroke –prone individuals.
Methods: Serum and salivary Malondialdehyde (MDA) levels , glutathione (GSH), superoxide dismutase (SOD) and uric acid (UA) were estimated for 150 individuals, fifty of them were patients having recently diagnosed ischemic stroke, seventy five were sex and age matched risk-group patients (patients with hypertension, type2 diabetes and ischemic heart disease) and other 25 sex and age matched healthy control individuals.
Results: Serum GSH is considered as the most powerful predictor for ischemic stroke with critical value (< 1.52µmol/L) followed by serum SOD with critical value (≥ 2.09 U/ml) and salivary SOD with critical range (1.54-1.80 U/ml) could be an alarming sign for stroke in patients with hypertension and patients with heart diseases.
Conclusions: Serum and salivary MDA, SOD, UA and GSH can be used as potential marker for monitoring patients with hypertension, diabetes mellitus and patients with angina or myocardial infarction to give us an idea about the disease progression toward ischemic stroke.

INTRODUCTION

Stroke (CVA) is considered as a third leading cause of death and an important cause of long-term disability. Ischemic stroke accounts for 80% of all strokes ([1]). Several mechanisms have been suggested in the pathogenesis of ischemic stroke. Oxidative stress is one of the mechanisms involved in neuronal damage induced by free radicals production due to ischemia-reperfusion ([2]). Oxidative stress is an imbalance between the generation of free radicals and antioxidant defense capacity of the body. This resulted in the alteration of the cellular components in term of DNA break, cytotoxicity and lipid peroxidation ([3]). Lipid peroxidation is the most common and most hazardous reaction encountered as a result of free radical generation ([4]). Lipid peroxidation is measured by lipid hydro peroxides ([5]) which are unstable and degrade to various secondary products like Malondialdehyde (MDA) and MDA-like substances which are jointly called Thiobarbituric Acid Reactive Substances (TBARS) which provide meaningful information upon measurements ([6]). MDA level is widely utilized as a marker of lipid peroxidation in states of elevated oxidative stress ([7]). It is well known that saliva has considerable antioxidant capacity, and lipid peroxidation may happen as a consequence of oxidative stress and impaired capacity of saliva antioxidant power([8]). The antioxidant activity may be an important factor providing protection from neuronal damage caused by oxidative stress. Enzymatic and non-enzymatic antioxidants have been proposed as indirect markers, among them: glutathione (GSH), Uric Acid (UA) and Superoxide dismutase (SOD) are related to brain damage and clinical outcome ([9]). The diagnostic value of salivary secretions to detect systemic diseases had long been recognized ([10]). Salivary assays present a lot of advantages when compared to blood assay: the sampling is very easy to do especially in a non-medical environment. It does not

disturb intimacy when control is needed ([11]). Multiple samples could be collected providing more information than that of single blood sample ([12]). The present study was designed to measure the levels of MDA as oxidative stress marker and (GSH, SOD and UA) as antioxidants in serum and saliva of newly-diagnosed ischemic stroke patients and patients with some stroke-related diseases as a monitoring tools in early prediction of ischemic stroke.

MATERIALS AND METHODS

One hundred fifty individuals from Al-Diwania province in Iraq were enrolled in this study. They were categorized into three groups:

The first group (Study group): Composed of 50 patients (24 males and 26 females) who were recently diagnosed clinically and radiographically (Brain CT scan) as having ischemic stroke, their age ranges between 45-75 years.

The second group (Risk group): Composed of 75 sex and age matched patients, served as case control or risk group.

This group involved 25 patients (12males and 13 females) with hypertension, which is determined when systolic pressure of more than 150mmHg or a diastolic blood pressure of more than 90mm Hg or both on 3 occasions. Other 25 patients (11 males and 14 females) with type 2 diabetes, which is determined when two fasting plasma glucose tests exceeds 6.1 mmol/L, and other 25 patients (11 males and 14 females) with ischemic heart diseases (angina or myocardial infarction), which is determined by recent ECG report.

The third group (Negative control): Composed of 25 sex and age matched healthy individuals (12 males and 13 females).

All individuals were evaluated by full medical history and clinical examination with laboratory investigations to exclude any other systemic or local disease that may affect the parameters examined in this study. Oral and periodontal examination was done for each individual and any patient with symptoms and signs of any active oral inflammation, advanced periodontitis or severe gingivitis were excluded from the study.

All participants were supplied with informed consent and the study protocol was approved by Local Ethics Committee of Al-Diwania general teaching hospital.

For laboratory analysis: Blood and saliva samples were taken from patients and control after overnight fasting (8.00-9.00 a.m) . For isolation of serum, 5 ml. of blood sample was taken from each individual, centrifuged at 3000 r.p.m at 4?C for 5 minutes; the supernatant was aspirated and stored in tubes at -20?C until analyzed.

Saliva samples were always collected in restful and quite circumstances, following flushing of mouth with 100ml. of distilled water, the whole saliva was collected for 5 minutes by the subject leaning forward and spiting saliva in test tubes that were kept in crushed ice and immediately after collection, samples were cold centrifuged at 3000 r.p.m at 4?C for 5 minutes. The supernatant was aspirated and stored at -20?C until analyzed.

Serum and salivary levels were assessed for MDA using thiobarbituric acid (TBA) method of Buege and Aust([13]), GSH levels according to the method described by Burtis and Ashwood([14]), SOD levels using modified photochemical Nitroblue Tetrazolium (NBT) method utilizing sodium cyanide as peroxidase inhibitor ([15]), Uric acid were also assessed using commercial kit (BioMerieux, France).

All data were statistically analyzed using SPSS statistical package (SPSS, Version13, Chicago,IL,USA). Data are expressed as mean ± standard deviation. Differences between groups were analyzed for significance using one-way ANOVA test. Correlation assessment was performed using the Spearman correlation analysis. To discriminate between ischemic stroke cases from case-control and to compare the diagnostic performance of the test, Receiver Operating characteristic (ROC) curve analysis was used. Statistical significance was defined as $p < 0.05$.

RESULTS

The mean age for ischemic stroke patients was about 58.2 years. The most affected age group was between 56-65 years. Forty one of them (82%) had hypertension, 34 of them had diabetes, 26 were heavy smokers and only 8 of them had previous transient ischemic attack (TIA). Since the levels of all tested variables (MDA, GSH, SOD and UA) in serum and saliva did not vary with age and sex in this study, the results from males and females were grouped together for each group.

Figure 1

Figure (1&2) showed salivary levels of MDA and all antioxidants measured in ischemic stroke group, case-control and negative control groups follows that recorded in serum.

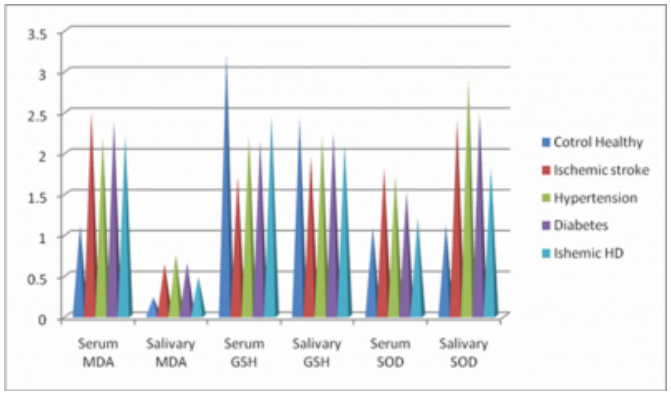
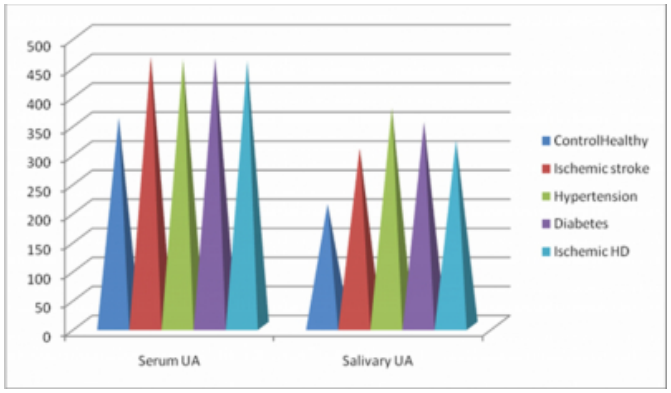


Figure 2

Figure 2: Serum and Salivary Uric acid levels.



Serum and salivary MDA, SOD and UA values were significantly higher in ischemic stroke group when compared with that of healthy control (p< 0.001). However GSH levels in serum of ischemic stroke patients were markedly lower than that of healthy control (p< 0.001)(table 1).

Figure 3

Table 1: Mean levels of MDA, GSH,SOD and UA in serum of Ischemic stroke, Risk group patients and Healthy control.

Serum	Healthy control N=25	Ischemic Stroke N=50	Healthy vs. Ischemic stroke	Case Control (Risk group)					
				Hypertension N=25	Hypertension vs Healthy	Diabetes N=25	Diabetes vs Healthy	Isch. Heart disease. N=25	IHD vs Healthy
MDA (µmol/L)	1.12 ± 0.35	2.51± 1.11	< 0.001	2.19 ± 0.83	< 0.001	2.39 ± 0.97	< 0.001	2.22 ±0.73	< 0.001
GSH (µmol/L)	3.22 ± 0.7	1.71 ± 0.76	< 0.001	2.2 ± 0.76	< 0.001	2.15 ± 0.87	< 0.001	2.44 ±0.77	< 0.005
SOD (U/ml)	1.09 ± 0.18	1.81 ± 0.57	< 0.001	1.72 ± 0.44	< 0.001	1.52 ± 0.53	< 0.027	1.2 ± 0.44	1 (NS)
UA (µmol/L)	358.4 ±38.9	463.3± 65.3	< 0.001	458.8 ±49.1	< 0.001	461.2± 61.2	< 0.001	455.8± 58.8	< 0.001

NS : Non significant at p< 0.05

On the other hand, salivary GSH levels of ischemic stroke patients were not significantly different from that of healthy control and case-control group (table 2).

Figure 4

Table 2: Mean levels of MDA, GSH,SOD and UA in saliva of Ischemic stroke, Risk group patients and Healthy control.

Saliva	Healthy control N=25	Ischemic Stroke N=50	Healthy vs. Ischemic stroke	Case Control (Risk group)					
				Hypertension N=25	Hypertension vs Healthy	Diabetes N=25	Diabetes vs Healthy	Isch. Heart disease. N=25	IHD vs Healthy
MDA (µmol/L)	0.23 ± 0.07	0.64 ± 0.22	< 0.001	0.75 ± 0.21	< 0.001	0.65 ± 022	< 0.001	0.48 ± 0.13	< 0.001
GSH (µmol/L)	2.43 ± 0.89	1.96 ± 0.68	0.2 (NS)	2.21 ± 0.91	1 (NS)	2.24 ± 0.91	1 (NS)	2.1 ±0.85	1 (NS)
SOD (U/ml)	1.12 ± 0.27	2.4 ± 0.9	< 0.001	2.91 ± 0.91	< 0.001	2.48 ± 0.94	0.027	1.82 ± 0.64	1 (NS)
UA (µmol/L)	209.9 ± 28.3	305.6± 62.8	< 0.001	375.2 ± 102	< 0.001	350.8 ±90.4	< 0.001	319.6 ± 56.2	< 0.001

Serum UA had a significant positive correlation with serum MDA (r =0.34) and SOD (r =0.26), whereas serum GSH had significant negative correlation with serum UA (r = -0.28) and with serum MDA (r = - 0.38) (table 3).

Figure 5

Table 3: Pearson correlation between serum estimates

Serum Estimates	Serum Uric acid (µmol/L)	Serum MDA (µmol/L)	Serum GSH (µmol/L)	Serum SOD (U/ml)
Serum MDA concentration (µmol/L)	0.34**			
Serum GSH concentration (µmol/L)	-0.28*	-0.38**		
Serum SOD activity (U/ml)	0.26*	0.12	0	

** p < 0.01 , * p < 0.05

Salivary UA, on the other hand, had significant positive correlation with salivary MDA (r = 0.33) and with salivary SOD (r = 0.21) as seen in table (4).

Table (5) displayed the critical values of the studied parameters in differentiating healthy individuals from those with ischemic stroke. Salivary critical value of MDA is ≥ 0.38µmol/L which was with higher accuracy rate (92%) than that of serum values which is ≥ 1.85µmol/L with accuracy rate of (81%). Salivary critical value of SOD is ≥ 1.54 U/ml. yields 89.3% accuracy and 100% specificity in comparison with serum critical SOD value of ≥ 1.49 U/ml with only 80% accuracy. Serum UA in a value of ≥ 375.5 µmol/L was accurate by 89.3% and sensitive by 96% in differentiating ischemic stroke patients from healthy individuals, whereas, salivary UA in concentration ≥ 238.5 µmol/L was accurate by 89.3% and sensitive by 92% only. Serum and salivary

GSH share the same critical value in differentiating ischemic stroke patients from otherwise healthy individuals which is ? 2.6μmol/L with reasonable accuracy (80%) and (86-90%) sensitivity.

Figure 6

Table 4: Pearson correlation between salivary estimates

Salivary Estimates	Salivary Uric acid (μmol/L)	Salivary MDA (μmol/L)	Salivary GSH (μmol/L)	Salivary SOD (U/ml)
Salivary MDA concentration (μumol/L)	0.33**			
Salivary GSH concentration (μmol/L)	0.09	-0.02		
Salivary SOD activity (U/ml)	0.21**	0.43**	-0.08	

** p < 0.01 , * p < 0.05

Figure 7

Table 5 :ROC test showing the tested variables ordered according to their significance in separating between IS patients and healthy controls.

Parameter	Cut-Off Values	ROC area	P	Accuracy
1-Salivary MDA	Positive if >= 0.38 (μmol/L)	0.969	<0.001	92%
2-Salivary UA	Positive if >= 238.5 (μmol/L)	0.950	<0.001	89.3%
3-Serum UA	Positive if >= 375.5 (μmol/L)	0.927	<0.001	89.3%
4-Salivary SOD	Positive if >= 1.54 (U/ml)	0.918	<0.001	89.3%
5-Serum GSH	Positive if < 2.60 (μmol/L)	0.912	<0.001	80%
6-Serum MDA	Positive if >= 1.85 (μmol/L)	0.885	<0.001	81%
7-Serum SOD	Positive if >= 1.49 (U/ml)	0.838	<0.001	80%
8-Salivary GSH	Positive if < 2.64 (μmol/L)	0.669	0.018	81%

ROC curve equation was also applied to diagnose cases of ischemic stroke and differentiating it from risk group patients. As seen in table (6), salivary UA with critical value (positive if < 260.5 μmol/L) is the most valid parameter in predicting ischemic stroke from hypertension with area under ROC curve (0.709; p = 0.003). The second parameter was serum GSH (positive if ≥1.52 μmol/L) with area under ROC (0.680; p =0.011). The third one was salivary SOD (positive if < 1.80 U/ml.) with ROC area (0.679; p = 0.012), followed by salivary MDA (positive if ≥ 0.86 μmol/L with ROC =0.646; p = 0.04).

Figure 8

Table 6: The most valid parameters in prediction of IS from HT

Parameter	Cut-Off Values	ROC area	P
Salivary UA	Positive if < 260.5 (μmol/L)	0.709	0.003
Serum GSH	Positive if < 1.52 (μmol/L)	0.680	0.011
Salivary SOD	Positive if < 1.80 (U/ml)	0.679	0.012
Salivary MDA	Positive if >= 0.86 (μmol/L)	0.646	0.04
Salivary GSH	Positive if < 2.54 (μmol/L)	0.598	0.17[NS]
Serum MDA	Positive if >= 2.98 (μmol/L)	0.590	0.2[NS]
Serum SOD	Positive if >= 2.09 (U/ml)	0.546	0.51[NS]
Serum UA	Positive if >= 491.1 (μmol/L)	0.517	0.81[NS]

For predicting ischemic stroke in diabetic patients, ROC test showed the most valid parameter which is serum SOD with cut-off value (≥ 2.09 U/ml), followed by salivary UA (positive if < 260.5 μmol/L) followed by serum GSH (positive if < 1.52 μmol/L) as shown in table (7).

Table (8) revealed the most valid parameters in predicting ischemic stroke from ischemic heart disease which are: serum SOD (positive if≥ 2.09 U/ml) followed by serum GSH(positive if < 1.52 μmol/L), then salivary MDA (positive if ≥ 0.86 μmol/L) and lastly salivary SOD (positive if < 1.80 U/ml).

Figure 9

Table 7: The most valid parameters in prediction of IS from DM

Parameter	Cut-Off Values	ROC area	P
Serum SOD	Positive if >= 2.09 (U/ml)	0.667	0.019
Salivary UA	Positive if < 260.5 (μmol/L)	0.660	0.025
Serum GSH	Positive if < 1.52 (μmol/L)	0.648	0.038
Salivary GSH	Positive if < 2.54 (μmol/L)	0.623	0.08[NS]
Salivary SOD	Positive if < 1.80 (U/ml)	0.533	0.65[NS]
Serum MDA	Positive if >= 2.98 (μmol/L)	0.532	0.65[NS]
Salivary MDA	Positive if >= 0.86 (μmol/L)	0.516	0.83[NS]
Serum UA	Positive if >= 491.1 (μmol/L)	0.513	0.85[NS]

Figure 10

Table 8: The most valid parameters in prediction of IS from ischemic heart disease.

Parameter	Cut-Off Values	ROC area	P
Serum SOD	Positive if >= 2.09 (U/ml)	0.806	<0.001
Serum GSH	Positive if < 1.52 (µmol/L)	0.765	<0.001
Salivary MDA	Positive if >= 0.86 (µmol/L)	0.705	0.004
Salivary SOD	Positive if < 1.80 (U/ml)	0.661	0.024
Salivary UA	Positive if < 260.5 (µmol/L)	0.596	0.18[NS]
Serum MDA	Positive if >= 2.98 (µmol/L)	0.570	0.33[NS]
Salivary GSH	Positive if < 2.54 (µmol/L)	0.562	0.39[NS]
Serum UA	Positive if >= 491.1 (µmol/L)	0.541	0.57[NS]

To differentiate ischemic stroke from the whole risk group, the most valid parameter is serum GSH with optimum cut-off value (< 1.52 µmol/L), followed by serum SOD (≥ 2.09 U/ml), then salivary UA (< 260.5 µmol/L),(table 9).

Figure 11

Table 9: ROC test showing the tested variables ordered according to their significance in separating IS patients from the whole RG patients.

Parameter	Cut-Off Values	ROC area	P
1-Serum GSH	Positive if < 1.52 (µmol/L)	0.698	<0.001
2-Serum SOD	Positive if >= 2.09 (U/ml)	0.673	0.001
3-Salivary UA	Positive if < 260.5 (µmol/L)	0.655	0.003
Salivary GSH	Positive if < 2.54 (µmol/L)	0.594	0.07[NS]
Serum MDA	Positive if >= 2.98 (µmol/L)	0.564	0.23[NS]
Serum UA	Positive if >= 491.1 (µmol/L)	0.524	0.66[NS]
Salivary SOD	Positive if < 1.80 (U/ml)	0.517	0.75[NS]
Salivary MDA	Positive if >= 0.86 (µmol/L)	0.514	0.79[NS]

DISCUSSION

Stroke remains the third leading medical cause of death and the second most frequent cause of morbidity in developed countries ([16,17]).Atherosclerosis of cerebral vasculature accounts for approximately 2/3 of ischemic stroke ([18]). Hypertension is the number one risk factor for ischemic stroke due to acceleration of arteriosclerotic process that leads to stenosis and embolism originating from large extra cranial vessels ([19]). The underlying risk factors that were reported in ischemic stroke patients in this study were hypertension which constituted (82%) of ischemic stroke sample. This result was in agreement with Oxfordshire Community Stroke Project study ([20]). Many studies have identified diabetes mellitus as an independent and significant risk factor for stroke ([21,22]). Diabetes was reported in (68%) of ischemic stroke sample in this study and ranked as a second risk factor after hypertension , this finding is in agreement with Mortel study ([23]). Diabetes mellitus accelerates atherosclerosis and induces both micro-angiopathic changes and large-vessel atherosclerosis ([24]). Smoking increases platelets activity and catecholamine levels, alters prostaglandins and decreases protective high density lipoprotein (HDL) levels ([25]). Smoking habit ranked the third in term of underlying risk factors recorded in this study, which indicated a significant effect of smoking on ischemic stroke incidence as reported in many studies ([16,26,27]). Ischemic heart diseases were reported in 15 patients (30%) of ischemic stroke sample in this study. Cardiac lesions were considered as a major potential source of emboli to the brain in 20% of ischemic stroke victims ([18]). Early detection and control of risk factors such as hypertension, diabetes mellitus and cardiac diseases are thought to be crucial in reducing the risk of stroke([9]). Oxidative stress and antioxidant activity is one of the mechanisms involved in neuronal damage induced by free radical production due to ischemia-reperfusion ([2]). In the present study, aim was directed to assess and measure the oxidative stress marker (MDA) and the antioxidants (UA, GSH and SOD) in serum and saliva of ischemic stroke and risk group patients. In an attempt to prevent or avoid the stroke attack, patients with hypertension, diabetes and ischemic heart disease were assessed since they are highly vulnerable for stroke attack. Up to our knowledge, this study is the first of its kind that evaluate the usefulness of saliva as diagnostic / monitoring tool in detection of ischemic stroke through measuring oxidative stress and antioxidant activity in patients with stroke and stroke-related diseases. Malondialdehyde (MDA) levels were assessed in serum and saliva of patients with recently diagnosed ischemic stroke (within first week of acute ictus) and in patients with stroke-related chronic illnesses like hypertension, type-2 diabetes and ischemic heart diseases. Serum MDA level was significantly higher in both groups when compared with that of healthy control. This finding means elevated oxidative stress as a result of free-radical –induced cerebral injury in ischemic stroke patients ([7, 28, 29]). This type of stress was also increased in risk group patients of the present study which showed elevated serum MDA levels. Salivary MDA levels are directly affected by systemic oxidative stress, since MDA levels were also elevated in saliva of ischemic stroke patients and patients with stroke-related diseases. These levels had no definite cut-off values to discriminate between the two groups, making MDA the least sensitive parameter in this discrimination for both serum and saliva. When risk group studied separately, salivary MDA level was significantly accurate ($p < 0.05$) in discriminating patients with ischemic heart disease and patients with hypertension

from ischemic stroke patients with optimum cut-off value (≥ 0.86μ mol/L).

Uric acid (UA) is the end product of purine metabolism, it acts as potent and significant antioxidant and free radicals scavenger ([30]).Elevated UA levels in patients with ischemic stroke and patients with stroke-related disease in the present investigation may reflect separate underlying disease process like atherosclerosis itself or increased xanthine oxidase enzymes which catalyzes the reaction of hypoxanthine to xanthine during the formation of uric acid. Uric acid in the early stages of the atherosclerotic process when its levels are known to be elevated this antioxidant paradoxically becomes prooxidant([31]). Elevated serum uric acid independently predicts stroke and mortality in patients with non-insulin dependent diabetes ([32]). Substantial evidence supports that serum uric acid is an important, independent risk factor for cardiovascular diseases, especially in patients with hypertension or heart failure. In this study, the mean serum UA levels in patients with ischemic stroke were not statistically different from that of risk group patients. For this reason, serum uric acid is not considered as reliable parameter in prediction of ischemic stroke from stroke-related diseases. This finding is not in agreement with other previous studies ([32,33]). However, serum uric acid levels were significantly accurate in differentiating healthy individuals from ischemic stroke patients with optimum cut-off value (≥ 375.5μmol/L). Salivary uric acid, on the other hand, revealed a significant positive correlation with salivary MDA (r =0.33) and with salivary SOD (r =0.21), this indicates that salivary UA is likely to be directly affected by systemic oxidative stress. Uric acid is the most important non-enzymatic antioxidant present in human saliva which correlate with plasma UA suggesting that the former is imported from plasma ([34]). Salivary UA level was significantly accurate in predicting ischemic stroke from hypertensive and diabetic patients for the optimum cut-off value (≥ 238.5μmol/L). This means that salivary UA values between (238.5-260.5 μmol/L) are critical for ischemic stroke attack.

Glutathione (GSH) plays a central role in antioxidant defense, its serum levels for patients with ischemic stroke were dramatically decreased when compared with that of healthy control. This finding is in accordance with Haruki et al ([35]) study, they suggested that the reduced plasma GSH levels are a risk factor for cerebrovascular diseases, especially for cerebral small vessel disease. GSH levels were significantly reduced in risk group patients as well, suggesting that GSH has consumed to counteract the oxidative damages associated with these diseases, mainly the detoxification of lipid hydroperoxides. This fact was supported by the significant negative correlation between serum GSH from one hand and serum MDA and UA from the other hand. The low values of serum GSH in patients with diabetes, hypertension and ischemic stroke could represent an adaptive response to increased oxidative stress and free radicals generation. On contrary, salivary GSH levels showed no significant differences among the three studied groups of the present study. This means that salivary GSH levels might not reflect the serum levels as suggested by Taro et al ([36]), who found that human parotid saliva possesses fatty acid hydroperoxide-reducing ability rendering its level in saliva not accurate in prediction of ischemic stroke in stroke- prone individuals. SOD is a metalloenzyme, its function is to dismutate superoxide to H_2O_2 ([37]). The generation of superoxide anion usually occurs at the time of reperfusion in patients with stroke resulting in a marked elevation of serum SOD, this make SOD a good indicator for high degree of oxidative stress in such patients. This fact is supported by a significant direct relationship between serum SOD and UA. Moreover, the levels of serum SOD in hypertensive patients and diabetic patients were also significantly elevated, since both hypertension and diabetes are considered as known risk factors for ischemic stroke and are associated with increased oxidative stress ([38,39,40]). ROC test results exhibited the diagnostic value of serum SOD in predicting ischemic stroke in diabetics and patients with ischemic heart diseases which is (≥ 2.09U/ml). Salivary total antioxidant activity and SOD activity were detected in saliva ([41]). In the present study, salivary SOD levels usually followed serum levels. Salivary SOD with values (1.54 -1.8 U/ml) are critical for ischemic stroke attack in hypertensive patients and patients with ischemic heart disease like angina and myocardial infarction. This finding made the measurement of SOD in human saliva is crucial for estimation of oxidative stress in those patients as part of routine biochemical investigation.

CONCLUSION

From the results of this study one can conclude the following:

1. Serum and salivary MDA, SOD, UA and GSH can be used as potential marker for monitoring patients with hypertension, diabetes mellitus and patients

with angina or myocardial infarction to give us an idea about the disease progression to ischemic stroke.

2. Serum GSH is the most powerful predictor for ischemic stroke with critical value (< 1.52µmol/L)

3. Serum SOD is the second most powerful parameter with critical value (≥ 2.09 U/ml). Moreover, salivary SOD with critical range (1.54-1.80 U/ml) could be an alarming sign for ischemic stroke attack in patients with ischemic heart diseases and hypertensive patients.

4. Salivary UA with critical range 238.5-260.5µmol/L could be alarming sign for stroke attack in patients with diabetes and hypertension.

5. Salivary MDA can be used with limited ability to alarm patients with hypertension and patients with ischemic heart diseases for stroke attack with value ≥0.86µmol/l.

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