

# INFLUENCE OF OBESITY ON ISCHEMIA-MODIFIED ALBUMIN (IMA) AND FRUCTOSAMINE LEVELS

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**ABSTRACT:** Obesity is excessive body fat accumulation that presents a potent risk factor, leading to reduced life expectancy. We evaluated the levels of Fructosamine and ischemia-modified albumin (IMA) and its association with body mass index (BMI) in obese patients. We found that obese subjects had significantly higher levels of IMA and lower levels of Fructosamine as compared with normal-weight persons. The linear regression analysis revealed that BMI and glucose level are partially determinants of Fructosamine concentration. We conclude that the effect of obesity on IMA is in opposite of its effect on Fructosamine.

**Keywords:** Obesity, body mass index, Ischemia-modified albumin, Fructosamine.

## I. INTRODUCTION

Obesity is a chronic metabolic disorder considered as an important risk factor leading to the development of health problems, such as diabetes, hypertension, stroke, some kinds of cancers, and arthritis [1]. The excess of adipose tissue, determined by the body mass index (BMI), releases several products such as free fatty acids (FFA), cytokines, and plasminogen activator inhibitor-1, which probably exacerbate some associated conditions such as insulin resistance, endothelial dysfunction, dyslipidemia, and cardiovascular disease [2]. Such conditions are possible mechanisms that generate oxidative stress in obesity [3]. Bad eating habits, stressful life, and sedentary lifestyle exacerbate this state of imbalance between the free radicals and the antioxidant defenses contributing to the structural function changes of some proteins, such as the serum albumin, which plays a vital role in the efficient antioxidant defense of the organism [4]. Overproduction of free radicals may modify the N-terminal region of albumin generating ischemia-modified albumin (IMA), a sensitive marker of ischemia that is also increased in diseases associated with obesity, such as hypercholesterolemia [5], type 2 diabetes [6], and metabolic syndrome [7].

Fructosamine is a glycated protein formed via a non-enzymatic mechanism that involves the binding of plasma glucose to serum proteins to form ketoamines. Fructosamine has a short half-life and reflects the physiology of glucose metabolism in the extracellular space; therefore, Fructosamine provides information on blood glucose over the previous 2-4 weeks. In Addition to the prevailing glucose concentration, Fructosamine concentration may be affected by the concentration and turnover of serum proteins [8].

We recently demonstrated that IMA level, but not Fructosamine level, might predict cardiovascular disorders (CVD) in type 2 diabetic patients [9]. Because obesity is one of the most important risk factors for the development of diabetes type 2 and CVD, we therefore investigated the effect of obesity on IMA and Fructosamine levels.

## II. MATERIALS AND METHODS

### A. Reagents

Cobalt chloride was purchased from Sigma-Aldrich (France). DTT was purchased from Vivantis (Malaysia). All diagnostic reagents were purchased from Roche (France).

### B. Patients

This study was performed at Albasel governmental Hospital, Aleppo, Syria. Peripheral blood was obtained from 95 participants. The subjects were divided into two groups: Normal group (included 49 subjects with normal BMI values ranged between 18.5 and 24.9 kg/ m<sup>2</sup>) and Obese group (included 46 obese subjects with BMI values  $\geq 30$  kg/m<sup>2</sup>). All participants provided written informed consent. All selected patients were without liver or kidney dysfunction, infection and corticosteroid or statin therapy. Each blood sample was placed in two separate tubes, tube without anticoagulant and a tube with heparin. The serum or plasma was separated and kept at -80°C until the biochemical evaluations

### C. IMA Measurements

The IMA levels was measured by albumin cobalt binding test (ACB test) [10,11]. Briefly, 50  $\mu$ l water solution of 0.1% cobalt chloride (CoCl<sub>2</sub>6H<sub>2</sub>O) was added to 200  $\mu$ l of serum, gently mixed and after 10 minutes the 50  $\mu$ l of Dithiothreitol (DTT) solution (1.5 mg/ml H<sub>2</sub>O) was added as a colorizing agent and the reaction was quenched two minutes later by adding 1.0 ml of 0.9 % NaCl. Color development with DTT was measured spectrophotometrically at 470 nm in comparison with a serum cobalt blank without DTT and reported in absorbance units (ABSU).

#### D. Fructosamine determination

Plasma Fructosamine was determined by SPOTCHEM II reagents strips using a SPOTCHEM Analyzer (Medical Group Company, distributor of Arkray, Syria) according to manufacturer's instructions.

#### E. Glucose, cholesterol, and triglycerides measurement

Glucose, cholesterol and triglycerides were analyzed using routine kits.

#### F. Statistical Analysis

Each sample was measured in duplicate and the mean value was reported. Statistical analyses were done with SPSS software. T test and Chi square were used to evaluate the significance of differences between test groups. Pearson's correlation was used to evaluate the association between IMA, Fructosamine and BMI. Linear regression analysis was used to examine the independent influence of other variables on plasma Fructosamine. A  $p < 0.05$  was considered statistically significant.

### III. RESULTS

We first investigated the basic characteristics of the total study population (Table 1).

**Table 1:** basic characteristic of the total study population

Parameters	Normal Group (n=49)	Obese Group (n=46)	P Value
Gender (M/F)	27/22	24/22	0.775
Age, Years	29.240±4.465	38.070±9.091	0.000
BMI (Kg/m <sup>2</sup> )	23.126±3.977	34.041±4.566	0.000
TGs (mg/dl)	68.660±25.018	96.913±44.149	0.000
Cholesterol (mg/dl)	123.500±30.266	140.804±38.862	0.016
Glucose (mg/dl)	77.660±10.709	89.391±17.803	0.000
IMA (ABSU)	0.755±0.115	0.895±0.191	0.000
Fructosamine	189.800±16.311	172.826±18.394	0.000

( $\mu$ mol/L)

Despite the difference in age between the groups, there was no influence of age on the other clinical parameters ( $p > 0.05$ ). The mean values of BMI, Fasting blood glucose, total cholesterol, triglycerides and IMA were distinctly higher in the obese population than among those in the Normal group. In contrast, Fructosamine levels were significantly lower in the obese population (Table 1).

We then examined the correlation between the IMA or Fructosamine levels and the BMI in the two groups. As shown in Table 2, There was a positive correlation between IMA and BMI ( $r = 0.223$ ,  $p = 0.029$ ), whereas the Fructosamine level was inversely correlated with BMI ( $r = -0.485$ ,  $p = 0.000$ ) (Table 2).

**Table 2:** The correlation between IMA or Fructosamine levels and BMI

	R	P value
Fructosamine ( $\mu$ mol/L)	-0.485	0.000
IMA (ABSU)	0.223	0.029

We finally analyzed the factors that influenced the Fructosamine concentration. Using linear regression analysis, we found that Fructosamine level was only affected by glucose concentration ( $p = 0.019$ ) and BMI ( $p < 0.001$ ).

### IV. DISCUSSION

Obesity is a chronic state that is related with the free radical production through diverse pathways. These free radicals may promote an increase of IMA levels [6]. It is known that serum albumin is the primary binder of FFA, and that plasma concentrations of such acids are increased in obesity. Bhagavan et al. [12] described that changes in IMA values during acute muscular heart tissue necrosis are likely to be caused by reversible conformational changes in serum albumin associated with FFA fluxes. Therefore, IMA levels were elevated in obesity associated with oxidative stress and FFA fluxes. In agreement with previous studies, our results showed that IMA levels of obese subjects were significantly higher than those of normal-weight controls [13,14]. This result is confirmed by positive correlations between IMA and BMI. Thus, obese subjects are under a high risk of ischemia, and IMA may be used as a prognostic marker of ischemia in these subjects.

Fructosamine concentrations are considered to reflect mean blood glucose changes, which have occurred the past 2-3 weeks [8]. We found that Plasma Fructosamine concentration was lower in obese subjects; perhaps because of decreased incorporation of

glucose in serum proteins of obese subjects, this means that caution must be taken in interpreting glycemic control from serum Fructosamine concentrations in obese subjects. It may not provide a reliable overview of glycemic status, and it may underestimate the degree of blood glucose elevation in this group of patients. This inverse association of BMI with Fructosamine has been observed in other studies [15-17]. In addition, multivariate analysis showed that the following factors: total cholesterol, triglycerides, IMA and age did not contribute to Fructosamine variation, whereas, both BMI and glucose mildly influenced Fructosamine concentration.

## V. CONCLUSION

Our study demonstrated that ischemia-modified albumin (IMA) is elevated in obese individuals that makes of these persons at high risk of CVD development. Therefore, it should integrate the IMA measurement routinely to supervise the obese persons. On the other hand, Fructosamine was decreased in obese people indicating that this parameter have a small value in prognosis of prediabetic status in the obese individuals.

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