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Association between Blood Sugar, Methyl-paraben, and Albumin Concentrations in Women with Hyperglycemic

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Abstract. Background: Type 2 diabetes is a type of metabolic disorder, and the role of parabens as endocrine-disrupting chemicals in the physiological process of diabetes and their effects on the function of serum albumin has always been a scientific paradox. Until now, there is little information about the correlation between parabens and sugar level of diabetic people as well as their effect on albumin concentration in Iranian society, which has been investigated as the most important objective of this research. Aim of Study: The study aimed to investigation the relationship between blood sugar, methyl-paraben, and albumin diabetic Women. Material and Method: 200 diabetic patients and 75 control were subjected to laboratory tests. Demographic data were prepared and analyzed. The concentration of methyl paraben and albumin were statistically analyzed. The results: The demographic data showed that there is a significant relationship between the diabetic group and the control in the age factor and body mass index (P=0.012). The analysis of laboratory data showed that there was no significant relationship between blood sugar concentration and albumin (P=0.577) and between blood sugar concentration and methyl paraben concentration (P=0.532). Furthermore, the statistical test showed that there was no significant relationship between the concentration of albumin and the concentration of methyl paraben (P=0.374). Conclusion: The results of this research show that there is no statistical relationship between the concentrations of FBS, methyl paraben and albumin, which can be the result of genetic diversity in the Iranian diabetic community with other populations in different parts of the world.

Highlights:

1. No significant correlation was found between blood sugar, methyl paraben, and albumin levels in Iranian diabetic women.
2. Demographic factors such as age and body mass index showed a significant association with diabetes risk.
3. Statistical tests confirmed non-normal data distribution and absence of meaningful correlations among the three studied biomarkers.

Keywords: Type 2 Diabetes, Methyl Paraben, Albumin, Iranian Women, Blood Sugar

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Introduction

Type 2 diabetes or non-insulin dependent diabetes refers to a group of metabolic disorders characterized by high blood sugar levels over a long period of time. Symptoms often include frequent urination, increased thirst, and increased appetite [1]. The prevalence of the disease is different in different countries, and according to the World Health Organization, people between the ages of 45 and 65 are more affected by the disease. The prevalence of the disease is increasing in developing countries [2]. Genetic and environmental factors are the etiological causes of the disease [3]. Parabens as endocrine-disrupting chemicals, include methyl, ethyl, propyl, butyl and benzyl, which are widely used in daily products (personal care products), among which methyl paraben is known as the most widely used food preservative or antifungal preservative in cosmetic products [4-7]. Several studies have reported the presence of parabens in human biological samples such as maternal urine, breast milk, amniotic fluid and placenta, and some sources have considered them as non-toxic compounds for humans [8-10]. Despite the widespread use of these chemicals, many issues related to their impact on human health have not yet been explained and remain in the dark. Another important factor closely related to diabetes is albumin [11,12]. Human serum albumin (HSA) is a highly abundant protein in plasma, which is mainly responsible for the binding and transport of various substances such as fatty acids, cholesterol and many drugs, therefore, it has a profound effect on the pharmacokinetic properties and efficacy of many drugs [13]. In diabetic patients, sugar units are added to albumin, which changes the structure and function of albumin, which causes severe pathological damage in different biological pathways in different organs of the body [14]. On Iranian women with diabetes, the role of parabens as well as the interaction of albumin and sugar in this category of patients have not been well investigated, therefore, the relationship between the amount of paraben (methyl paraben), the amount of increase in sugar and serum albumin in women as objective are the basis of this research.

Materials and Method

A. Sample Selection

This descriptive-analytical research was performed (based on ethics number IR.TUMS.REC.1400.041) in a comprehensive group of 275 people including 200

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diabetes patients with an average age of 44.44±6.553 years, and 75 people with an average age of 34/23± 7.610 years old as a normal, referred to the Endocrine and Metabolism Center of Tehran University. All clinical and demographic data of patients and normal people, including age, body mass index, smoking and alcohol consumption, as well as pregnancy and abortion status before and after diabetes, were prepared and collected, and then to ensure If the patients are diabetic, the blood sugar test was done again and after the final confirmation and review of the medical records by the endocrinologist, all the patients were included in the plan and subjected to laboratory analysis to check the amount of serum albumin and methyl paraben.

B. Laboratory Tests Analysis

Whole blood was prepared from patients and controls individuals. Separation of serum from blood was performed using 2500 rpm centrifuging for 15 min in laboratory temperature. The amount of albumin in serum was measured by Bromcresol Green (BCG) method (albumin pars azmoon kit-Iran, in this method, albumin creates a blue-green colored complex in an acidic environment (PH<7) in the presence of citrate buffer. After ten minutes, they were incubated at 37°C and read with a spectrophotometer at a wavelength of 546 nm.). The concentration of methyl paraben in the samples was evaluated by solid phase extraction (SPE) method and then completed by reverse phase HPLC method. Then Carbowax (Polyethylene Glycols) 20M FPSE sol-gel membrane was used to separate methyl paraben from the samples.

C. Statistical Analysis

The analysis of laboratory findings obtained from the quantitative measurements of blood sugar; serum albumin and methyl paraben concentration were carried out using statistical tests and based on the data distribution test based on the normality or non-normality of the data distribution. In order to reach this goal, the Kolmogorov-Smirnov test was used to check the normality of the data. A QQ Plot was prepared for each variable and P-Value was measured for each test (p-value ,0.05 considered as significant). Furthermore, the Mann-Whitney statistical test was used to compare the mean between two non-paired groups with non-normal distribution, and the ROC diagram was drawn for each variable. The Spearman two-tailed test was used to check the correlation between data with non-normal distribution of quantitative data [15].

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Results and Discussion

A. Results

1. Clinical and Demographical Data Analysis

Based on the demographic analysis of the data, the average age of diabetic patients was estimated to be 44.44±6.553 years and normal volunteers were 33.23±7.610 years, which statistical analysis shows a significant difference between the two age groups (p=0.012, Figure 1A.) According to table 1, the body mass index is shown as a percentage in two groups. Since, according to authoritative articles, the increase in body mass percentage has a direct linear relationship with the risk of diabetes, the demographic results show the highest body mass percentage equal to 60% and 64% in patients and normal group respectively with index of 18.5-24.5 kg/m2. There was no statistically significant difference in the consumption of alcoholic beverages and cigarettes before and after diagnosis of diabetes (P>0.05). Furthermore, a statistically differences was observed in FBS and HBA1c value in two groups of study (P<0.05). the results of this analysis have been presented in Table 1.

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Table1. Demographic and laboratory information of individuals (control and patients) in the current research

	Individuals n=275	Youngest Age	Oldest Age	Median Age	Standard Deviation	Standard Error	*p*-Value
Age (Year)	Patients(n=200)	28	48	44.44± 6.533	6.533	1.466	0.012
	Control(n=75)	23	46	34.23± 7.61	7.61	1.646	

	Individuals n=275	Slim (<18.5)	Normal (18.5-24.9)	Additional Weight (25-30)	Fat (30>)	*p*-Value
Body Mass Index BMI (Kg/m2)	Patients(n=200)	20(10%)	120(60%)	29(14.5%)	31(15.5%)	<0.001
	Control(n=75)	10(13.3%)	48(64%)	10(13.3%)	7(9.3%)	

	Individuals n=275	Statues	Before the Diagnosis of Diabetes	After the Diagnosis of Diabetes	*p*-Value
Alcohol Consumption	Patients(n=200)	Yes	5(2.5%)	3(1.5%)	>0.05
		No	195(97.5%)	197(98.5%)	
	Control(n=75)	Yes	1(1.33%)	0(0%)	
		No	74(98.6%)	75(100%)	

	Individuals n=275	Statues	Before the Diagnosis of Diabetes	After the Diagnosis of Diabetes	*p*-Value
Smoking	Patients(n=200)	Yes	5(2.5%)	3(1.5%)	>0.05
		No	195(97.5%)	197(98.5%)	
	Control(n=75)	Yes	2(2.66%)	0(0%)	
		No	73(97.33%)	75(100%)	

	Individuals n=275	Statues	Value (70-110 normal range)	*p*-Value
FBS (Mean)	Patients(n=200)	Diabetes	199.3±2.1	<0.05
	Control(n=75)	Non Diabetes	87.76±1.34	

	Individuals n=275	Statues	Value/ <42mmol normal, >48mmol diabetes	*p*-Value
HBA1c(Mean)	Patients(n=200)	Diabetes	50±1.02	<0.05
	Control(n=75)	Non Diabetes	39±0.06	

2. Data Distribution Test Results

Based on the data distribution of Kolmogorov-Smirnov test, the data distribution for fasting blood sugar concentration (Figure 1B), methyl paraben

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(Figure 1C) and serum albumin (Figure 1D) concentrations are in the range of P-Value <0.05, which confirms non-normal distribution for each data.

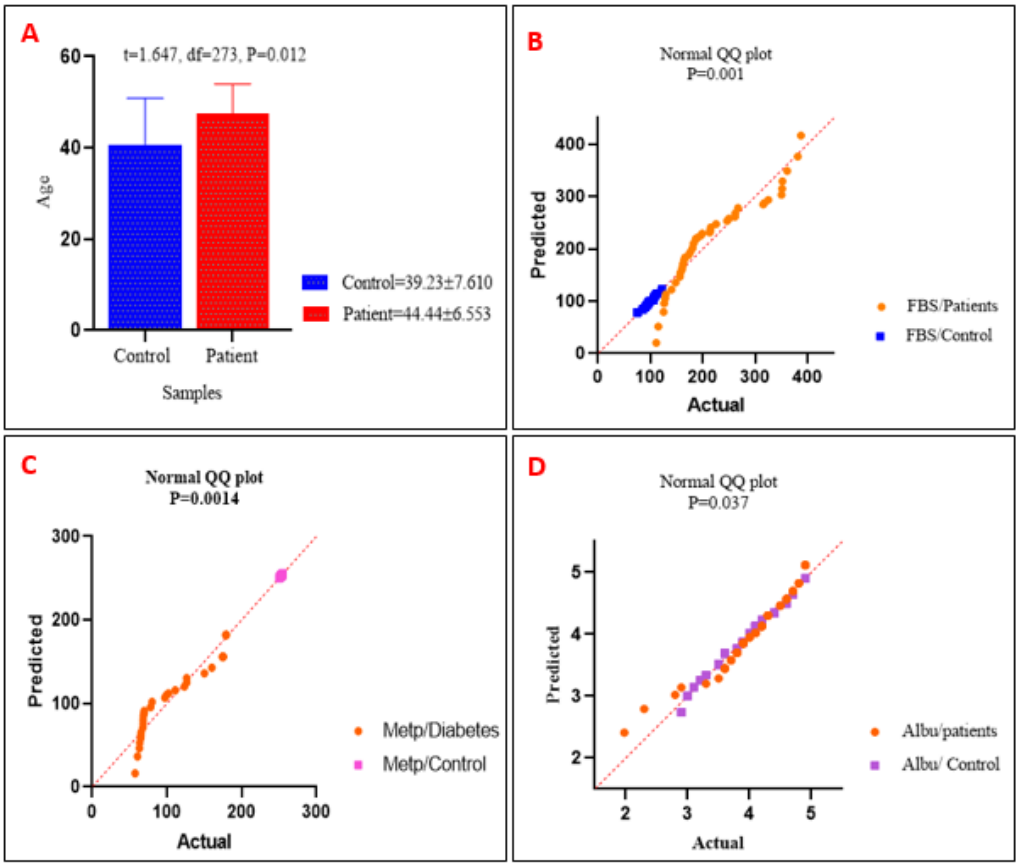

Figure 1. Data distribution of age, FBS, methyl Paraben, and Albumin. The P<0.05 considered as non-parametric distribution

3. A Rock Plot of the Mean between the Data

The non-parametric statistical analysis between the data shows (Figure 2) that there is a significant relationship between the control group and diabetic patients in the level of blood sugar concentration, so that the rock diagram with the level below the equivalent diagram is AUC=0±1 and P- Value=0.0001 confirms it (Figure 2A). Also, this analysis has proven that although there are statistically significant changes in the albumin concentration, the rock diagram resulting from this analysis does not show a significant level (Figure 2B) (AUC=0.7035±0.04541, P=0.157)) There is no statistical significance in the amount of methyl paraben in patients and control group (Figure 2C, AUC=0.6760±0.043 and P=Value=0.0860). All the analyzes are shown in the figures with the calculation of the standard deviation.

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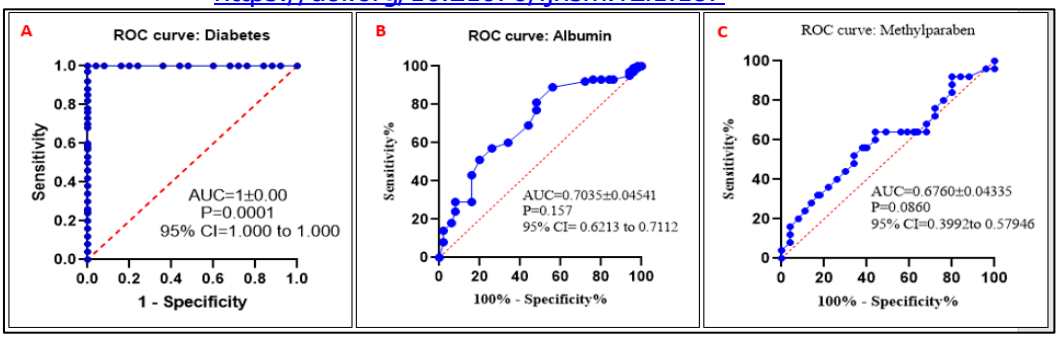

Figure 2. A rock plot of the mean between the data. Based on the ROC analysis curve, the only AUC of diabetes data was significant. P=0.001

4. The Correlation between Paraben, Sugar and Albumin of Patients

The correlation between methyl paraben and albumin (Y = -0.003613*X + 4.392, P=0.3741 (Figure 3A) and also the correlation between the concentration of methyl paraben and sugar of patients (Y = -0.0004218*X + 3.168, P=0.5328 (Figure 3B) shows statistically insignificant (P>0.05). This analysis also shows that there is no significant relationship between the blood sugar concentration of the patients and their serum albumin (Y = - 0.05344 X + 2.446, P = 0.5776) (Figure 3C). Correlation analysis between three factors of blood sugar, albumin concentration and methyl paraben concentration shown in Figure D confirms the lack of correlation between them (P>0.05).

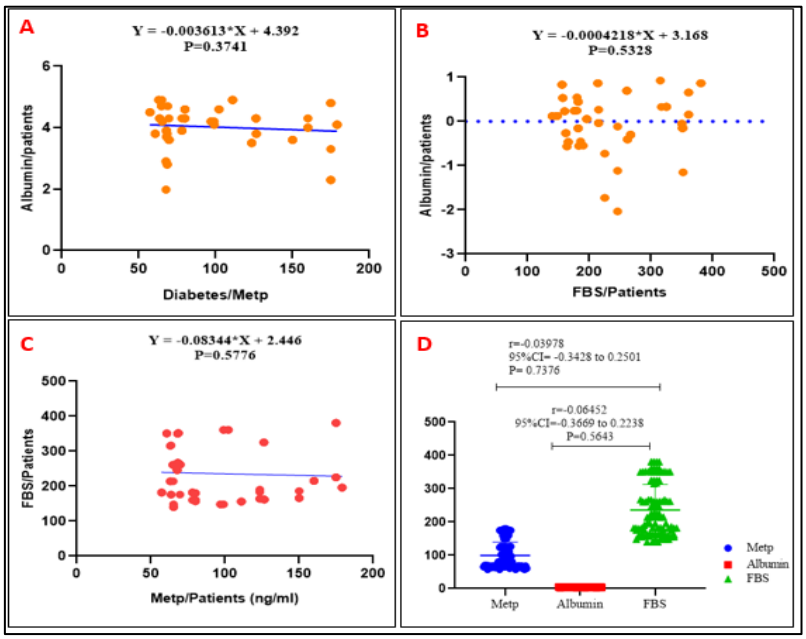

Figure 3. Correlation analysis between sugar concentration, serum albumin concentration and methyl paraben concentration in diabetic patients. There was not observed any statistically correlation among blood sugar, albumin and methyl paraben concentrations (p>0.05).

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B. Discussion

Type 2 diabetes (T2DM) is one of the most common chronic metabolic disorders in which various factors can play a role in the etiology and pathogenesis of the disease [16]. Among the risk factors that have been reported in the pathophysiology of the disease is the existence of different types of parabens, which with their different effects on the insulin secretion system can cause metabolic imbalance in the neck [17-21].Different types of parabens are capable of binding to serum albumin and disrupting the function of albumin [22,23].In the present research, the relationship and possible correlation between blood sugar concentration, methyl paraben concentration and serum albumin concentration in the population of Iranian women with type 2 diabetes have been investigated. There is limited information about the effects of sugar on albumin and paraben in Iranian society. In this study, 275 female subjects including, 200 diabetics and 75 normal subjects were selected as the control group. The analysis of demographic information shows that age is an effective factor in the occurrence of type 2 diabetes, and our data shows that the average age of 47 years can increase the risk of the disease. (P Value=0.012). Furthermore, the increase in body mass index is directly related to the occurrence of the disease (P=0.0001).This finding is in agreement with the results of the research of other researchers who considered increasing age and body mass index to be related to the risk of diabetes [24].In the present study, there was no significant relationship between blood sugar concentration, methyl paraben and albumin concentration in Iranian diabetic women (P>0.05).Albumin has always been known as a biomarker for the pathophysiological monitoring of diabetes. This molecule causes structural changes in diabetic patients, which in turn will have an adverse effect on the function of this protein [25]. In a test conducted in 2013 by Adele Bahar and her colleagues on disorders in glucose tolerance and fasting sugar as pre-diabetic diagnosis factors, it was shown that the albumin concentration value decreases strongly [26].

Findings in diabetic patients of the Chinese population show that the decrease in albumin has an inverse relationship with the level of hemoglobin A1c (HbA1c), so that the decrease in serum albumin causes an increase in this type of hemoglobin in patients [27]. The studies and results of Douglas C. Chang et al [28] have shown that the reduction of serum albumin can increase the risk of type 2 diabetes and also cause the activation of adipose tissue macrophages. In various reports that Ji Eun Jun et al

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presented, the increase in serum albumin can be effective in diagnosing prediabetes, which shows the different behavior of albumin in the occurrence of the disease. As mentioned, this increase can prevent the development of type 2 diabetes [29].

There have been reports of the amount and relationship of albumin with diabetes in Iranian society. The results of tests on the statistical population of Iranian diabetic patients have shown that the amount of albumin in the urine (more than 30 mg in 24-hour urine) of male patients has increased significantly compared to female patients [30]. The studies of Hajizadeh et al, on the Iranian community have proven the effective role of HbA1c, the amount of cholesterol and HDL in the level of albumin concentration [31]. In a study conducted on the statistical population, it was shown that the amount of methyl paraben in the urine of people who have high consumption of hygiene products (such as body wash shampoo, makeup products) has increased significantly (32).

In 2018, Huo W et al, reported a statistical association between parabens and gestational diabetes [33]. Although the results obtained from our data did not show a significant relationship between the blood sugar level of diabetic people and the level of methyl paraben concentration and albumin levels, but their pathophysiological role in the occurrence of diabetes or other diseases cannot be ignored. According to the results of our research, it seems that compared to other societies in different parts of the world, the Iranian society will have different genetic and physio pathological responses to the factors that cause diabetes. It is suggested that this project be checked on other diseases in the Iranian society.

Author Contributions

LM and FD conceived of the presented idea, carried out the experiment and wrote the manuscript with support from NH. FD is the main supervisor of the project.

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Data Availability Statement

All raw data are available under request.

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Conflicts of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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