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New Approach for Analysis the Correlation of Some Oxidative Markers in Type 2 Diabetes Mellitus by Data Wavelet Analysis

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Abstract

Diabetes mellitus is a common disease. This disease also has several complications, which is the main reason for the development of other diseases. For the study of diabetes, various markers are considered. Analysis of such markers allows us to draw conclusions about the degree of development of diabetes mellitus. We are considering expanding the analysis of various markers in diabetes. To do this, we use wavelet ideologists - the wavelet coherence method. We have identified periods of agreement between FBS and serum vitamin A, FBS and serum vitamin C, serum vitamin A and serum vitamin C, serum vitamin A and MDA for different levels of HbA1c. This allows us to evaluate the effect of various markers on the development of diabetes. To conduct this study, a group of 300 patients with type 2 diabetes was considered.

Keywords: *Diabetes mellitus, correlation, wavelet coherence, glyclated hemoglobin, fasting blood sugar, malondialdehyde.*

Introduction

Diabetes mellitus is one of the common chronic diseases. According to the World Health Organization (WHO), diabetes will be the 7th leading cause of death worldwide by 2030[1]. At the same time, 90% of all patients with diabetes are diagnosed with type 2 diabetes[2]. Type 2 diabetes is a metabolic disease. This type of diabetes occurs as a result of a violation of the interaction of insulin with tissue cells. Diabetes mellitus is a risk factor for other diseases and complications. In particular, this is a violation of vascular permeability and, as a consequence, the development of vascular atherosclerosis. Violation of vascular permeability can also be the basis of various heart diseases [3]. Diabetes is also the basis for the early development of cataracts, retinopathy, kidney damage, changes in the psyche and mood [4]. As a result of diabetes, oxidative stress often occurs, which in turn leads to various diseases, including the further development of diabetes. Therefore, an important task is the process of controlling the development of diabetes. This can be done by analyzing various markers that identify and show the development of diabetes. It is important to analyze such markers correctly. Therefore, the main objective of this study is to consider a new approach for the analysis of such markers in their relationship with each other.

Materials and Method

Brief overview of the research topic: The work[5] addresses several issues that are devoted to various markers of type 2 diabetes. Moreover, such markers allow you to control changes in renal decline. The authors consider plasma and urinary markers. Among these markers are considered: the level of antioxidant vitamins in plasma, the level of triglycerides in the blood and cholesterol, the level of malondialdhehyde and much more. To analyze such markers, the authors use method of descriptive statistics, factor and variance analysis. A similar study can be found in [6], where the authors also use classical method of statistical analysis to study the corresponding markers. In[7], markers are considered that allow one to consider the relationship between type 2 diabetes and cardiovascular diseases. The authors, first of all, study the effect of various vitamins on the development of diabetes mellitus, the possibility of slowing down the rate of development of cardiovascular disease. For their conclusions, the authors of the study use the method of correlation and regression analysis.

DNA methylation markers, level glucose and HbA_{1c} are discussed in [8]. For this analysis, the authors used multidimensional linear models. Markers of oxidative stress are the basis of the study in S. Seyyedebrahimi, H. Khodabandehloo, E. N. Esfahani and R. Meshkani [9]. For such an analysis, descriptive and comparative statistics method were used. A comprehensive review of various markers for studying the development of type 2 diabetes mellitus was considered in [4, 10]. Here, the authors also use classical statistical method to carry out the corresponding analysis: descriptive statistics, linear regression analysis, factor analysis, correlation analysis. Thus, based on the foregoing, we can say that there are various markers for the analysis of the development of diabetes and the manifestation of its influence in the form of complications of certain diseases. This allows you to conduct multifaceted research and draw various conclusions. However, the analysis apparatus used for such studies is standard. This limits the possibility of carrying out advanced analysis. Therefore, we will consider one of the tools that can be used in this study.

Wavelet ideology as a tool for analyzing data markers: Data markers for diabetes analysis can be represented as a sequence. The structure of such a sequence is a time series or a set of data for a certain period of time. Thus, for analysis we can use the ideology of wavelets. The input for wavelet ideology method is data that has the structure of a time series [11, 12]. In general, the ideology of wavelets makes it possible to identify singular points in the data structure that is being studied. Such an analysis is based on a series of different maternal wavelets [12, 13]. We can also analyze the mutual influence of two data sets. For this, the wavelet coherence methodology is used. This methodology is based on an analysis of a cross-reference for data series (z and z_1), which are analyzed[14,15]

$$R^2(z,z_1)=\frac{\left|\Psi(z_1^{-1}\Delta_{xy}(z,z_1)\right|}{\Psi(z_1^{-1}\left|\Delta_x(z,z_1)\right|^2)\Psi(z_1^{-1}\left|\Delta_y(z,z_1)\right|^2)}$$

where ψ – is a smoothing operator,

$\Delta(z, z_1)$ – cross wavelet spectra for different time series z and z_1

x – data number in the test series,

y – characterizes the depth of cross-references,

$$0 \le R^2(z,z_1) \le 1.$$

If we have several series of data for a certain date, then we can use one of these series as a ranking tool. To do this, we select one of the data series and perform ranking on this series for other data series. Thus, we determine the cross wavelet spectra by some series u $\Delta^u(z, z_1)$, which allows us to rank the data and apply the wavelet coherence methodology:

$$R^2(z,z_1)=\frac{\left|\Psi(z_1^{-1}\Delta^u_{xy}(z,z_1)\right|}{\Psi(z_1^{-1}\left|\Delta^u_x(z,z_1)\right|^2)\Psi(z_1^{-1}\left|\Delta^u_y(z,z_1)\right|^2)}$$

This approach allows you to structure the data series and carry out the corresponding analysis. Then along the axis x we have some parameter that is structured. This allows you to evaluate the reciprocity of some data series relative to another parameter. Therefore, we are expanding the possibilities of analysis.

Data: We review the data that was obtained for patients with the second type of diabetes. This group of patients consists of 300 people. This study was conducted by the Jabber Abu Ezz Center for treatment and care of diabetics in Khartoum– Sudan [4].

As individual markers are considered: Glyclated hemoglobin (HbA_{1c})% in human whole blood; fasting blood sugar (FBS), mg/dl; serum vitamin A, µg/dl; serum vitamin C, µg/ml; malondialdehyde (MDA), mol/l.

Some statistical parameters of markers are presented in Table 1.

Table 1: Statistical indicators markers

Markers	Diabetics (n=300)	P value
Vitamin A means (Max-Min)	50.3±20.0 (14.0-95.0)	0.001*
Vitamin C means (Max-Min)	3.9±1.3 (1.2-6.9)	0.0003*
MDA means (Max-Min)	6.7±6.2 (1.0-35.0)	0.001*
HbA_{1c}% means (Max-Min)	7.5±1.4 (6.0-13.3)	0.001*
FBS means (Max-Min)	160.4±65.5 (75.0-480.0)	0.0002*

*Significant differences in all blood parameters between control and test group (P value < 0.05).

These are the most commonly used markers for analyzing the development of diabetes. At the same time, our task is to show the possibility of applying the ideology of wavelet analysis to study the development of diabetes.

Results

One of the key markers in the study of the development of diabetes is the marker HbA_{1c}. HbA_{1c} shows the average blood sugar over a long period. Therefore, for further analysis, we chose the HbA_{1c} marker as the data for the ranking base. We do this ranking by increasing values of HbA_{1c}. These values are in the range: 6.0-13.3%.

Data for the remaining markers are given in accordance with the ranking of HbA_{1c}. Thus, we consider wavelet coherence for different marker groups, subject to the ranking of the HbA_{1c} marker. Then we can evaluate the change in the relationship between different markers for different levels of the HbA_{1c} marker.

In Fig. 1 shows the wavelet coherence between the values of the FBS and serum vitamin A.

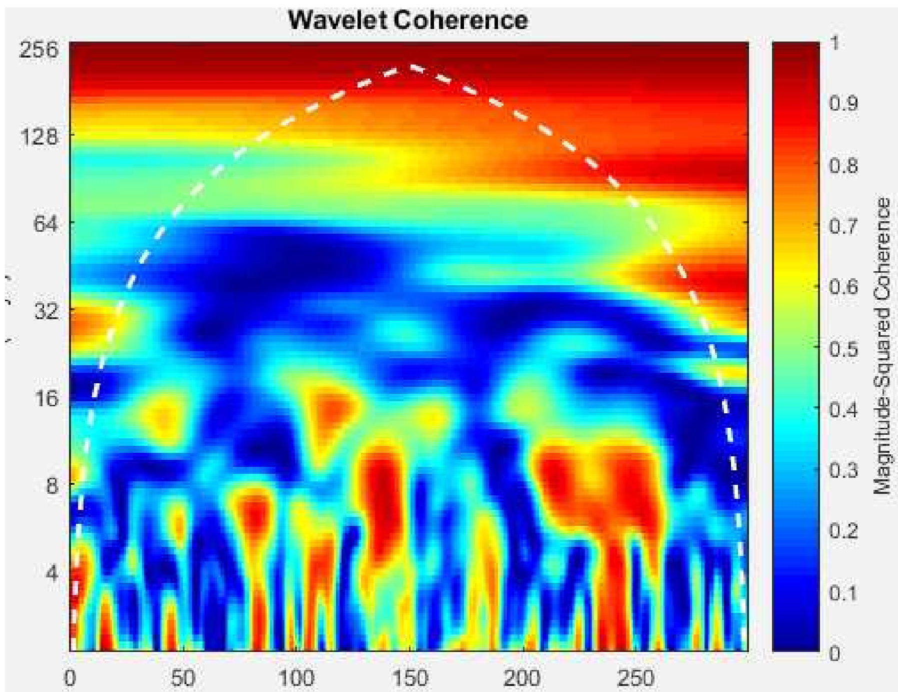

Fig. 1. Wavelet coherence between the values of the FBS and serum vitamin A markers when ranking by the HbA_{1c} marker

In Fig. 1 (and for other similar figures that are presented below) shows: along the axis *x*, the ranked values of the HbA_{1c} marker for 300 patients from the group (for Fig. 5, this is the ranking by the FBS marker); along the axis *y*, the depth of the relationship between the data values for the FBS and serum vitamin A markers (for other figures, this is the depth of the relationship between the other markers that are considered); the dashed white line limits the region of reliable values of wavelet coherence (at a confidence level of not less than 0.95). These values are inside the dashed line; the figure also shows a scale for analyzing the significance of wavelet coherence data. The significance of wavelet coherence is in the range from 0 to 1. Such data for clarity also have color values. Separate areas are the localization of the consistency (the significance of the wavelet coherence tends to 1) or the inconsistency of the data (the significance of the wavelet coherence tends to 0), which are investigated.

Fig. 1 show, that the consistency between the values of the FBS and serum vitamin A markers is different depending on the values of the HbA_{1c} marker. The greatest consistency between the values of the FBS and serum vitamin A markers is characteristic for the range of changes in the HbA_{1c} marker: 8.0-8.7%. We can also observe the alternation of such significance that is associated with certain values of the HbA_{1c} marker.

In Fig. 2 shows the wavelet coherence between the values of the FBS and serum vitamin C.

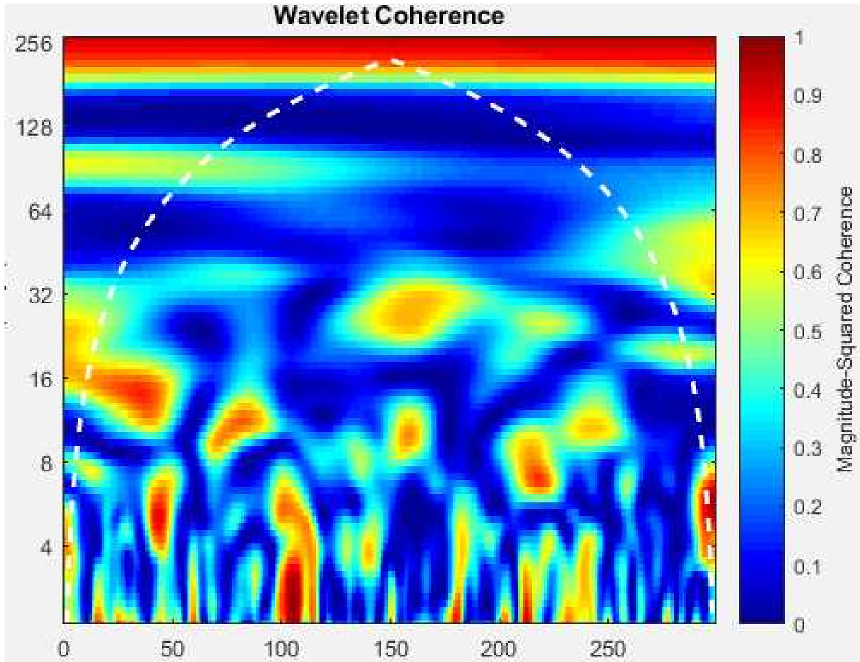

Fig. 2. Wavelet coherence between the values of the FBS and serum vitamin C markers when ranking by the HbA_{1c} marker

Comparing Fig. 1 and Fig. 2 we can see different consistency between the markers that are considered. The consistency for the data in Fig. 1 is higher than for the data in Fig. 2.

In Fig. 3 shows the wavelet coherence between the values of the serum vitamin A and serum vitamin C.

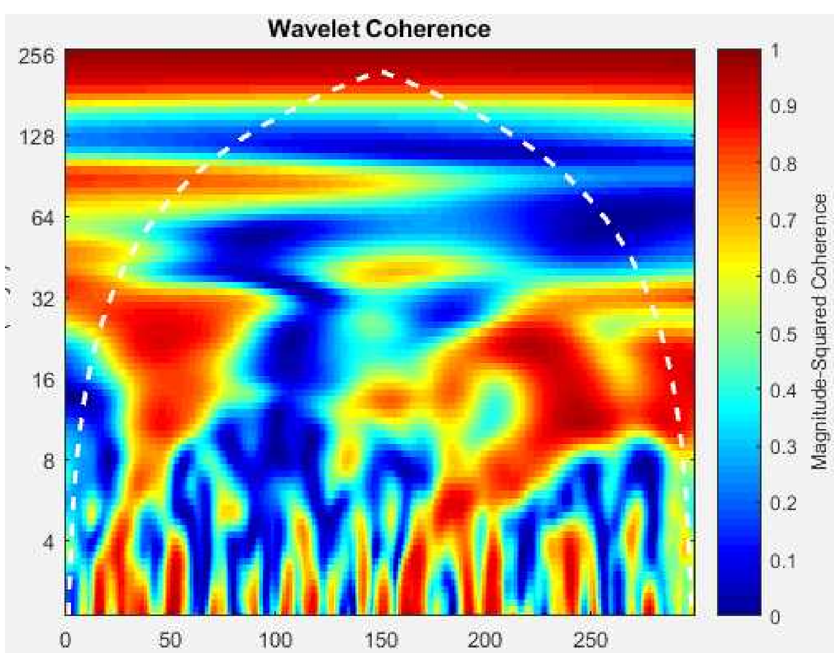

Fig. 3. Wavelet coherence between the values of the serum vitamin A and serum vitamin C markers when ranking by the HbA_{1c} marker

In Fig. 3, we see a significant agreement between the values of the serum vitamin A and serum vitamin C. Thus, serum vitamin A and serum vitamin C play an important role from the standpoint of analysis of the conditions for the development of diabetes mellitus, the effect on the change in the level of the HbA_{1c} marker.

In Fig. 4 shows the wavelet coherence values between serum vitamin A and MDA.

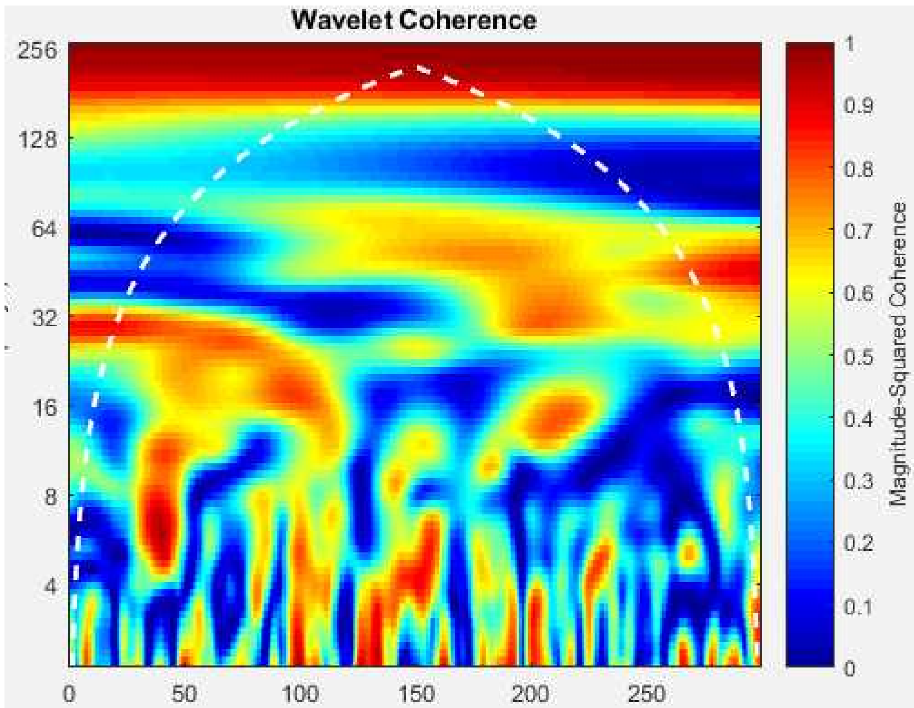

Fig. 4. Wavelet coherence between the values of the serum vitamin A and MDA markers when ranking by the HbA_{1c} marker

At the same time, in Fig. 5 shows the wavelet coherence between the values of the serum vitamin A and MDA when ranking by the FBS marker.

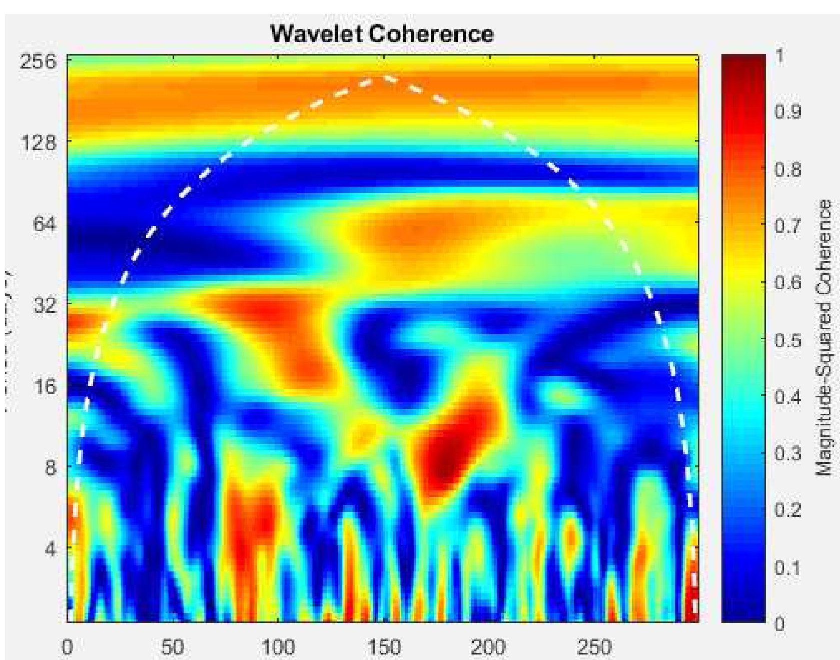

Fig. 5. Wavelet coherence between serum vitamin A and MDA values when ranking by FBS marker

Comparing the data in Fig. 4 and Fig. 5, we can see a different degree of consistency between serum vitamin A and MDA markers when ranking by HbA_{1c} or FBS. However, the greatest consistency is characteristic for lower values of HbA_{1c} or FBS.

Discussion

The high prevalence of diabetes and the possibility of its influence on the development of other diseases make it necessary to conduct various studies. Such studies involve the analysis of markers that characterize the development of diabetes. Among such studies, a special place is occupied by the analysis of correlation between individual markers. This allows us to analyze the development of diabetes and evaluate the effect of various components on such a process.

In[16], based on the analysis of correlation relationships, the relationship between neutrophil-lymphocyte ratio and insulin resistance is considered. This allows you to correctly diagnose patients with diabetes.

In the study[17], on the basis of correlation analysis between different markers, connections with complications that arise in diabetes were determined.

We can also note other studies, where the basis of the study of various markers in the study of the development of diabetes is a correlation analysis[3,5,18,19].

However, when considering correlations, we consider the pairwise influence of markers. In some cases, this can lead to mixed results [20]. For example, when we compare several markers, we can have different correlation values. As a result, it is difficult to draw general conclusions.

In this study, we are expanding the possibilities of conducting correlation analysis. This is possible through the use of wavelet ideology. For this we use wavelet coherence. As a result, we are able to estimate the correlation value between three different markers. This makes it possible to expand the conclusions based on the studies.

Conclusion

We considered the possibility of expanding the correlation analysis to study various markers in diabetes mellitus. For this, we used wavelet coherence. In particular, periods of agreement between FBS and serum vitamin A, FBS and serum vitamin C, serum vitamin A and serum vitamin C, serum vitamin A and MDA for different levels of HbA1c are shown. This allows us to evaluate the effect of various markers on the development of diabetes. Different periods between serum vitamin A and MDA were also observed, taking into account the analysis of HbA1c and FBS levels.

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