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A Study of Correlation Ratios for Low- and High-Density Lipoprotein in Comparison with Antioxidant Vitamins A, E, C at Different Levels of Glycosylated Hemoglobin among Type 2 Diabetes Patients

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ABSTRACT

Diabetes is one of the chronic diseases in which the number of patients increases every year. Moreover, diabetes mellitus is a risk factor for the risk for the development of other diseases. Therefore, the number of studies that address various aspects of the diagnosis and control of the processes of diabetes is increasing. Among such studies, an important place is taken by the analysis of the relationship between low and high density lipoprotein and antioxidant vitamins A, E, C. Such an analysis can be done using various analytical methods. This expands medical diagnostics and treatment options for diseases. The study was based on a sample of 300 patients with type 2 diabetes. For analysis, we used: correlation analysis and the wavelet coherence method. The values of wavelet coherence between low and high density lipoprotein and antioxidant vitamins A, E, C for different levels of glycosylated hemoglobin were obtained. This provides an explanation of the differences in the relationship between low and high density lipoprotein and antioxidant vitamins. Also a more consistent dynamics is observed between antioxidant vitamins A, E, C and HDL, taking into account changes in glycosylated hemoglobin levels. This is a key factor in understanding the greater correlations between antioxidant vitamins A, E, C, and HDL.

Key words: Diabetes Mellitus, Correlation, Wavelet Coherence, Low Density Lipoprotein, High Density Lipoprotein, Antioxidant Vitamins, Glycosylated Hemoglobin

1. INTRODUCTION

Disruption of the immune system, when, in particular, the interaction of insulin with tissue cells ceases, leads to the development of a disease such as diabetes. Uncontrolled development of such a disease leads to various complications and poor human health. As a result, this is a risk factor for the emergence of new diseases, among which a characteristic violation of vascular permeability [1], [2] [3].

Thus, diabetes is a complex disease of an endocrine nature, in which insulin secretion is impaired in the human body. One type of diabetes is type 2 diabetes. This type of diabetes is the prevailing disease in its group. At the same time, patients with diabetes are at risk of disease, a characteristic feature of which is death.

One of the elements of the treatment of this disease is constant monitoring. Moreover, such control applies to lifestyle, diet, and medication. The basis of this control is the analysis of various markers that identify and show the development of diabetes. Therefore, the control of various markers is the basis for the successful treatment of this disease. However, it is important not only to control the various markers, but also to analyze them correctly. For this, it is necessary to apply various analysis methods that help to present and describe the clinical picture that develops as a result of a particular disease.

As the main objective of this work is to consider individual methods of analysis for the study of various markers that characterize the development of diabetes. Moreover, such methods should expand the capabilities of the analysis necessary to understand the development of diabetes.

2. BRIEF REVIEW OF RECENT RESEARCH

Diabetes mellitus is a key subject that has been examined by many researchers. These are works where the general problems of diabetes mellitus are studied, various markers, as well as research methods for such markers.

The work [4] addresses a wide range of issues related to the diagnosis, prevention and treatment of diabetes. Particular attention is paid to primary care, the dissemination of information on the care of patients with diabetes. The issues of improving the quality of control over the course of diseases associated with diabetes mellitus were also considered.

A study by I. Romera, A. Cebrián-Cuenca, F. Álvarez-Guisasola, F. Gomez-Peralta and J. Reviriego focuses on practical issues related to the treatment of type 2 diabetes [5]. Safety issues and precautions for the use of medicines were also considered.

M. S. Aravind, T. M. Joy and P. S. Rakesh analyze the prevalence of diabetes mellitus by the level of income of the population [6]. It also provides an analysis of the behavior of people with diabetes mellitus, and examines the practice of caring for patients.

The study [7] addresses the symptoms of diabetes. It also analyzes the use of antidepressants in the prevention of diabetes. Particular attention is paid to markers that allow you to control the development of diabetes.

S. Sangeeta, J. Ambekar, T. Sudhakar and N. Dongre study markers of diabetes that are associated with kidney disease [8]. The basis of such a study is the methods of statistical analysis. The authors conclude that it is necessary to consider individual markers of diabetes in the diagnosis of kidney disease.

For the analysis of markers that characterize the development of diabetes, as a rule, use the classical methods of statistical analysis [9], [10]. At the same time, neural networks and methods of the theory of fuzzy sets are also used to derive certain relations between different markers [11].

Also, special attention is paid to the influence of various vitamins on the development of diabetes mellitus and their ratio with corresponding markers. An example of such a study is [12]–[14]. However, such an analysis is insufficient. This applies to cases where the correlation between vitamins and other markers in diabetes is not sufficiently pronounced. This served as the basis for this study with the aim of possible concretization of the relevant relationships or their refinement.

3. WAVELET IDEOLOGY AS A TOOL FOR ANALYZING MEDICAL DATA

To solve this problem, we will use the ideology of wavelets. This ideology showed itself well in the analysis of various medical data [15]– [17].

The ideology of wavelets is based on the analysis of various groups of data that can be interpreted as a time series. For this analysis, special functions are used – the mother wavelet [18], [19]. This makes it possible to reveal hidden features in the data set that is being investigated. Then we can draw extended conclusions about the phenomena under study.

Using wavelets, we can also compare different groups of data. This comparison is based on the analysis of cross-references between data groups. This allows an analysis of the mutual influence of various data groups. As a result, we can identify periods of data consistency (there is a strong mutual influence between data groups) and data inconsistency (there is no mutual influence). For such an analysis, the wavelet coherence method should be used, which allows one to determine the values of wavelet coherence [19, 20]. In doing so, we can rank data groups by a specific group. This allows the data to be presented in the form of a series that has a structure similar to a time series. For analysis, we use the formula [20], [21]:

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

where Ψ – is a smoothing operator,

z and z_1 – data groups, which are investigated;

g – data group for ranking;

$\Delta(z,z_1)$ – 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,

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

This allows you to evaluate the reciprocity of some data series relative to another parameter. Therefore, we are expanding the possibilities of analysis.

4. DATA

For analysis, we consider a group of data for 300 patients with type 2 diabetes mellitus. These data were obtained by the Jabber Abu Ezz Center for treatment and care of diabetics in Khartoum - Sudan [22], [23].

As individual data we consider: glycosylated hemoglobin (HbA_{1c})% in human whole blood; serum vitamin A, µg/dl; serum vitamin E, µg/ml; serum vitamin C, µg/ml; low density lipoprotein (LDL), mg/dl; high density lipoprotein (HDL), µg/dl .

Some statistical parameters of data are presented in Table 1.

Table 1: Some statistical parameters of data

Data	Diabetics (n=300)	P value
Vitamin A: means (Max-Min)	50.3±20.0 (14.0-95.0)	0.001*
Vitamin E: means (Max-Min)	5.2±1.8 (1.0-9.0)	0.001*
Vitamin C: means (Max-Min)	3.9±1.3 (1.2-6.9)	0.0003*
HbA_{1c}%: means (Max-Min)	7.5±1.4 (6.0-13.3)	0.001*
LDL: means (Max-Min)	41.8±11.9 (20.0-88.0)	0.0008*
HDL: 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).

The choice of HbA_{1c} is based on the fact that it is one of the key markers of the process of diabetes mellitus. The choice of LDL, HDL and antioxidant vitamins A, E, C is due to the fact that these parameters have insignificant correlation relationships. At the same time, it is also important data for the analysis of diabetes mellitus.

5. RESULTS AND DISCUSSION

First of all, consider correlation ratios for low and high density lipoprotein (LDL and HDL) in comparison with antioxidant vitamins A, E, C. In Fig. 1 – Fig. 3 shows the correlation between antioxidant vitamins A, E, C, and LDL or HDL, respectively.

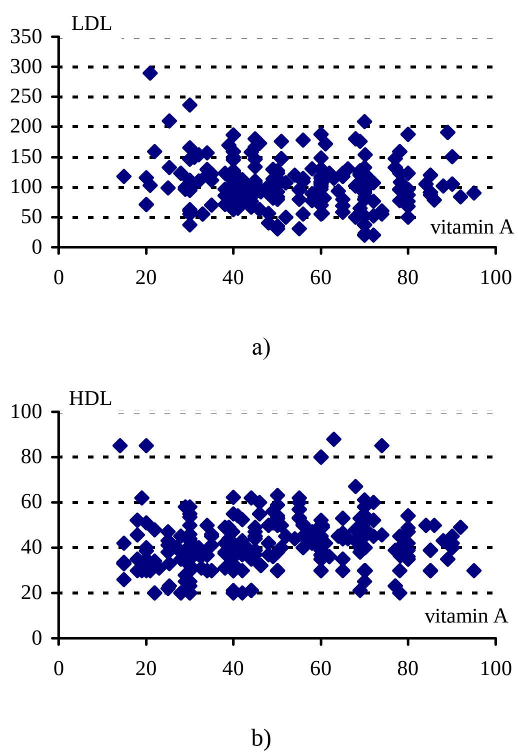


Figure 1: Scatter plot shows the relationship between serum vitamin A and LDL (r=0.04, P value = 0.548; Fig. 1a); serum vitamin A and HDL (r=0.18, P value = 0.02; Fig. 1b)

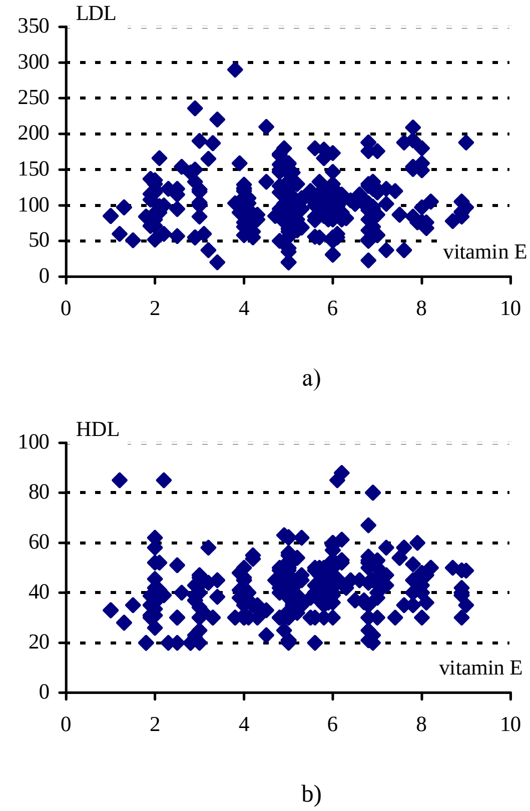


Figure 2: Scatter plot shows the relationship between serum vitamin E and LDL (r=0.03, P value = 0.663; Fig. 2a); serum vitamin E and HDL (r=0.23, P value = 0.04; Fig. 2b)

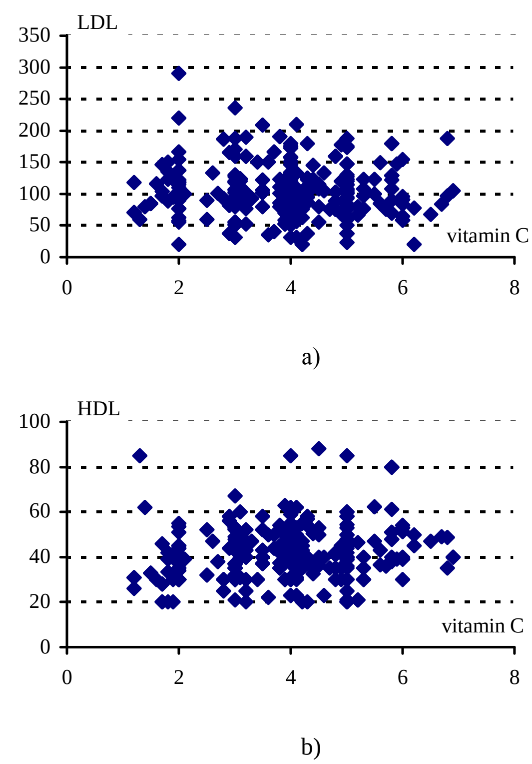


Figure 3: Scatter plot shows the relationship between serum vitamin C and LDL (r=0.09, P value = 0.134; Fig. 3a); serum vitamin C and HDL (r=0.19, P value = 0.04; Fig. 3b)

We can see that these correlations are not significant enough. Moreover, the correlation between the level of LDL and vitamins A, E, C are insignificant, and the correlation between the level of HDL and vitamins A, E, C are moderate, but quite significant. Therefore, we will consider the values of wavelet coherence for a possible understanding of such processes. We will consider such relationships with respect to HbA1c, where HbA1c is considered as a ranking element for other data groups (LDL, HDL, antioxidant vitamins A, E, C). Then we obtain the wavelet coherence values for the groups under consideration, taking into account the different values of HbA1c. This will allow us to draw conclusions about reciprocal links. Moreover, such an analysis will take into account different levels of HbA1c.

It should also be noted that the figures below show:

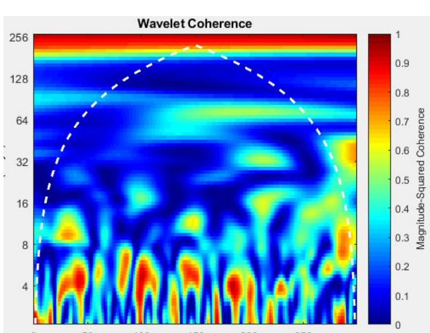
along the axis are the ranked values of HbA1c. These values are in the range: 6.0-13.3%. In the figures, these values are represented by serial numbers in accordance with the number of patients in the sample (300 patients);

along the axis is the depth of the relationship between the data values that are being investigated. This depth correlates with values for HbA1c and displays different analysis intervals for HbA1c values;

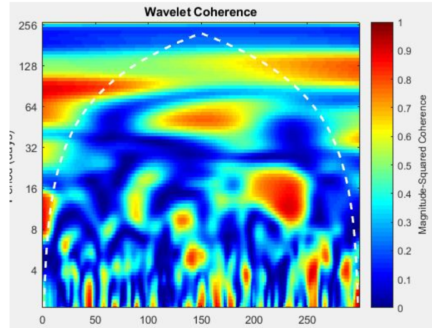
the dashed white line limits the region of reliable values of wavelet coherence (with a confidence level of at least 0.95). These values are inside the dashed line;

the figure also shows a scale for analyzing the significance of wavelet coherence data. The value 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 wavelet coherence tends to 1) or the inconsistency of the data (the significance of wavelet coherence, as a rule, 0), which are studied.

In Fig. 4 – Fig. 6 shows the wavelet coherence between antioxidant vitamins A, E, C, and LDL or HDL, respectively.

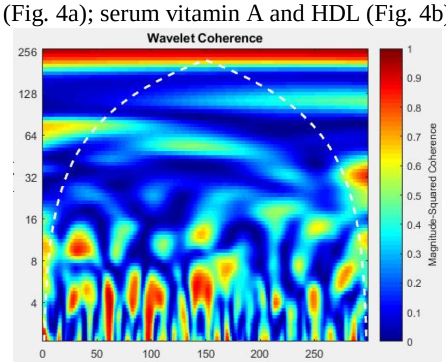


a)

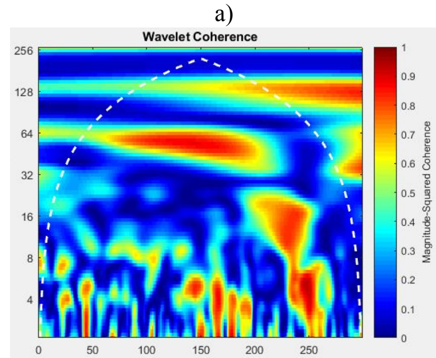


b)

Figure 4: Wavelet coherence between serum vitamin A and LDL (Fig. 4a); serum vitamin A and HDL (Fig. 4b)

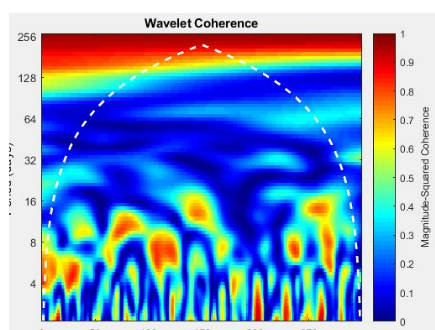


a)

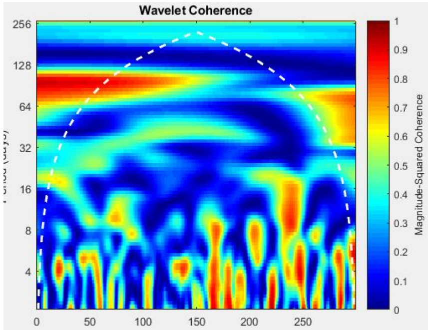


b)

Figure 5: Wavelet coherence between serum vitamin E and LDL (Fig. 5a); serum vitamin E and HDL (Fig. 5b)



a)



b)

Figure 6: Wavelet coherence between serum vitamin C and LDL (Fig. 6a); serum vitamin C and HDL (Fig. 6b)

Analyzing the data of Fig. 4 – Fig. 6 should be noted:

wavelet coherence between antioxidant vitamins A, E, C and LDL, as well as between antioxidant vitamins A, E, C and HDL, respectively, is similar. This allows us to talk about the same processes affecting the dynamics of the corresponding correlation relationships (see Fig. 1 – Fig. 3);

wavelet coherence is generally fragmented. This means that we can observe a correspondence between the data being analyzed for the same levels of HbA_{1c}. This could be a factor that affects the corresponding values of correlation estimates;

wavelet coherence between antioxidant vitamins A, E, C and LDL is more regular than between antioxidant vitamins A, E, C and HDL;

wavelet coherence between the antioxidant vitamins A, E, C and HDL has a greater depth of consistency than that between the antioxidant vitamins A, E, C and LDL. This means that we can observe more consistent dynamics between antioxidant vitamins A, E, C, and HDL, taking into account changes in HbA_{1c} levels. This is a key factor in understanding the greater correlations between antioxidant vitamins A, E, C, and HDL. Then the relationship between antioxidant vitamins A, E, C and HDL is more significant for understanding the development of diabetes.

LDL, HDL and antioxidant vitamins A, E, C play an important role in the study and understanding of the processes that occur in diabetes mellitus.

S. Singha, R. Gupta, and A Goyle conducted a detailed analysis to study the effects of antioxidant vitamins A, E, C in coronary heart disease [24]. It is emphasized that diabetes is one of the factors in the development of coronary heart disease. This study also noted a weak relationship between LDL, HDL and antioxidant vitamins A, E, C. However, a more detailed analysis between LDL, HDL and antioxidant vitamins A, E, C was not performed.

A. W. Ashor, M. Siervo, and J. C. Mathers examine the interaction of vitamin C with LDL and HDL when considering conditions for changing levels of cholesterol in the blood [25]. This is an important element in the study of diabetes. Such an analysis was carried out on the basis of clustering and linear regression methods. However, the relationship between the interaction of vitamin C with LDL and HDL at different levels of glycosylated hemoglobin has not been disclosed.

In [26], it was noted that it was not possible to establish a significant relationship between LDL, HDL and antioxidant vitamins E, C. Such a study was conducted on the basis of classical statistical methods. However, in this work, the relationship of the studied markers with the level of glycosylated hemoglobin in the blood was not evaluated.

J. Zalaket, L. H. Wakim, and J. Matta note the different effects of antioxidant vitamins on LDL and HDL [27].

Thus, it should be noted that almost all researchers pay attention to the relationship between LDL, HDL and antioxidant vitamins A, E, C. However, the mutual influence of this relationship at different levels of glycosylated hemoglobin is not considered. This is due to the fact that only pairwise comparison of markers is taken into account. We consider a group of three markers to analyze the relationship between LDL, HDL, and antioxidant vitamins. This allows you to expand the capabilities of the correlation analysis, to draw new conclusions.

6. CONCLUSION

We examined the relationship between LDL, HDL and antioxidant vitamins A, E, C for a group of patients with type 2 diabetes mellitus (300 patients). For research, we used the method of correlation analysis and the wavelet coherence method. This allowed us to consider the changes in the correlation between LDL, HDL and antioxidant vitamins A, E, C at different levels of glycosylated hemoglobin. The differences in wavelet coherence between LDL and antioxidant vitamins A, E, C, and between HDL and antioxidant vitamins A, E, C are shown. It is noted that the relationship between antioxidant vitamins A, E, C and HDL is more significant for understanding the development of sugar diabetes.

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CONFLICTS OF INTEREST

There are no conflicts of interests between authors.

REFERENCES

1. N. M. Kady, and et al.. **ELOVL4-mediated production of very long-chain ceramides stabilizes tight junctions and prevents diabetes-induced retinal vascular permeability**, *Diabetes*, Vol. 67, no. 4, pp. 769-781, 2018.
https://doi.org/10.2337/db17-1034
2. F. Mo, G. Hu, W. Liu, L. He, and H. Wang. **Prostaglandin E1 protects the peripheral nerve in diabetics through preventing vascular permeability changes**, *Exp Clin Endocrinol Diabetes*, Vol. 126, no. 02, pp. 113-122, 2018.
https://doi.org/10.1055/s-0043-112351
3. ALTOUM, A.E.A., OSMAN, A.L. and BABKER, A.M., 2018. **Comparative study of levels of selective oxidative stress markers (malondialdehyde, zinc, and antioxidant vitamins A, E, and C) in ischemic and non-ischemic heart disease patients suffering from type-2 diabetes**. Asian J Pharm Clin Res, 11(8), pp.508-510.
4. G. Meyerowitz-Katz, and et al.. **Effectiveness of joint specialist case conferences for building general practice capacity to enhance diabetes care: a pilot study in Western Sydney, Australia**, *J Integrated Care*, Vol. 26, no. 3, pp. 199-210, 2018.
https://doi.org/10.1108/JICA-09-2017-0029
5. I. Romera, A. Cebrián-Cuenca, F. Álvarez-Guisasola, F. Gomez-Peralta, and J. Reviriego. **A review of practical issues on the use of glucagon-like peptide-1 receptor agonists for the management of type 2 diabetes**, *Diabetes Therapy*, Vol. 10, no. 1, pp. 5-19, 2019.
https://doi.org/10.1007/s13300-018-0535-9
6. M. S. Aravind, T. M. Joy, and P. S. Rakesh. **Self-Care Practices among People with Type II Diabetes Mellitus in an Urban Area of Ernakulam, Kerala**, *Indian Journal of Public Health Research & Development*, Vol. 10, no. 8, pp. 1-5, 2019.
https://doi.org/10.5958/0976-5506.2019.01843.6
7. M. de Groot, and et al.. **Depressive symptoms, antidepressant medication use, and inflammatory markers in the diabetes prevention program**, *Psychosom Med.*, Vol. 80, no. 2, pp. 167-177, 2018.
https://doi.org/10.1097/PSY.0000000000000535
8. S. Sangeeta, J. Ambekar, T. Sudhakar, and N. Dongre. **Evaluating the Efficacy of Myeloperoxidase and other Biochemical Parameters in the Diagnosis of Chronic Kidney Disease among Diabetic Patients: A Cross-sectional Study**, *Indian Journal of Public Health Research & Development*, Vol. 10, no. 8, pp. 422-426, 2019.
https://doi.org/10.5958/0976-5506.2019.01919.3
9. C. Pouvreau, A. Dayre, E. Butkowski, B. De Jong, and H. Jelinek. **Inflammation and oxidative stress markers in diabetes and hypertension**, *J Inflamm Res.*, Vol. 11, pp. 61-65, 2018.
https://doi.org/10.2147/JIR.S148911
10. J. M. Dennis, and et al.. **Precision medicine in type 2 diabetes: clinical markers of insulin resistance are associated with altered short-and long-term glycemic response to DPP-4 inhibitor therapy**, *Diabetes care*, Vol. 41, no. 4, pp. 705-712, 2018.
https://doi.org/10.2337/dc17-1827
11. E. Y. Suda, A. B. Matias, S. A. Bus, and I. C. Sacco. **Impact of diabetic neuropathy severity on foot clearance complexity and variability during walking**, *Gait posture*, Vol. 74, pp. 194-199, 2019.
https://doi.org/10.1016/j.gaitpost.2019.09.014
12. K. M. Swart, and et al.. **Effects of vitamin D supplementation on markers for cardiovascular disease and type 2 diabetes: an individual participant data meta-analysis of randomized controlled trials**, *The American journal of clinical nutrition*, Vol. 107, no. 6, pp. 1043-1053, 2018.
https://doi.org/10.1093/ajcn/nqy078
13. M. Shang, X. Dong, and L. Hou. **Correlation of adipokines and markers of oxidative stress in women with gestational diabetes mellitus and their newborns**, *J Obstet Gynaecol Res.*, Vol. 44, no. 4, pp. 637-646, 2018.
https://doi.org/10.1111/jog.13586
14. Y. Xiao, and et al.. **Effects of nut consumption on selected inflammatory markers: A systematic review and meta-analysis of randomized controlled trials**, *Nutrition*, Vol. 54, pp. 129-143, 2018.
https://doi.org/10.1016/j.nut.2018.02.017
15. T. Shu, B. Zhang, and Y. Y. Tang. **Computer-Assisted Non-Invasive Diabetes Mellitus Detection System via Facial Key Block Analysis**, *In 2018 International Conference on Wavelet Analysis and Pattern Recognition (ICWAPR). IEEE*, pp. 101-106, 2018.
https://doi.org/10.1109/ICWAPR.2018.8521271
16. V. Lyashenko, A. Babker, and O. Kobylin. **The methodology of wavelet analysis as a tool for cytology preparations image processing**, *Cukurova Medical Journal*, Vol. 41, no. 3, pp. 453-463, 2016.
https://doi.org/10.17826/cukmedj.237468
17. A. Kimata, and et al.. **Temporally stable frequency mapping using continuous wavelet transform analysis in patients with persistent atrial fibrillation**, *J Cardiovasc Electrophysiol*, Vol. 29, no. 4, pp. 514-522, 2018.
https://doi.org/10.1111/jce.13440
18. M. Dadkhah, V. Lyashenko, Z. Deineko, S. Shamshirband, and M. Jazi. **Methodology of wavelet analysis in research of dynamics of phishing attacks**, *International Journal of Advanced Intelligence Paradigms*, Vol. 12, no. 3-4, pp. 220-238, 2019.
https://doi.org/10.1504/IJAIP.2019.098561
19. V. Lyashenko, O. Kobylin, and Y. Baranchykov. **Ideology of Image Processing in Infocommunication**

Systems, *In 2018 International Scientific-Practical Conference Problems of Infocommunications. Science and Technology (PIC S&T)*, pp. 47-50, 2018. https://doi.org/10.1109/INFOCOMMST.2018.8632124

20. C. Torrence, and P. **Webster, Interdecadal changes in the ENSO-monsoon system**, *J Clim.*, Vol. 12, no. 8, pp. 2679-2690, 1999. https://doi.org/10.1175/1520-0442(1999)012<2679:ICITEM>2.0.CO;2
21. A. Grinsted, J. C. Moore, and S. Jevrejeva. **Application of the cross wavelet transform and wavelet coherence to geophysical time series**, *Nonlinear Process Geophys.*, Vol. 11, no. 5/6, pp. 561-566, 2004.
22. H. M. Mohamed, I. M. Sadik, A. Eltom, A. L. Osman, and A. M. Babker. **A Study of Correlation of Serum Chromium Level with Glycosylated Haemoglobin (HbA1c), Total Cholesterol and Triglycerides, among Type 2 Diabetes Patients**, *Open J Blood Dis.*, Vol. 9, no. 1, pp. 1-8, 2019. https://doi.org/10.4236/ojbd.2019.91001
23. A. E. A. Altoum, A. L. Osman, and A. M. Babker. **Impact of body mass index in malondialdehyde, antioxidant vitamins A, E, C and plasma zinc among type 2 diabetic patients**, *Kuwait medical journal*, Vol. 51, no. 1, pp. 16-21, 2019.
24. S. Singhal, R. Gupta, and A. Goyle. **Comparison of antioxidant efficacy of vitamin E, vitamin C, vitamin A and fruits in coronary heart disease: a controlled trial**, *J Assoc Phys India*, Vol. 49, pp. 327-331, 2001.
25. A. W. Ashor, M. Siervo, and J. C. Mathers. **Vitamin C, Antioxidant Status, and Cardiovascular Aging**, *In Molecular basis of nutrition and aging*. *Academic Press*, pp. 609-619, 2016. https://doi.org/10.1016/B978-0-12-801816-3.00043-1
26. A. Gawron-Skarbek, and et al.. **Dietary vitamin C, E and β-carotene intake does not significantly affect plasma or salivary antioxidant indices and salivary c-reactive protein in older subjects**, *Nutrients*, Vol. 9, no. 7, pp. 729-740, 2017. https://doi.org/10.3390/nu9070729
27. J. Zalaket, L. H. Wakim, and J. Matta. **The difference in antioxidant vitamins consumption between obese and non-obese Lebanese individuals**, *Prim Care Diabetes*, Vol. 11,pp. e3-e4, 2017. https://doi.org/10.1016/j.pcd.2017.10.013