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ABSTRACT of the dissertation for the degree of philosophy doctor of medicine

Efficiency mark of carbohydrate metabolism management in diabetes mellitus with Continuous Glucose Monitoring Systems

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INTRODUCTION

Relevance and development of the topic. Diabetes mellitus is one of the most serious medical problems that affects both the functioning of the healthcare system, social and economic aspects of life in all countries of the world, as well as the psychological climate in the families of patients and the psycho-emotional state of every person with diabetes¹. Poor control of this chronic condition can lead to multi-organ damage leading to disability and life-threatening complications such as cardiovascular disease, nerve damage, kidney damage, lower limb amputations and vision loss^{2,3}. However, with appropriate management, these serious complications can be delayed or completely prevented. One of the important management factors is self-monitoring of glucose, which has been replaced by long-term glucose monitoring^{3,4}, allowing 288 glucose measurements per day⁵. Although long-term glucose monitoring measures glucose levels in the interstitial fluid, an analogy with capillary blood glucose has been proven⁶.

The method of long-term glucose monitoring is recommended by the US Food and Drug Administration, the effectiveness of the

 $^{^1} Non$ communicable diseases country profiles / World Health Organization. – Switzerland. -2018. -223 p.

² IDF Diabetes Atlas. Ninth edition / International Diabetes Federation. –Brussels. - 2019.-9, -169 p.

³Falkentoft A.C. Risk of first-time major cardiovascular event among individuals with newly diagnosed type 2 diabetes: data from Danish registers/A.C. Falkentoft, T.A.Gerds, B.Zareini[et al]//Diabetologia.-2023.66.-p.2017-2029.

⁴Standards of Medical Care in Diabetes – 2023/American Diabetes Association.-USA:"Diabetes Care", -2023, - v.46, -298 p.

⁵ Adam B. Abbats FreeStyle Libre Approved in US to Replace Routine Fingersticks [Electronic resource] / Diatribe Learn. -2017, 10 Mach. https://diatribe. org/abbottsfreestyle-libre-approved-us-replace-routine-fingersticks

⁶ Cengiz E. New generation diabetes management: Glucose sensor augmented insulin pump therapy/ E. Cengiz, J.L. Sherr, S.A.Weinzimer [et al]// Expert Rev. Med. Devices. -2011. 8. - p. 449-458.

system has received serious confirmation ⁷. To evaluate the results obtained, at the 79th scientific session of the American Diabetes Association⁸ "Clinical standards" of indicators were proposed, the analysis which can help improve the control of diabetes mellitus and reduce hypoglycemic conditions⁴. Long-term glucose monitoring has recently gained significant support as a method of monitoring glucose regulation, including in the context of the COVID 19 pandemic.⁹.

Recently, extremely important indicators obtained when using long-term glucose monitoring systems have been proposed, such as "Time in Range" and/or "Glucose Management Indicator". According to the US Food and Drug Administration, the Glucose Management Indicator can replace glycosylated hemoglobin in the future, the importance of which in modern diabetology is difficult to overestimate.

Object and subject of the study. The object of the study were patients with diabetes mellitus admitted to the clinic. The subject of observation was glucose levels recorded every 5 minutes using the CGMS MiniMed, Dexcom 4G, FreeStyle Libre continuous glucose monitoring systems.

The purpose of the study was to use continuous glucose monitoring systems (CGMS MiniMed, Dexcom 4G, FreeStyle Libre)

⁷ U.S. Food and Drug Administration. FDA news release. FDA expands indication for continuous glucose monitoring system, first to replace fingerstick testing for diabetes treatment decisions [electronic resource]. -2016, Des. 20. <u>https://www</u>. fda.gov/news-events/press-announcements/fda-expands-indication-continuousglucose-monitoring-system-first-replace-fingerstick-testing

⁸ American Diabetes Association. New Recommendations for Time-in-range Targets During Continuous Glucose Monitoring: [Electronic recourse]/ Press release.-San Francisco, California. -2019. <u>https://www.diabetes.org</u> /newsroom/ press-releases/2019/new-recommendations-for

⁹ Skoler E. Changes to CGM in Hospitals: Updated Rules and Generous CGM Donations: [Electronic resource]/diatribe Learn.-2020. https://diatribe.org/changes-cgm-hospitals-updated-rules-and-generous-cgm-donations

to evaluate the effectiveness of carbohydrate metabolism management in patients with diabetes mellitus.

Objectives of the study:

1. Determine the significance of the average glucose value obtained from the results of continuous glucose monitoring using CGMS MiniMed, Dexcom 4G, FreeStyle Libre, and also explore its relationship with:

- ✓ glycosylated hemoglobin;
- ✓ Glucose Management Indicator (GMI);
- ✓ the value of the standard deviation of glucose indicators (SD) and

other indices reflecting the quality of regulation of carbohydrate metabolism Conga, LI, J-index, LBGI, HBGI, MODD, ADDR, M Value, MAG, MAGE, GRADE..

2. Determine "time in range" (70 mg/dl-180 mg/dl or 3.9 mmol/l-10 mmol/l) and frequency of occurrence of "target range" glucose values:

- \checkmark for type 1 diabetes mellitus.
- \checkmark for type 2 diabetes mellitus on insulin therapy;
- ✓ for type 2 diabetes mellitus on non-insulin therapy;
- ✓ in the absence of diabetes mellitus (persons with normal carbohydrate metabolism and prediabetes);

3. To determine the frequency of occurrence of glucose values more than 180 mg/dl (10 mmol/l) and more than 250 mg/dl (13.9 mmol/l) in people with type 1 diabetes mellitus, type 2 diabetes mellitus on insulin therapy, patients with type 2 diabetes mellitus on non-insulin therapy, in persons without diabetes mellitus.

4. To determine the frequency of occurrence of glucose values less than 70 mg/dl (3.9 mmol/l) and less than 54 mg/dl (3.0 mmol/l) in patients with type 2 diabetes mellitus on non-insulin therapy, type 2 diabetes mellitus on insulin therapy, type 1 diabetes mellitus.

5. To develop a new indicator for assessing glucose variability based on continuous glucose monitoring data, determine its effectiveness and justify the possible range of application of the proposed indicator. The methods of the study: All patients underwent continuous glucose monitoring using CGMS MiniMed, Dexcom 4G, FreeStyle Libre devices with the study of the following indicators:

- SD standard deviation;
- Conga continuous overlapping net glycemic action;
- LI lability index;
- J-index index J;
- LBGI low blood glucose index;
- HBGI high blood glucose index;
- MODD mean of the day differences;
- ADRR average daily risk ratio;
- M Value average mean glucose index;
- MAG mean absolute glucose;
- MAGE mean amplitude of glycemic excursions;
- GRADE glycemic risk assessment in diabetes equation;
- Average glucose level;
- GMI- glucose management indicator;

• TIR- time in range- frequency and time of occurrence of glucose values 70-180 mg/dl (3.9-10 mmol/l);

• TAR-time above range-frequency and time of occurrence of glucose values greater than 180 mg/dl (10 mmol/l) and 250 mg/dl (13.9 mmol/l);

• TBR-time below range-frequency and time of occurrence of glucose values less than 70 mg/dl (3.9 mmol/l) and 54 mg/dl;

- Glucose rate of change indicator;
 - Determination of glycohemoglobin level
 - statistical analysis of the obtained results.

Main points of the disseratation submitted for defence:

• The average glucose value reflected the degree of carbohydrate metabolism disorder, correlated well with the level of glycohemoglobin and was maximally correlated with the GMI index. The average glucose value is also statistically significantly correlated with all indicators reflecting the quality of glucose regulation (Conga, LI, J-index, LBGI,

HBGI, MODD, ADDR, M Value, MAG, MAGE, GRADE), that is, indicators associated with both glucose values, and with its variability.

- The duration of time that glucose values remained in the target range and the frequency of occurrence of "target glucose values" differed statistically significantly between all groups, being maximum in the absence of carbohydrate metabolism disorders and minimum in type 1 diabetes mellitus.
- The frequency of occurrence of glucose values more than 180 mg/dl (10 mmol/l) is maximum in type 1 diabetes mellitus and decreased stepwise in type 2 diabetes mellitus on insulin therapy, without insulin therapy, in persons without diabetes, respectively. A more severe increase in glucose concentration of more than 250 mg/dl (13.9 mmol/l) had a qualitatively the same picture.
- Hypoglycemia with a decrease in glucose levels of less than 70 mg/dl (3.9 mmol/l) most rarely occurred with non-insulin therapy for type 2 diabetes mellitus, more often with insulin therapy for this type of diabetes, and most often occurred with type 1 diabetes. The incidence pattern is more deep hypoglycemia with a glucose level less than 54 mg/dl (3.0 mmol/l) of the total number of hypoglycemia also had the picture described above. Accordingly, the time of glucose values below 54 mg/dl (3.0 mmol/l) per person examined per day was minimal in patients with type 2 diabetes mellitus on non-insulin therapy, intermediate in patients with type 2 diabetes mellitus on insulin therapy, and maximum in the group with type 2 diabetes mellitus 1.
- A new indicator has been proposed for assessing the state of control of carbohydrate metabolism based on the results of long-term glucose monitoring the rate of change in glucose over 5 minutes. The incidence of 5-minute glucose rate of change in the range from 0 to 10 mg/dl (0-0.6 mmol/l) decreased in the following order: non-diabetes mellitus group → type 2 diabetes mellitus group on non-insulin therapy →

type 2 diabetes mellitus group on insulin therapy \rightarrow type 1 diabetes mellitus group.

• The incidence rate of glucose change of more than 10 mg/dl (0.6 mmol/l) increased in the following order: group without diabetes mellitus → group of type 2 diabetes mellitus on noninsulin therapy → group of type 2 diabetes mellitus on insulin therapy → group of type 1 diabetes mellitus.

Scientific innovations of the study results:

- For the first time, the use of the rate of change in glucose over 5 minutes has been proposed to assess glucose variability using continuous glucose monitoring.
- The "Glucose Management Indicator" was studied and its maximum correlation with the average glucose value was proven ($r = 1.00\pm0.000$, p<0.001).
- The relative "risk" of identifying glucose levels in the target range, in the range of hyperglycemia and hypoglycemia for groups of people without impaired carbohydrate metabolism, patients with diabetes type 2 on non-insulin therapy, patients with diabetes type 2 on insulin therapy and patients with type 1 diabetes mellitus.
- It is proposed to calculate group average glucose values to evaluate the results of continuous glucose monitoring using a technique for combining samples by their variances.

Practical significance of the study results:

- 1. It has been shown that devices for continuous glucose monitoring currently used in our country, such as CGMS MiniMed, Dexcom 4G, FreeStyle Libre, are a reliable factor for the management of diabetes mellitus, however, they require careful training of patients in the rules of selfmonitoring and strict adherence to the instructions included to the list to these devices.
- 2. It has been shown that in patients with diabetes mellitus, continuous glucose monitoring contributes to a better understanding of individual glucose regulation and an increase

in the time that glucose remains in the target state, reducing the risk of hypoglycemia.

➤ 3. It has been shown that during continuous glucose monitoring, the following indicators are of particular importance for the analysis of electronic materials: "time in range"; time of hyperglycemia above 180 mg/dl (10 mmol/l), including time of hyperglycemia above 250 mg/dl (13.9 mmol/l); time of occurrence of hypoglycemia, depth and duration of hypoglycemia.

Approbation of the study: The main points of the work were presented at «Azərbaycan Endokrinoloqlar Elmi Cəmiyyətinin iclası» (Bakı, 2016), conference "Diabet Yenilikləri" (Baku, 2017), International Diabetes Federation Congress (Abu Dhabi, 2017), «4-cü Beynəlxalq Metabolik və Bariatri k Cərrahiyə Konqressi» (Bakı, 2018), 3rd EASD Postgraduate Course (Tbilisi, 2018), «I Azərbaycan Diabet Konqresi» (Bakı, 2018), «5-ci Beynəlxalq Metabolik və Bariatrik Cərrahiyə Konqressi» (Bakı, 2019), «II Azərbaycan Diabet Konqresi» (Bakı, 2019), «III Azərbaycan Diabet Konqresi» (Bakı, 2020).

Publications: On the subject of the thesis 8 scientific papers were published, including 5 articles (2 abroad) and 3 abstracts (2 abroad).

Implementation of the study results: The results of the study were introduced into the educational process of the Department of Therapy of the Azerbaijan State Advanced Training Institute for Doctors named after A. Aliyev, as well as into the work of the diabetes department of the Azerbaijan Medical University Educational and Therapeutic Clinic, The Republic Endocrinological Center and the "Azer Turk Med" Clinic.

Name of the organization where the work was performed: Department of Therapy of Azerbaijan State Advanced Training Institute for Doctors named after A. Aliyev of the Ministry of Health of the Azerbaijan Republic, collection of clinical material was carried out in "VM Endokrinologiya, Diabet və Metabolizm Center", in the clinic "Azər Türk Med" and the Educational and Therapeutic Clinic of the Azerbaijan Medical University.

Scope and structure of the dissertation. The dissertation is includes 70 tables, 64 figures. The work consists of an introduction (11974 characters), a literature review (Chapter I – 35053 characters), a description of materials and research methods (Chapter II - 14894 characters), results and their discussion (Chapter III - 94592 findings conclusion (21919 characters), characters). (3498 recommendations (2524)characters), characters). practical bibliography, which includes 271 sources, of which 5 are in Azerbaijani, 10 in Russian, 256 in English. Total number of characters -184454.

MATERIALS AND METHODS OF RESEARCH

During the study, 125 people (52 men and 73 women) aged from 7 to 80 years were examined. The continuous glucose monitoring device CGMS MiniMed examined 57 people, Dexcom 4G - 47 people, FreeStyle Libre - 21 people.

In 4 subjects, 1 man and 3 women; age from 36 to 57 years (3.2%) there were no carbohydrate metabolism disorders (NCD). 4 subjects - 1 man and 3 women aged from 40 to 61 years (3.2%) had prediabetes (PD). 117 examined people - 49 men and 68 women, ages from 7 to 80 years (93.6%) had diabetes, and 47 of them - 17 men and 30 women, ages from 5 to 47 years (37.6%) had diabetes mellitus. diabetes mellitus type 1 (DM1), and in 70 examined people - 33 men and 37 women, ages from 13 to 80 years (56.0%) - diabetes mellitus type 2 (DM2).

Of the 47 patients with T2DM, 25 (21 men and 4 women, ages from 13 to 78 years) (20.0%) did not receive insulin therapy and were treated only with oral hypoglycemic drugs. A total of 34 patients (20%) received treatment with oral hypoglycemic drugs. From the data obtained, it can be calculated that 9 patients (7.2%) with diabetes type 2 had combination therapy: insulin + oral hypoglycemic drugs. 92 subjects (73.6%) received insulin treatment, and in 47 patients with diabetes type 1 and 36 patients with diabetes type 2 (66.4% in total), insulin treatment was monotherapy.

The average age of the subjects was 42.2 ± 1.85 years. The average height was 161.0 ± 1.05 cm, body weight - 73.0 ± 1.94 kg, body mass index - 27.8 ± 0.64 kg/m2.

Systolic blood pressure averaged 124.8±1.86 mmHg, while diastolic blood pressure averaged 78.2±1.03 mmHg.

The patients were divided into the following groups:

- Persons without carbohydrate metabolism disorders (without NCD) (n = 4)
- Prediabetes (PD) (n =4)
- Diabetes type 2 on non-insulin therapy (T2DM NIT) (n =25)
- Diabetes mellitus type 2 on insulin therapy (T2DM IT) (n =45)
- Diabetes mellitus type 1 (T1DM) (n =47)

Subsequently, the groups of practically healthy and prediabetes were combined into a group of people without diabetes mellitus (no diabetes) (n = 8). Thus:

- group 1 persons without diabetes ND (n =8);
- group 2 persons with T2DM NIT (n = 25);
- group 3 T2DM IT (n =45);
- group 4 T1DM (n =47).

All subjects were measured for height and body weight. Body mass index was calculated using the formula: BMI = body weight / height², where body weight was expressed in kilograms and height in meters. According to generally accepted rules, systolic and diastolic blood pressure was measured for each examinee, the values of which were expressed in mmHg. Venous blood tests to determine glucose were taken after an overnight fast of 8-12 hours. The results of the analysis were expressed in mg/dL. Glycated hemoglobin levels were measured. The results of the analysis were expressed in "%". Indicators of carbohydrate metabolism were assessed as normal in accordance with the recommendations of the Azerbaijan Association of Endocrinology, Diabetology and Therapeutical Education and the American Diabetes Association.

During statistical data analysis, the sample mean, standard deviation and error of the mean were determined. Statistical analysis was carried out using the standard computer program Microsoft Excel.

The confidence interval of mean values (CI) was determined on line with a probability level of 95% using the "Confidence Limits for Mean Calculator" calculator.

Using the MEDCALC calculator, on line using the χ^2 method and Fisher's exact test, the significance of the differences between the shares was determined. Differences between means for small samples were calculated using the Mann–Whitney–Wilcoxon method. Calculation of relative risk with a 95% confidence interval was carried out using the online calculator "Medical Statistics".

A correlation analysis of the relationship between various indicators of long-term glucose monitoring was carried out using the standard computer program Microsoft Excel.

The average glucose value in the group ND was 107.8 ± 4.84 mg/dl, and in the group with PD 107.5 ± 5.54 mg/dl, which was even slightly lower than the values in the group without ND. The differences in the mean values of the ND group and the PD group were not statistically significant (p>0.05). The data obtained show that the average glucose level calculated in a standard way did not distinguish the group without ND from the PD group.

In the group with T2DM NIT, the average glucose value was 155.5 ± 7.76 mg/dl. The differences in the average glucose values between the T2DM NIT group and the group without ND, as well as the differences between the T2DM NIT group and the PD group were statistically significant (in both cases p<0.001). Thus, the average glucose value made it possible to clearly differentiate diabetes mellitus from normal and prediabetes.

In the T2DM IT group, the average glucose value was $173.3 \pm 6.15 \text{ mg/dL}$. The average glucose value in the T2DM IT group and the group without ND differed statistically significantly (p<0.001). A similar picture occurred when comparing the T2DM IT groups with the PD group (p<0.001). The difference between the T2DM IT and T2DM NIT groups was also statistically significant (p<0.05), which

indicates the presence of higher glucose values in the T2DM IT group, that is, worse glucose regulation in this group. This assumption is clinically confirmed since the initiation of insulin therapy in these patients with diabetes type 2 was a consequence of the inability to further continue non-insulin therapy.

In the T1DM group, the average glucose value was 177.5 ± 7.56 mg/dL. This indicator was statistically significantly higher than in the group without ND (p<0.001), in the PD group (p<0.001) and did not differ statistically significantly from the indicators in the group T2DM NIT (p>0.05) and T2DM IT (p>0, 05).

It should be noted that the average values of the indicators were calculated based on the number of patients in the group. For example, in the group without ND we had 4 examined:

- Examined G.N. the average glucose value in the intercellular fluid is 104.95 mg/dl;
- Examined M.R. the average glucose value in the intercellular fluid is 119.1 mg/dl;
- Examined G.M. the average glucose value in the intercellular fluid is 99 mg/dl;
- Examined by B.G. the average glucose value in the intercellular fluid is 108.26 mg/dl;

However, this calculation does not take into account the number of measurements of which the examined G.N. was 1105, M.R. -1612, from G.M. -1124, from B.G. -1646.

That is, the average value in our example would be calculated not from 4 values, but from 5487 glucose determinations. Based on this n, the Standard Deviation and the average error were calculated.

Although such a technique optimizes the differentiation between groups of subjects, it still has one drawback: it does not take into account the differences in the number of glucose tests in different patients, which can lead to a distortion of the overall result, when the data of the examined person who had the most glucose tests will dominate.

It may be more appropriate to use a standard method of combining samples by their variances, which will allow taking into account both the average values for each person examined and the variances of these average values, and thus the number of glucose studies.

As a result of using this technique, the average glucose value in the group without ND was 108.9 ± 0.35 mg/dL, in the PD group 110.9 ± 0.32 mg/dL, in the T2DM NIT 151.7 ± 0.12 mg/dL, in the T2DM IT was 165.5 ± 0.17 mg/dL and in the T1DM group 192.6 ± 0.24 mg/dL. All these indicators have statistically significant differences (p<0.001).

As would be expected, the average glucose level correlated with the level of glycohemoglobin ($r=+0.55\pm0.065$; p<0.001).

A new indicator has been proposed by the International Consensus Group⁷ to be included in all routine continuous glucose monitoring reports. This indicator is recognized as the equivalent of glycohemoglobin, which is the "gold standard" for assessing carbohydrate metabolism, but, unfortunately, has a number of disadvantages. FDİ decided to call this indicator the "GMI"-glucose management indicator. To date, this indicator has not been studied in any of the studies conducted in Azerbaijan. We conducted a study of the correlation of the average glucose value with GMI and glycohemoglobin in all groups of subjects. As a result, the correlation between the average glucose value and the "GMI" index (r =+1.0\pm0.00; p <0.001), as well as glycohemoglobin and GMI (r =+0.55\pm0.06; p<0.001) was extremely high, which is to be expected, since GMI is calculated based on the average glucose value.

It turned out to be extremely important that all indicators of the state of carbohydrate metabolism (SD, Conga, LI, J-index, LBGI, HBGI, MODD, ADDR, M Value, MAG) to a greater or lesser extent, better or worse, reflect different aspects of regulation glucose, such as glycemic variability, frequency of hypo- and hyperglycemia, etc. Moreover, they statistically significantly (p < 0.05 - p < 0.001) correlate with the average glucose value.

The average number of results in the "target range" (70-180 mg/dl or 3.9-10.0 mmol/l) per 1 examined person per day in the group without diabetes was 273.3 ± 0.20 ; in the group T2DM NIT

214.0 \pm 0.29; in the group T2DM IT was 168.7 \pm 0.32 and in the T1DM group 150.7 \pm 0.35 (in all cases p<0.001). Glucose levels within the target parameters in the group without diabetes occurred in 93.99% of cases, in the T2DM NIT group – in 74.58% of cases, in the T2DM IT group – in 62.35% of cases, and, finally, in the T1DM group – in 47.90% of cases (p < 0.0001).

Thus, target glucose parameters in the group without diabetes mellitus were more common than in people with diabetes type 2 and diabetes type 1.

The average duration of "target time" in the group without diabetes was 22 hours 33 minutes; in the group T2DM NIT – 17 hours and 51 minutes; in the group T2DM IT – 14 hours and 57 minutes. In the T1DM group, the duration of the "target time" was minimal and amounted to 11 hours 29 minutes.

Considering the relative risk of occurrence of time in range in various groups of subjects, the following results were obtained (Table 1)

Table 1.

Values of the relative risk of occurrence of time in the target range in various groups of patients

	ND		_
T2DM NIT	1,134	T2DM NIT	
T2DM IT	1,261	1,112	T2DM IT
T1DM	1,496	1,319	1,186

The summarized results of determining the relative risk of occurrence of "time in range" in the analyzed groups of patients showed that in groups with diabetes type 2 mellitus, target parameters occurred more often than in diabetes type 1.

The number of cases of glucose levels above 180 mg/dl (10 mmol/l) in the group without diabetes was 179 (1.61%), in the T2DM NIT group -9218 (23.93%), in the T2DM IT group -27260 (35. 16%) and in the T1DM group -39,127 (47.61%).

The average number of hyperglycemia results per 1 examined person per day in the group without diabetes was 6.34 ± 0.47 ; in the group T2DM NIT 81.00 ± 0.71 ; in the group T2DM IT was 116.00 ± 0.47 and in the T1DM group it was maximum and amounted to 121.01 ± 0.39 (in all cases p<0.001).

Examining the duration of time of glucose more than 180 mg/dl (10 mmol/l) in the group without diabetes, the duration was 22 minutes 48 seconds; in the group T2DM NIT – 5 hours 44 minutes 24 seconds; in the group T2DM IT – 8 hours 25 minutes 48 seconds. In the T1DM group, the duration of glucose values more than 180 mg/dl (10 mmol/L) was maximum and amounted to 11 hours 25 minutes 12 seconds.

The number of hyperglycemia results (>250 mg/dl or >13.8 mmol/l) in the ND group was 0, in the group T2DM NIT 1548 (5.39%), in the group T2DM IT 8987 (18.59%) and in group T1DM 19111 (48.54%).

The average number of hyperglycemia results per 1 examined person per day in the group without diabetes was zero; in the group T2DM NIT 35.63 ± 1.46 ; in the group T2DM IT was 52.07 ± 0.51 and in the T1DM group 63.56 ± 0.42 (in all cases p<0.001). Thus, as we expected, in the group of people without diabetes, the frequency of glucose more than 250 mg/dl (13.8 mol/l) was 0, and in the group with diabetes type 1it was the highest and amounted to 48.54% of cases.

In the group without diabetes, the duration of time for glucose levels greater than 250 mg/dL (13.8 mol/L) was 0 hours 00 minutes; in the group T2DM NIT – 0 hours 57 minutes 52 seconds; in the group T2DM IT – 2 hours and 46 minutes 48 seconds. In the T1DM group, the duration of glucose values greater than 250 mg/dl (13.8 mol/l) was maximum and amounted to 5 hours 34 minutes 48 seconds.

In the group without diabetes, there was no risk of detecting glucose levels above 250 mg/dl.

The occurrence of hypoglycemia is possible both during insulin therapy and during therapy with oral glucose-lowering drugs. Hypoglycemia is the most striking and acute sign of the excessive effect of glucose-lowering therapy and is associated with serious damage to the cardiovascular and nervous systems.

In this study, the incidence of glucose levels less than 70 mg/dl (3.9 mmol/l) was examined in 4 groups: a group of people without diabetes (persons without disturbance of carbohydrate metabolism and people with PD), patients with T2DM NIT, patients with T2DM IT, patients with T1DM. However, due to the fact that in people ND, a hypoglycemic level is considered to be below 60 mg/dl (3.3 mmol/l), as well as the small sample size of the group without ND (n = 4), the indicators of people without diabetes were not included in the study.

The number of hypoglycemia results <70 mg/dl (<3.9 mmol/l) in the T2DM NIT group was 574 (1.49%), in the T2DM IT group 1925 (2.48%) and in the T1DM group 3692 (4.49%).

The average number of hypoglycemia results per 1 examined person in the group T2DM NIT was 12.19 ± 0.75 ; in the group T2DM IT was 11.19 ± 0.43 and in the T1DM group 20.68 ± 0.39 (in all cases p<0.001).

The average duration of time for glucose values less than 70 mg/dl (3.9 mol/l) in the T2DM NIT group was 21 minutes 27 seconds; in the T2DM IT group – 35 minutes 45 seconds. In the T1DM group, the duration of glucose values less than 70 mg/dl (3.9 mol/l) was maximum and amounted to 1 hour 42 minutes.

In the T2DM NIT group, the time of hypoglycemia per 1 examined person per day was 61 minutes; in the group T2DM IT was 60 minutes and was the largest in the T1DM group and amounted to 86 minutes.

The number of low glucose results <54 mg/dl (<3.0 mmol/l) in the T2DM NIT group was 176 (0.46%), in the T2DM IT group 733 (0.95%) and in the T1DM group 1463 (1.78%).

The average number of hypoglycemic indicators per 1 examined person per day in the T2DM NIT group was 8.6 ± 0.66 ; in the T2DM IT group was 10.9 ± 0.67 and in the T1DM group 12.2 ± 0.42 . The differences between the groups T2DM NIT and T2DM IT, T2DM NIT and T1DM were statistically significant (p<0.01). There were no statistically significant differences between the T2DM IT and T1DM groups (p>0.05).

Assessing the data for various groups on the average duration of time when glucose was less than 54 mg/dl (3.0 mol/l) during the day, we obtained the following data. In the group T2DM NIT – 6 minutes 32 seconds; in the group T2DM IT – 13 minutes 35 seconds. In the T1DM group, the duration of glucose values less than 54 mg/dl (3.0 mol/l) was maximum and amounted to 25 minutes 24 seconds.

Data were reviewed on the percentage of patients with glucose levels less than 54 mg/dl (3.0 mol/l) in the groups T2DM NIT, T2DM IT, T1DM. The incidence of patients with glucose levels less than 54 mg/dL (3.0 mol/l) in the group of T2DM NIT was 20%, in the group with T2DM IT it was 27% and in the group with T1DM it was 53%, respectively. The differences between the T2DM NIT and T2DM IT groups were not statistically significant (p > 0.05). The incidence of patients with glucose less than 54 mg/dl (3.0 mol/l) was statistically significantly higher in the T1DM group than in the T2DM NIT group (p = 0.01) and in the T2DM İTgroup (p < 0.01).

The average number of glucose values is less than 54 mg/dl (3.0 mol/l) per 1 examined person per day (taking into account all patients in the group, regardless of the presence or absence of hypoglycemia) in the group T2DM NIT 1.7 ± 0.37 ; in the group T2DM IT was 2.8 ± 0.36 and in the T1DM group 6.9 ± 0.35 (p<0.001).

Data on the time of glucose values less than 54 mg/dl (3.0 mol/l) per person examined per day for patients in 3 groups were analyzed. It is important to note that in this case, only those patients in the groups who had hypoglycemic indicators were taken into account. The time for glucose values below 54 mg/dl (3.0 mmol/l) per person examined per day in the T2DM NIT group was 42 minutes, in the T2DM IT group 53 minutes and was the longest in the T1DM group - 1 hour 9 minutes.

Analysis of the average frequency of occurrence of glucose values below 54 mg/dl (3.0 mmol/l) among the total number of indicators less than 70 mg/dl (3.0 mmol/l) in the group T2DM NIT was 45%, in the group with T2DM IT was 52% and in the group with

diabetes type 1 the highest was 71%. The differences between the groups, in all cases, were statistically significant: T2DM NIT, T2DM IT p = 0.003, while in the groups with T2DM NIT and T1DM, T2DM IT and T1DM were highly statistically significant (p < 0.0001).

The work examined the frequency of occurrence of the rate of change in glucose every 5 minutes in the range from 0 to 10 mg/dl (0-0.6 mmol/l) and above 10 mg/dl (0.6 mmol/l). Number of cases of changes in glucose rate in the range from 0 to 10 mg/dl (0-0.6 mmol/l) in the group without diabetes 10805, in the group T2DM NIT 37265, in the group T2DM IT 74895 and in the T1DM group 75338. Number of cases of changes in glucose rate in the range above 10 mg/dl (0.6 mmol/l) in in the group ND 272, in the group T2DM NIT 1194, in the group T2DM IT 2595 and in the T1DM group 6803.

The rate of glucose change in the range from 0 to 10 mg/dL (0-0.6 mmol/l) in the group ND was 97.54%; in the group T2DM NIT -96.80%. In the group T2DM IT was 96.65% and in the T1DM group 91.72%. The incidence rate of glucose change in the range above 10 mg/dl (0,6 mmol/l) in the group ND was 2.46%; in the group T2DM NIT - 3.10%; in the group T2DM IT - 3.35% and in the T1DM group - 8.28%. Differences, according to the Fisher exact method, in the frequency of occurrence of the rate of change in glucose from 0 to 10 mg/dl (0-0.6 mmol/l) and above 10 mg/dl (0.6 mmol/l) in 5 minutes between the groups ND and T2DM NIT were statistically significant (p = 0.0003). The difference between the T2DM NIT and T2DM IT groups was also statistically significant (p=0.0283). Differences in the frequency of occurrence of the rate of change in glucose in the groups without DM and T2DM IT, without DM and T1DM, T2DM NIT and T1DM, and T2DM IT and T1DM, respectively, were highly statistically significant (p<0.00001).

Table 2 presents data on the probability ("relative risk") of finding glucose values in the range of glucose change rates above 10 mg/dl (0.6 mmol/l) in the group ND compared to the group T2DM NIT.

The "absolute risk" of detecting values in the range of glucose change rates above 10 mg/dl (0.6 mmol/l) in the ND was 0.186.

Table 2.

Data on the likelihood ("relative risk") of finding glucose values in the range of glucose change rates above 10 mg/dl (0.6 mmol/l) in the group ND compared with the group T2DM NIT

"Absolute risk" of detecting changes in glucose rate greater than 10 mg/dl (0.6 mmol/l) in the ND (EER)	0,186
"Absolute risk" of detecting values of change in glucose rate above 10 mg/dl (0.6 mmol/l) in the group T2DM of NIT (CER)	0,225
Relative risk: group ND/T2DM NIT(RR)	0,825
Standard error of relative risk (S)	0,055
Lower limit of 95% confidence interval (CI)	0,741
Upper limit of 95% confidence interval (CI)	0,920

The "absolute risk" of detecting glucose values in the range of glucose change rates above 10 mg/dl (0.6 mmol/l) in the T2DM NIT group was 0.225. Relative risk: group ND/T2DM NIT 0.825 with standard error 0.055, lower limit of 95% CI (confidence interval) 0.741 and upper limit of 95% CI 0.920. The data obtained indicate the statistical significance of the existing differences p<0.05. Thus, the "risk" of detecting glucose values in the range of glucose change rates above 10 mg/dl in the ND is 0.825 times less than in the presence of T2DM NIT.

Table 3 presents data on the probability ("relative risk") of finding glucose values in the range of glucose change rates above 10 mg/dl (0.6 mmol/l) in the group ND compared with the T2DM IT group.

As can be seen from Table 3, the "Absolute risk" of detecting values in the range of the rate of change in glucose above 10 mg/dl (0.6 mmol/l) in the ND group was 0.095. The "absolute risk" of detecting glucose values in the range of glucose change rates above 10 mg/dl in the T2DM IT group was 0.126. Relative risk: group ND/T2DM IT 0.752 with standard error 0.058, lower limit of 95% CI (confidence interval) 0.671 and upper limit of 95% CI 0.844.

Table 3.

Data on the probability ("relative risk") of finding glucose values in the range of glucose change rates above 10 mg/dl (0.6 mmol/l) in the group ND compared with the T2DM group IT

"Absolute risk" of detecting changes in glucose rate greater than 10 mg/dl (0.6 mmol/l) in the ND group (EER)	0,095
"Absolute risk" of detecting changes in glucose rate above 10 mg/dl (0.6 mmol/l) in the T2DM IT group (CER)	0,126
Relative risk: group ND/T2DM IT(RR)	0,752
Standard error of relative risk(S)	0,058
Lower limit of 95% confidence interval (CI)	0,671
Upper limit of 95% confidence interval (CI)	0,844

The data obtained indicate the statistical significance of the existing differences p<0.05. Thus, the "risk" of detecting glucose values in the range of glucose change rates above 10 mg/dl (0.6 mmol/l) in the absence of diabetes is 0.752 times less than in the presence of T2DM IT.

Table 4 presents data on the probability ("relative risk") of finding glucose values in the range of glucose change rates above 10 mg/dl (0.6 mmol/l) in the group ND compared with the group with T1DM.

As can be seen from Table 4, the "Absolute risk" of detecting values in the range of the rate of change in glucose above 10 mg/dl (0.6 mmol/l) in the group ND was 0.038. The "absolute risk" of detecting glucose values in the range of glucose change rates above 10 mg/dl (0.6 mmol/l) in the T1DM group was 0.125. Relative risk: group ND/DM1 0.307 with standard error 0.060, lower limit of 95% CI (confidence interval) 0.272 and upper limit of 95% CI 0.345.

The data obtained indicate the statistical significance of the existing differences p<0.05. Thus, the "risk" of detecting glucose values in the range of glucose change rates above 10 mg/dl (0.6

mmol/l) in the absence of diabetes is 0.307 times less than in the presence of diabetes type 1.

Table 4.

Data on the probability ("relative risk") of finding glucose values in the range of glucose change rates above 10 mg/dl (0.6 mmol/l) in the group ND compared to the group with type 1 diabetes

"Absolute risk" of detecting changes in glucose rate greater	
than 10 mg/dl (0.6 mmol/l) in the group ND (EER)	
"Absolute risk" of detecting changes in glucose rate above	0,125
10 mg/dl (0.6 mmol/l) in the T1DM group (CER)	
Relative risk: ND/T1DM group (RR)	0,307
Standard error of relative risk (S)	0,060
Lower limit of 95% confidence interval (CI)	0,272
Upper limit of 95% confidence interval (CI)	

Table 5 presents data on the probability ("relative risk") of finding glucose values in the range of glucose change rates above 10 mg/dl (0.6 mmol/l) in the T2DM NIT group compared with the T2DM IT group.

Table 5.

Data on the likelihood ("relative risk") of finding glucose values in the range of glucose change rates above 10 mg/dl (0.6 mmol/l) in the T2DM NIT group compared with the T2DM IT group

"Absolute risk" of detecting values of change in glucose rate	0,315
above 10 mg/dl (0.6 mmol/l) in the group of T2DM NIT	
(EER)	
"Absolute risk" of detecting values of change in glucose rate	0,332
above 10 mg/dl (0.6 mmol/l) in the T2DM IT group (CER)	
Relative risk: group T2DM NIT/T2DM IT (RR)	0,948
Standard error of relative risk (S)	0,024
Lower limit of 95% confidence interval (CI)	0,904
Upper limit of 95% confidence interval (CI)	0,995

As can be seen from Table 5, the "Absolute risk" of detecting values in the range of the rate of change in glucose above 10 mg/dl (0.6 mmol/l) in the group T2DM NIT was 0.315. The "absolute risk" of detecting glucose values in the range of glucose change rates above 10 mg/dl in the T2DM IT group was 0.332. Relative risk: group T2DM NIT/T2DM IT 0.948 with standard error 0.024, lower limit of 95% CI (confidence interval) 0.904 and upper limit of 95% CI 0.995. The data obtained indicate the statistical significance of the existing differences p<0.05. Thus, the "risk" of detecting glucose values in the range of glucose change rates above 10 mg/dl (0.6 mmol/l) in the T2DM NIT group is 0.948 times less than in the T2DM IT group.

Table 6 presents data on the probability ("relative risk") of finding glucose values in the range of glucose change rates above 10 mg/dl (0.6 mmol/l) in the T2DM NIT group compared to the T1DM group.

Table 6.

Data on the likelihood ("relative risk") of finding glucose values in the range of glucose change rates above 10 mg/dl (0.6 mmol/l) in the T2DM NIT group compared with the T1DM group

"Absolute risk" of detecting values of change in glucose rate above 10 mg/dl (0.6 mmol/l) in the group of T2DM NIT (EER)	0,149
"Absolute risk" of detecting changes in glucose rate above	0,331
10 mg/dl (0.6 mmol/l) in the T1DM group (CER)	
Relative risk: group T2DM NIT/T1DM (RR)	0,451
Standard error of relative risk(S)	0,027
Lower limit of 95% confidence interval (CI)	0,428
Upper limit of 95% confidence interval (CI)	

As can be seen from Table 6, the "Absolute risk" of detecting values in the range of the rate of change in glucose above 10 mg/dl (0.6 mmol/l) in group T2DM NIT was 0.149. The "absolute risk" of detecting glucose values in the range of glucose change rates above

10 mg/dl (0.6 mmol/l) in the T1DM group was 0.331. Relative risk: group T2DM NIT/T1DM 0.451 with standard error 0.027, lower limit of 95% CI (confidence interval) 0.428 and upper limit of 95% CI 0.476. The data obtained indicate the statistical significance of the existing differences p<0.05. Thus, the "risk" of detecting glucose values in the range of glucose change rates above 10 mg/dl (0.6 mmol/l) in the T2DM NIT group is 0.451 times less than in the T1DM group.

Table 7 presents data on the probability ("relative risk") of finding glucose values in the range of glucose change rates above 10 mg/dl (0.6 mmol/l) in the T2DM IT group compared to the T1DM group.

Table 7.

Data on the probability ("relative risk") of finding glucose values in the range of glucose change rates above 10 mg/dl (0.6 mmol/l) in the T2DM IT group compared with the T1DM group

"Absolute risk" of detecting changes in glucose rate above 10 mg/dl (0.6 mmol/l) in the T2DM IT group (EER)	0,276
"Absolute risk" of detecting changes in glucose rate above 10 mg/dl (0.6 mmol/l) in the T1DM group (CER)	0,499
Relative risk: T2DM IT/T1DM group (RR)	0,554
Standard error of relative risk (S)	0,017
Lower limit of 95% confidence interval (CI)	0,536
Upper limit of 95% confidence interval (CI)	0,573

As can be seen from Table 7, the "Absolute risk" of detecting values in the range of the rate of change in glucose above 10 mg/dl (0.6 mmol/l) in the T2DM IT group was 0.276. The "absolute risk" of detecting glucose values in the range of glucose change rates above 10 mg/dL in the T1DM group was 0.499. Relative risk: group T2DM IT/DM1 0.554 with standard error 0.017, lower limit of 95% CI

(confidence interval) 0.536 and upper limit of 95% CI 0.573. The data obtained indicate the statistical significance of the existing differences p<0.05. Thus, the "risk" of detecting glucose values in the range of glucose change rates above 10 mg/dl (0.6 mmol/l) in the T2DM IT group is 0.554 times less than in the T1DM group.

Thus, the data obtained indicate that a high rate of change in glucose is not typical for people without diabetes and people with prediabetes. Indicators of the rate of change in glucose above 10 mg/dl (0.6 mmol/l)/5 min are statistically significantly more common in diabetes, while the greater the degree of degradation of the glucose regulation system, the higher the frequency of cases of rate of change in glucose above 10 mg/dl (0.6 mmol/l)/5 min or more. The resulting indicator can be used to evaluate the results of continuous glucose monitoring. It is advisable to further study it as a diagnostic parameter and a parameter for assessing the state of glucose control.

CONCLUSIONS

- 1. The average glucose value reflects the degree of disturbance of carbohydrate metabolism (in the group ND: 107.8 ± 4.84 mg/dl; in the group of diabetes mellitus type 2 on noninsulin therapy: 155.5 ± 7.76 mg/dl; in the group of diabetes mellitus type 2 on insulin therapy: 173.3 ± 6.15 mg/dl; in the diabetes type 1 group: 177.5 ± 7.56 mg/dl (p < 0.001). The average glucose correlated with the glycohemoglobin (r=+0,55±0,065; p<0,001) and indicators reflecting the quality of glucose regulation (r from "-0.27" to "+0.96"; p from "<0.05" to "<0.001") maximally correlated with the GMI (r=1.00\pm0.000, p<0.001).
- 2. The frequency of "time in range" was 93.99% in the group of persons without diabetes; 74.58% in the group of people with T2DM NIT; 62.35% in the group with T2DM IT; 47.90% in the group with T1DM (differences between groups in all cases were statistically highly significant (p < 0.0001); while the time spent in the target range was 22 hours 33 minutes in the group without diabetes, 17 hours 51 minutes in the group with T2DM NIT, 14 hours 57 minutes in the

group with T2DM IT, 11 hours 29 minutes in the group with T1DM. The relative "risk" of determining glucose levels outside the target range was minimal in individuals without diabetes and was 1,134; 1,261; 1,496 with the T2DM NIT, T2DM IT and T1DM groups, respectively. The relative "risk" of determining glucose values outside the target range was greatest in the T1DM group [5].

- 3. The frequency of occurrence of glucose values more than 180 mg/dl (10 mmol/l) in the group without diabetes was 1.61%; with T2DM NIT 23.93%; with T2DM IT 35.16%; for T1DM 47.61%. A more severe increase in glucose concentration (> 250 mg/dL or 13.9 mmol/L) was absent in the ND group, occurring in 5.39% of studies in the T2DM NIT group, in 18.59% of studies in the T2DM IT group and in 48. 54% of analyzes in the T1DM group.
- 4. Hypoglycemia with a decrease in glucose levels of less than 70 mg/dl (3.9 mmol/l) was examined in three groups of patients and occurred in 1.49% of studies in people with T2DM NIT, in 2.48% of studies in patients with T2DM IT and in 4.49% of analyzes in patients with T1DM. More profound hypoglycemia with a glucose level of less than 54 mg/dl (3.0 mmol/l) accounted for 30.6% of the total number of hypoglycemia in the T2DM NIT group, 38.2% in T2DM IT and 40.3% in T1DM. The average number of glucose values is less than 54 mg/dl (3.0 mol/l) per 1 examined person per day (taking into account all patients in the group, regardless of the presence or absence of hypoglycemia) in the group T2DM NIT 1.7±0.37; in the group T2DM IT was 2.8±0.36 and in the T1DM group 6.9±0.35. At the same time, the time of glucose values below 54 mg/dl (3.0 mmol/l) per 1 examined person per day in the group with T2DM NIT was 42 minutes, in the group T2DM IT was 53 minutes and was the longest in the T1DM group - 1 hour 9 minutes. The differences in the incidence of hypoglycemic conditions between the study groups were statistically significant (p<0.001) [6].
- 5. The frequency of occurrence of the rate of change in glucose for every 5 minutes in the range from 0 to 10 mg/dl (0.6 mmol/l) was maximum in the group without diabetes and amounted to 97.54%; in the group T2DM NIT 96.80%; in the group T2DM IT 96.65% and in the

T1DM group – 91.72%. The incidence rate of glucose change of more than 10 mg/dl in the group without diabetes was 2.46%; in the group T2DM NIT was 3.10%; in the group T2DM IT 3.35%; in the T1DM group was maximum and amounted to 8.28%. The differences between all groups were statistically significant (p 0.0283 to <0.00001). It is proposed to use the rate of change in glucose over 5 minutes to assess the state of control of carbohydrate metabolism based on the results of continuous glucose monitoring [7].

PRACTICAL RECOMENDATIONS

- 1. The devices for continuous glucose monitoring currently used in our country are a reliable tool for managing diabetes mellitus, provided that the patient is carefully trained in the rules of self-control and accurately follows the instructions included with these devices.
- 2. In patients with diabetes, continuous glucose monitoring helps to better understand the characteristics of individual glucose regulation and, thereby, increase the time that glucose remains in the target range. Continuous use of glucose monitoring may be considered absolutely necessary in diabetes type 1, which is characterized by a minimum incidence of glucose values in the target range, a maximum incidence of glucose values greater than 180 mg/dL (10 mmol/L) and 250 mg/dL (13, 9 mmol/l), as well as the maximum frequency of occurrence of hypoglycemic conditions, including deep hypoglycemia.
- 3. Continuous use of glucose monitoring is also advisable in diabetes type 2 on insulin therapy, since these patients are characterized by a high incidence of glucose values more than 180 mg/dl (10 mmol/L) and 250 mg/dl (13.9 mmol/l) and hypoglycemia.
- 4. For diabetes type 2 without insulin therapy, the use of continuous glucose monitoring can be carried out

intermittently due to a lower risk of hypoglycemia and a higher frequency of occurrence of time in the target range.

- 5. When conducting continuous glucose monitoring, indicators are of particular importance for the analysis of the obtained materials:
 - time in range 70 mg/dl-180 mg/dl (3.9 mmol/l-10 mmol/l),
 "Time In Range"
 - time of hiperglycemia above 180 mg/dl (10 mmol/l), including time above 250 mg/dl (13.9 mmol/l), - «Time Above Range»
 - time of occurrence of hypoglycemia, depth and duration of hypoglycemia.
 - Glucose management indicator "GMİ", which correlates well with average glucose levels and glycated hemoglobin levels.
- 6. For a more in-depth study of the characteristics of glucose regulation in a patient, the following indicators can also be used:

✓ Characterizing glucose variability:

Conga, LI, MODD, ADDR, MAGE, SD.

✓ Characterizing the quality of glucose control: LBGI, HBGI, M Value, MAG, GRADE, J-index, ADDR.

LIST OF PUBLISHED ARTICLES ON THE TOPIC OF THE DISSERTATION

- 1. Mustafayeva S.A. Мотивации больного и длительное мониторирование глюкозы как факторы эффективного влияния на течение сахарного диабета //-Baki: Azərbaycan Metabolizm Jurnalı, -2016. 1 (13), -s.16-20
- Mustafayeva S.A., Mirzazade V.A. Clinical case of type 2 diabetes remission // Georgiya: Georgian Medical News, -2018. 4 (277), p.34-39
- Mustafayeva S.A., Mirzazade V.A. Применение длительного мониторирования глюкозы аппаратом «DEXCOM» для оценки эффективности комбинированной терапии «метформин-гликлазид» у больного с первые выявленным сахарным диабетом типа 2 //-Baki: Azərbaycan Metabolizm Jurnali, -2018. 1 (15), -s.15-20
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- 5. Mustafayeva S.A. Показатель «Time in Range» в зависимости от степени нарушения системы контроля глюкозы // -Украина: Высник проблем быологии и медицини, -2020. 1(155), с. 167-170
- 6. Mustafayeva S.A., Mirzazade V.A. Frequency of hypoglycemia at patients with diabetes type 2 in Azerbaijan / Internation Diabetes Federation Congress, Abu Dhabi: -2017, 1p.
- 7. Mustafayeva S.A. Скорость изменения глюкозы как показатель функционального состояния островков Лангерганса / I Azərbaycan Diabet Konqressi, -Bakı, -2018, s.106-108
- Mustafayeva S.A., Mirzazade V.A. Rapid glucose changes as a feature of glycaemic instability in insulin-treated diabetes / V Beynəlxalq Bariatrik-Metabolik Cərrahiyyə Konqressi, -2019, p.146

ABBREVIATIONS

SD - standard deviation;

Conga – continuous overlapping net glycemic action;

LI - lability index;

J-index – index J;

LBGI – low blood glucose index;

HBGI – high blood glucose index;

MODD – mean of the day differences;

ADRR - average daily risk ratio;

M Value - average mean glucose index;

MAG - mean absolute glucose;

MAGE – mean amplitude of glycemic excursions;

GRADE – glycemic risk assessment in diabetes equation;

GMI- glucose management indicator;

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