Diabetes mellitus (DM) is a major public health concern that has serious social implications. By the end of 2017, type 2 DM had been diagnosed in 425 million of the world population. By 2045, this number will have reached 629 million. It is estimated that 212.4 million people worldwide do not know that they have type 2 DM [1]. In January 2018, the National Diabetes Registry reported that of 4.6 million Russian citizens diagnosed with DM, 4.1 million had type 2 DM [2]. Extrapolated results of the NATION cross-sectional study conducted in Russia suggest that about 20.7 million Russian residents are prediabetic and another 4.2 million do not know that they already have type 2 DM. Thus, the actual prevalence of type 2 DM in Russia is at least 5.5% (8 million people); 19.3% of Russians are prediabetic. The current situation with diabetes poses a serious threat to public health: at least 50% of the population do not know they are ill, do not receive any treatment and, therefore, are at high risk for complications [3, 4].

Between 2007 and 2012, the number of Russian patients with DM was increasing steadily by 6.23% (or 173,640) a year [5]. According to the report of the Federal Diabetes Mellitus Registry published on January 17, 2018, the prevalence of type 2 DM in Tambov region was 4,044.3 per 100,000 population.
Fig. 1. The study included 91 patients, who were then distributed into 3 groups depending on their blood sugar levels. Patients with FPG ≥ 7.0 mmol/L (measured in two repeated tests) were diagnosed with type 2 DM and prescribed adequate treatment. Patients with FPG between 6.1 and 6.9 mmol/L underwent an oral glucose tolerance test (OGTT). Patients with FPG between 5.6 and 6.0 mmol/L who were at risk for developing type 2 DM and metabolic syndrome also underwent OGTT.

FPG — fasting plasma glucose

<table>
<thead>
<tr>
<th>FPG test</th>
<th>n = 91</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.6–6.0</td>
<td>n = 35</td>
</tr>
<tr>
<td>6.1–6.9</td>
<td>n = 34</td>
</tr>
<tr>
<td>≥ 7.0</td>
<td>n = 22</td>
</tr>
</tbody>
</table>

Second FPG test

Type 2 DM

n = 22

Treatment

Fig. 1. The study included 91 patients, who were then distributed into 3 groups depending on their blood sugar levels. Patients with FPG ≥ 7.0 mmol/L (measured in two repeated tests) were diagnosed with type 2 DM and prescribed adequate treatment. Patients with FPG between 6.1 and 6.9 mmol/L underwent an oral glucose tolerance test (OGTT). Patients with FPG between 5.6 and 6.0 mmol/L who were at risk for developing type 2 DM and metabolic syndrome also underwent OGTT. FPG — fasting plasma glucose
The following exclusion criteria were applied: type 2 DM; type 1 DM; an exacerbation of any chronic disease; inflammation; a severe comorbidity; FPG < 5.6 mmol/L.

The patients were examined for the symptoms of metabolic syndrome and assessed for the risk of developing type 2 DM. According to IDF (2005), the main clinical manifestations of MS in Caucasian patients include abdominal obesity (waist circumference > 94 cm in men and > 80 cm in women) and two or more factors listed below [11]:
1) elevated triglycerides > 1.7 mmol/L or lipid-lowering therapy in progress;
2) low HDL (< 1.03 mmol/L in men and < 1.29 mmol/L in women) or lipid-lowering therapy in progress;
3) elevated blood pressure ≥ 130/85 mmHg or antihypertensive therapy in progress;
4) fasting blood sugar ≥ 5.6 mmol/L or previously diagnosed type 2 diabetes.

All patients with FPG falling in the range between 5.6 and 6.0, MS or at least one risk factor for type 2 DM underwent a 75-gram oral glucose tolerance test (OGTT). The schematic representation of the study is provided in Fig. 1.

The obtained data were processed in Statistica ver 6.1 (StatSoft; Russia). Because the Kolmogorov–Smirnov normality test revealed non-normal distribution, the nonparametric Mann–Whitney U-test was applied.

RESULTS

Of 91 patients included in the analysis, 22 (24.2%) had presented with complaints of fatigue, dry mouth, increased thirst, frequent urination, itchy skin, weight gain, or unstable blood pressure. Type 2 DM was confirmed in 22 patients (4 men; 18 women) aged 34 to 69 years whose FPG was ≥ 7.0 mmol/L in two repeated tests.

Thirty-five patients (38.4%) had FPG in the range from 5.6 to 6.0 mmol/L, metabolic syndrome and at least one risk factor for developing type 2 DM. In 34 patients (37.3%), FPG ranged from 6.1 to 6.9 mmol/L; 97.0% of such patients (or 33 out of 34) had symptoms of metabolic syndrome. An oral glucose tolerance test was ordered for all those patients.

Carbohydrate metabolism disorders were observed in 64.8% (n = 59) of the patients with borderline fasting blood sugar and at least one risk factor for type 2 DM; 34.0% (n = 31) of those individuals had never been diagnosed with type 2 DM before, and 30.7% (n = 28) were prediabetic. Twenty-two (24.1%) prediabetic patients had IGT.

All patients with new-onset type 2 DM (n = 31) had signs of metabolic syndrome. In 9 patients, type 2 DM was diagnosed based on OGTT.

Figure 3 shows the distribution of the patients depending on the severity of carbohydrate metabolism disorders revealed by OGTT in the group of 35 individuals with initial FPG between 5.6 and 6.0 mmol/L.

Figure 4 shows the distribution of the patients depending on the severity of carbohydrate metabolism disorders revealed by OGTT in the group of 34 patients with initial FPG between 6.1 and 6.9 mmol/L.

Clinical and demographic characteristics of the patients grouped by the severity of carbohydrate metabolism disorders (n = 91) are shown in Table 1.

OGTT conducted in 69 participants revealed that 13.0% (9 patients) had type 2 DM, 31.8% (22 patients) had IGT, and 8.7% (6 patients) had IFG. Normal fasting blood sugar levels were observed in 48.3% (32) of the participants (Table 2). Interestingly, the frequency of IFG cases was low.

Of 9 patients with new-onset type 2 DM, 3 had FPG between 5.6 and 6.0 mmol/L and 6 had FPG between 6.1 and 6.9 mmol/L.

The distribution of the patients depending on the severity of carbohydrate metabolism disorders (OGTT) in the groups with initial IFG levels ranging from 5.6 to 6.0 mmol/L (n = 35) and from 6.1 to 6.9 mmol/L (n = 34) is shown in Table 2.

OGTT demonstrated that 2.8% of the participants from the group with initial FPG between 5.6 and 6.0 mmol/L had IFG; the frequencies of IGT and type 2 DM cases were 11.5% and 4.3%, respectively. Thus, there were 14.4% prediabetic patients in the studied cohort.

Glucose tolerance was significantly less prevalent in the patients with FPG ranging from 6.1 to 6.9 mmol/L.

Most patients were over 45 years of age. This was true for 100% of the patients in the IFG and IGT groups and for 84.3% and 90.3% of the patients in the groups with normal carbohydrate metabolism and new-onset type 2 DM, respectively. All groups were dominated by overweight or obese patients. All patients had increased waist circumference. No significant differences were observed in the number of patients with a family history of type 2 DM (Table 1).

The number of patients with elevated blood pressure was significantly higher in the group with normal carbohydrate metabolism and prediabetes in comparison with the group with new-onset type 2 DM (p < 0.05).

No significant differences were detected between the groups in terms of lipid counts, chronic pancreatitis or the history of cardiovascular diseases (p > 0.05).

It should be noted that there were more patients with a history of elevated glucose levels in the group with new-onset DM (p > 0.05). Of 8 patients, only 2 had had their carbohydrate metabolism disorder and impaired glucose tolerance verified. Those patients had been receiving metformin for no longer than one year before the study and terminated the drug without consulting their physician. No diagnostic tests had been previously performed in the rest of the patients to assess their metabolic status.

Among 4 patients with IGT who had been diagnosed with elevated blood sugar between 2013 and 2018, one woman had been taking metformin for 6 years continuously (500 mg per day). This allowed her to stay at the prediabetic stage.
DISCUSSION

The incidence of type 2 DM in 91 study participants who had borderline fasting glucose levels and at least one risk factor for this condition was 34.0% (n = 31). IFG was diagnosed in 6.5% (n = 6) of patients and IGT, in 24.1% patients (n = 22). Thirty-two participants (35.1%) had normal glucose tolerance.

According to the NATION study, about 21 million Russian residents aged 20 to 79 years are prediabetic; another 4.2 million do not know they have type 2 DM [3]. In this study, a glycated hemoglobin test was used as a diagnostic criterion. This approach is an alternative to [12]; it has its advantages (higher specificity for type 2 DM) and drawbacks (lower specificity for prediabetic conditions) [13, 14].

Because at least 50% of patients with type 2 DM do not know they have it, we could be facing a situation when the criteria for patient eligibility for DM screening are not sufficiently sensitive. Depending on the country, different criteria are applied to identify groups at risk for type 2 DM. The Canadian Diabetes Association highlights the necessity of conducting screening for type 2 DM in all patients older than 40 regardless of the presence of specific risk factors [15]. The criteria proposed by the American Diabetes Association (ADA) include age over 45 years (regardless of the risk factors present) or

Table 1. Clinical and demographic characteristics of patients

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Norm  (n = 32)</th>
<th>IFG  (n = 6)</th>
<th>IGT  (n = 22)</th>
<th>Type 2 DM (n = 31)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>10 (31.2%)</td>
<td>3 (50.0%)</td>
<td>5 (22.7%)</td>
<td>6 (19.3%)</td>
</tr>
<tr>
<td>Women</td>
<td>22 (68.7%)</td>
<td>3 (50.0%)</td>
<td>17 (77.2%)</td>
<td>25 (80.6%)</td>
</tr>
<tr>
<td>Age ≥ 45 years</td>
<td>27 (84.3%)</td>
<td>6 (100%)</td>
<td>22 (100%)</td>
<td>28 (90.3%)</td>
</tr>
<tr>
<td>Family history of type 2 DM</td>
<td>2 (6.2%)</td>
<td>1 (16.6%)</td>
<td>6 (27.2%)</td>
<td>7 (22.5%)</td>
</tr>
<tr>
<td>BMi ≥ 25</td>
<td>30 (93.7%)</td>
<td>6 (100%)</td>
<td>21 (95.4%)</td>
<td>31 (100%)</td>
</tr>
<tr>
<td>WC &gt; 80 cm (women)</td>
<td>22 (100%)</td>
<td>3 (100%)</td>
<td>17 (100%)</td>
<td>25 (100%)</td>
</tr>
<tr>
<td>WC &gt; 94 cm (men)</td>
<td>10 (100%)</td>
<td>3 (100%)</td>
<td>5 (100%)</td>
<td>6 (100%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>32 (100.0%)</td>
<td>6 (100%)</td>
<td>22 (100.0%)</td>
<td>25 (80.6%)</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>21 (65.6%)</td>
<td>6 (100%)</td>
<td>15 (68.1%)</td>
<td>18 (58.0%)</td>
</tr>
<tr>
<td>Chronic pancreatitis</td>
<td>3 (9.3%)</td>
<td>1 (16.6%)</td>
<td>3 (13.6%)</td>
<td>5 (16.1%)</td>
</tr>
<tr>
<td>Cardiovascular diseases</td>
<td>9 (28.1%)</td>
<td>2 (33.3%)</td>
<td>4 (18.1%)</td>
<td>8 (25.8%)</td>
</tr>
<tr>
<td>AMI</td>
<td>3 (9.3%)</td>
<td>1 (16.6%)</td>
<td>2 (9.0%)</td>
<td>3 (9.8%)</td>
</tr>
<tr>
<td>ACE</td>
<td>3 (9.3%)</td>
<td>0 (0%)</td>
<td>1 (4.5%)</td>
<td>0 (0%)</td>
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<tr>
<td>TIA</td>
<td>1 (3.1%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>2 (6.4%)</td>
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<tr>
<td>Peripheral artery disease</td>
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<td>1 (16.6%)</td>
<td>1 (4.5%)</td>
<td>3 (9.6%)</td>
</tr>
<tr>
<td>History of hyperglycemia</td>
<td>3 (9.3%)</td>
<td>2 (33.3%)</td>
<td>4 (18.1%)</td>
<td>8 (25.8%)</td>
</tr>
</tbody>
</table>

Note: *— differences are significant, p < 0.05; BMI — body mass index; IFG — impaired fasting glucose; IGT— impaired glucose tolerance; AMI — acute myocardial infarction; ACE — acute cerebrovascular event; WC — waist circumference; OGTT— oral glucose tolerance test; DM — diabetes mellitus; TIA — transient ischemic attack.

Table 2. The distribution of the patients depending on the severity of carbohydrate metabolism disorders (OGTT)

<table>
<thead>
<tr>
<th>Carbohydrate metabolism</th>
<th>FPG 5.6–6.0</th>
<th>FPG 6.1–6.9</th>
<th>X2/ρ</th>
<th>ρ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>22 (31.8%)</td>
<td>10 (14.4%)</td>
<td>6.5</td>
<td>0.011*</td>
</tr>
<tr>
<td>IFG</td>
<td>2 (2.8%)</td>
<td>4 (5.7%)</td>
<td>0.43</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>IGT</td>
<td>8 (11.5%)</td>
<td>14 (20.2%)</td>
<td>1.9</td>
<td>0.17</td>
</tr>
<tr>
<td>DM</td>
<td>3 (4.3%)</td>
<td>6 (8.6%)</td>
<td>0.3</td>
<td>&gt; 0.05</td>
</tr>
</tbody>
</table>

Note: *— differences are significant, p < 0.05; FPG — fasting plasma glucose; IFG — impaired fasting glucose; IGT— impaired glucose tolerance; OGTT— oral glucose tolerance test; DM — diabetes mellitus. In the subgroup of patients with FPG levels ranging from 5.6 to 6.0 mmol/L, there were 2.8% cases of IFG, 11.5% cases of IGT and 4.3% cases of type 2 DM (based on OGTT results). Thus, the frequency of prediabetic conditions in the subgroup was 14.4%. The frequency of IGT was significantly lower in the subgroup with FPG between 6.1 and 6.9 mmol/L.
Fig. 3. The distribution of the patients depending on the severity of carbohydrate metabolism disorders revealed by OGTT in the group of 35 individuals with initial FPG between 5.6 and 6.0 mmol/L. IFG — impaired fasting glucose; IGT — impaired glucose tolerance; OGTT — oral glucose tolerance test.

Fig. 4. The distribution of the patients depending on the severity of carbohydrate metabolism disorders revealed by OGTT in the group of 34 individuals with initial FPG between 6.1 and 6.9 mmol/L. IFG — impaired fasting glucose; IGT — impaired glucose tolerance; OGTT — oral glucose tolerance test.

Our study has demonstrated the need for covering broader populations in the groups at risk for type 2 DM. We have provided a rationale for performing a 75-gram oral glucose tolerance test in all individuals with FPG between 5.6 and 6.0 mmol/L who have at least one risk factor for type 2 DM and/or metabolic syndrome. In our study, DM was diagnosed in 4.3% of such patients; another 14.4% were prediabetic. Early diagnosis of carbohydrate metabolism disorders and timely medication therapy would help to prevent development of DM 2 in prediabetic patients. Timely diagnosis and treatment of type 2 DM could prevent possible complications.

CONCLUSIONS

1) Screening for carbohydrate metabolism disorders in patients with borderline fasting glucose has revealed that the actual prevalence of type 2 DM is three times higher than reported.

2) Screening should be performed in patients at risk for type 2 DM using a FPG test even in the absence of clinical manifestations of diabetes in such patients.

3) A 75-gram oral glucose tolerance test should be performed in all patients with metabolic syndrome and/or one or more risk factors for type 2 DM with FPG between 6.1 and 6.9 mmol/L, as well as those who have FPG ranging from 5.6 to 6.0 mmol/L.

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