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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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GESTATIONAL DIABETES: PREVALENCE AND RISKS FOR THE MOTHER AND CHILD (REVIEW)

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Abstract.

Gestational diabetes mellitus (GDM) is chronic hyperglycemia during gestation in women without previously diagnosed diabetes. This hyperglycemia is caused by impaired glucose tolerance due to pancreatic β-cell dysfunction in the setting of chronic insulin resistance. GDM has been found to affect approximately 4-16.5% of pregnant women worldwide. The large range of prevalence is associated with different approaches to the diagnosis of gestational diabetes, which are addressed in recent organizational documents but have not yet been introduced into wide clinical practice, and therefore prevalence figures vary between countries, as well as between regions of one country. Studies have shown that overweight and obese patients or people with a family history of any form of diabetes are more likely to have GDM and the incidence of GDM increases with the age of the pregnant woman. It has been proven that half of the cases of GDM occur as a relapse in a subsequent pregnancy. Consequences of GDM include an increased risk of maternal cardiovascular disease and type 2 diabetes, as well as macrosomia and birth complications in the infant. There is also a long-term risk of obesity, type 2 diabetes, and cardiovascular disease in the child.

Conclusion: Despite the fact that management strategies, insulin therapy, and behavioral therapy have been discussed for a long time, the effectiveness of these methods is insufficient. This review discusses what is currently known about the epidemiology, pathophysiology of GDM, and maternal and child outcomes.

Keywords. Gestational diabetes, pregnancy, epidemiology, pathophysiology, effects on the mother, effects on the fetus.

Introduction.

Gestational diabetes mellitus (GSD) is a formidable complication of pregnancy in which an increased level of glycemia leads to severe consequences for the child and mother. The high prevalence of this condition explains the growing relevance of studying all aspects of this pathology. According to the report of the International Diabetes Federation (IDF) for 2019, 12.8% of pregnant women suffer from it worldwide [1]. Overweight and obesity, a family history of diabetes, a history of stillbirth, a history of abortions, chronic hypertension and previous GSD, malnutrition, macro, and micronutrients were recognized as risk factors [2-4]. In most cases, glycemia may return to normal after childbirth, but short- and long-term consequences include an increased risk of type 2 diabetes, cardiovascular diseases, and the development of obesity, which affects the health of the population as a whole [5,6].

In some studies, it has been demonstrated that the recurrence of gestational diabetes was repeated in subsequent pregnancies in about half of the cases [7,8]. For example, the total recurrence rate of GSD was 48%. A significant relationship was found between ethnicity and the frequency of recurrent GSD [9].

Treatment strategies, including diet, exercise, and insulin therapy, do not meet the expectations of most specialists due to the low effectiveness and adherence of patients. Insulin therapy is often limited due to insulin resistance [10].

Epidemiology.

According to the Atlas of the International Diabetes Federation, in 2019, the prevalence of hyperglycemia in pregnant women was about 15.8%, of which 83.6% of cases were associated with GSD [11]. The diagnosis of GSD has been undergoing changes in recent years. Studies of maternal glycemia and glucose metabolism in childhood by HAPO conducted in 2000-2008 set the task of revising the WHO diagnostic criteria for GSD. It turned out that among the observed women, unfavorable pregnancy outcomes increased in direct proportion, starting with a significantly lower level of glycemia than was accepted at that time as a criterion of GSD [12]. Back in 2008-2010, the International Association of Diabetes and Pregnancy Study Groups (IADPSG) proposed for discussion new criteria for the diagnosis of GSD, which were independently adopted by the USA, Japan, Germany, Israel [13,14]. These criteria are given in internationally recognized documents of organizations such as the World Health Organization, the American Diabetes Association, and the European Association for the Study of Diabetes [15,16]. In Kazakhstan, in 2022, the Association of Endocrinologists of Kazakhstan under the leadership of Bazarbekova R.B. has already released the sixth edition of the "Consensus on the diagnosis and treatment of diabetes mellitus", which takes into account all the updated criteria of GSD. According to this document, GSD is set during PGTT (oral test with a load of 75 grams of glucose) with fasting plasma glycemia more than or equal to 5.1 and less than 7.0 mmol/l, an hour after the load – more than or equal to 10 mmol/l, after 2 hours no more or equal to 8.5 mmol/l [17].

In the light of the new recommendations, prevalence studies have already been conducted in which diagnosis is carried out according to updated criteria. However, studies of pregnant women with GSD in Kazakhstan are still insufficient.

A recent analysis of 51 population studies of 5,349,476 pregnant women conducted in 2019 showed that the cumulative overall prevalence of GSD, regardless of the type of threshold screening categories, was 4.4%. At the same time, the cumulative overall prevalence of GSD at the diagnostic threshold used in the IADPSG criteria was 10.6%, which is the highest prevalence of GSD among the included studies. It turned out that the prevalence of GSD among studies that used the IADPSG criteria was significantly higher (6-11 times) than in other subgroups. The highest and lowest prevalence of GSD, regardless of screening criteria, was recorded in East Asia (11.4%) and Australia (3.6%), respectively [18].

In 2018, the prevalence of GSD in the United States of America among 8185 women was found to be equal to 7.6%. Mexican American women (compared to non-Hispanic whites), most had a family history of diabetes or were obese, and they also had a higher age-standardized prevalence of GSD. Among women with a history of GSD, 19.7% were subsequently diagnosed with diabetes mellitus, they also had a family history of diabetes and obesity and was associated with a lower level of education and income [19]. Another large-scale American study of 12,610,235 women showed an increase in GSD from 2011 to 2019 of all indicators of gestational diabetes in all racial and ethnic subgroups from 47.6 to 63.5 per 1,000 live births. The level of gestational diabetes was highest in participants of Asian origin, the indicator of gestational diabetes was 129.1 per 1000 live births [20].

In Europe, the prevalence situation was different depending on the regions. The overall weighted prevalence of GSD in 24 European countries was estimated at 10.9%. At the same time, higher prevalence values were observed in Eastern and Southern Europe than in Northern and Central Europe. The prevalence of GSD was highest in Eastern Europe (31.5%), followed by Southern Europe (12.3%) Western Europe (10.7%) and Northern Europe (8.9%). The prevalence of GSD was 2.14 times higher in pregnant women with maternal age ≥30 years (compared with 15-29 years), 1.47 times if the diagnosis was made in the third trimester (compared with the second trimester), and 6.79 times in obese women and 2.29 times in overweight women (compared to normal weight) [21].

In the Eastern Mediterranean region, 33 studies involving 887,166 people showed that the overall prevalence of GSD was 11.7%. An analysis of the situation in six countries showed that the cumulative prevalence in Saudi Arabia was 3.6 times higher than in Israel (17.6 *vs.* 4.9%), and in Pakistan, Qatar, Bahrain, and Iran — 15.3%, 14.7%, 12.2% and 8.6%, respectively [22]. Another study analyzing data from 2000-2019 with the inclusion of 279,202 women from the Middle East and North Africa region showed an increase in the prevalence of GSD from 10.6% in studies conducted before 2009 to 14.0% in studies conducted later [23].

The prevalence of GSD in Turkey was calculated as 7.7%. It was noted that the highest combined prevalence of GSD was 17.6% in the Black Sea region, and the lowest was 5.1% in the Central Anatolian region. The most frequent risk factors were the elderly age of the mother, overweight before pregnancy, weight gain during pregnancy, diabetes in the family, a history of GSD or the birth of a large child [24].

Studies conducted in India in 2019 revealed significant differences in the prevalence of gestational diabetes depending on the state, socio-economic status and demographic factors. A survey of 1,746 pregnant women with an average age of 24.3 years showed a weighted prevalence of gestational diabetes adjusted for age-1.3%. The prevalence of gestational diabetes increased with age, from 1.0% aged 15 to 19 years to 2.4% aged 35 years and older. The age-adjusted prevalence of gestational diabetes was higher among women with a body mass index of 27.5 and higher (1.8%); compared with women with a body mass index of less than 18.5 (0.8%). Researchers explain such low prevalence figures by insufficient diagnosis of GSD at the primary stage, the non-use of modern methods for detecting gestational diabetes [25]. At the same time, other studies in India, for example, in the state of Tamil Nadu, revealed the prevalence of GSD in three conditions: 17.8% in cities, 13.8% in suburbs and 9.9% in rural areas, which is more close to the truth and confirmed by similar studies [26-28].

The combined prevalence of GSD in Africa was 13.61% and 14.28% in sub-Saharan Africa. The prevalence was highest in the subregions of Central Africa — 20.4% and lowest in the subregions of North Africa — 7.57%. The study data also showed that overweight and obesity, macrosomia, family history of diabetes, a history of stillbirth, a history of abortions, chronic hypertension and previous GSD are positively associated with GSD [29].

According to recent researchers in Asia, the overall prevalence of GSD according to the latest data was 11.5%. The prevalence of GSD in Asian countries with lower or higher middle income was about 64% higher than in high-income countries, and the one-stage screening method was twice as often used for the diagnosis of GSD compared to the two-stage screening procedure [30].

The overall incidence of GSD in mainland China was higher and amounted to 14.8% when analyzing studies with a total of 79,064 pregnant women examined. The analysis of the subgroups also showed that age, body weight and family history of diabetes mellitus can significantly increase the incidence of GSD [31].

According to a few epidemiological studies in Russia, it was found that GSD complicates the course of pregnancy in 2-9.2% of cases [32,33].

In Kazakhstan, data on the prevalence of gestational diabetes are few. One study is available where the complications of GSD were assessed in 66 women; the manifestation of gestational hypertension was revealed in 36.1%, preeclampsia was diagnosed in 14.8%, it was also revealed that disorders of uteroplacental and fetoplacental blood flow, diabetic fetopathy, preterm labor, predominance of labor induction and intranatal trauma were more common in the group of pregnant women with GSD [34].

Pathogenesis.

In GSD, the most important factor is considered to be the loss of the ability of beta cells to adequately determine the concentration of glucose in the blood or release a sufficient amount of insulin in response (beta cell dysfunction). Studies have shown that pancreatic cells containing significant glycogen stores showed increased apoptosis, that is, the onset of cell destruction, while beta cells containing no glycogen were protected [35].

B-cell dysfunction is aggravated by insulin resistance. A decrease in insulin-stimulated glucose uptake also contributes to hyperglycemia, overloading beta cells, which in response must produce additional insulin. The direct contribution of glucose to β-cell failure is described as glucose toxicity [36]. Thus, as soon as β-cell dysfunction begins, a vicious cycle of hyperglycemia, insulin resistance and further β-cell dysfunction begins.

The role of hyperlipidemia is also important in the pathogenesis of GSD. When studying the placenta using microchip profiling of women with type 1 diabetes and GSD, it was found that diabetes was associated with 49 changes in gene expression at key stages of placental energy metabolism, while 67% of the changes were associated with lipid pathways and 9% of the changes were associated with glucose pathways. Predominant activation of lipid genes was observed during pregnancy with GSD [37].

It is claimed that the production of placental leptin increases with GSD, probably as a result of the placenta's resistance to insulin, which further contributes to hyperleptinemia. It is also believed that it facilitates the transport of amino acids through the placenta, contributing to fetal macrosomia [38].

No small importance is attached to failures in the work of antioxidant systems [39]. Thus, homocysteine levels were significantly increased in women with GSD compared to women without GSD. This evidence was more consistent when measuring homocysteine in the second trimester and for women over 30 years of age [40].

Consequences of GSD for the mother.

Patients with GSD have higher rates of maternal and perinatal morbidity. GSD is an independent risk factor for the future long-term risk of developing type 2 diabetes mellitus (DM2), metabolic syndrome, cardiovascular diseases, malignant neoplasms, ophthalmological, mental and renal diseases in the mother. Long-term adverse effects on the health of offspring include DM2, subsequent obesity, effects on the outcomes of the development of the nervous system, increased neuropsychiatric morbidity and ophthalmological diseases [41].

In 2019, an analysis of studies involving 1,332,373 people showed that women with a history of GSD had a risk of developing DM2 almost 10 times higher than women with normoglycemic pregnancy. In populations of women with previous GSD, the cumulative incidence of DM2 was 16.46% in women of mixed ethnicity, 15.58% in the predominantly non-white population, and 9.91% among the white population [42].

In a recent study in Kazakhstan, when studying the outcomes of pregnant women with 4 types of diabetes, it turned out that gestational diabetes mellitus, in comparison with other types of diabetes, causes premature rupture of fetal membranes more. Some types of maternal pregnancy complications were registered in almost 85% of the examined patients with diabetes in the cohort. Noteworthy in this study is the relative favorable outcome of pregnancy for children, the average score on the Apgar scale was above 7. Fetal malformations were most common in women with pre-existing diabetes who did not require insulin therapy. At the same time, 36.85% of children had early neonatal complications [43].

It is indicative of the observation of 435 women with GSD after childbirth for 5.7 years, which showed that 28% of them developed metabolic syndrome. However, 13% of them had this syndrome within one year after pregnancy, in addition, 8% were diagnosed with manifest diabetes after pregnancy [44].

An analysis of the consequences of 4,928 deliveries of patients with GSD found higher rates of cardiovascular morbidity, including non-invasive cardiological diagnostic procedures, simple cardiovascular events and the total number of hospitalizations for cardiovascular diseases [45].

A retrospective cohort study conducted in 2019 found that the frequency of outcomes of patients with GSD with good glycemic control and GSD with poor glycemic control was as follows: DM2 -38% and 57%; arterial hypertension 18% and 20%; obesity 48% and 58%; and dyslipidemia 29% and 48%, respectively, which indicates about the need for good glycemic control and the risks of complications [45].

There is also a risk of neoplasms. A long-term cohort study of 753 women in New Zealand who underwent a glucose test at 13 weeks of pregnancy found a positive association between higher glucose levels and an increased risk of breast cancer [46]. However, another broader study of African women on the association of breast cancer with GSD showed negative results [47].

Israeli scientists observed 37926 women and found five cases of pancreatic cancer in women with gestational diabetes. The interval between the registration of diabetes mellitus during pregnancy and the diagnosis of pancreatic cancer ranged from 14-35 years. The subjects with a history of gestational diabetes showed a relative risk of pancreatic cancer of 7.1, which indicates that GSD is closely associated with the risk of developing cancer in this category of women [48].

When studying the frequency of long-term maternal ophthalmological diseases in a cohort of women with GSD, it was shown that patients with GSD had a significantly higher frequency of ophthalmological diseases, such as glaucoma, diabetic retinopathy and retinal detachment, compared with the control group [49].

As a result of a study of 97,968 women, it was found that GSD is a significant risk factor for renal pathology in the mother in the future. The risk was more significant for patients with recurrent episodes of GSD [50].

Data from a recent Greek cohort study established a close relationship between gestational diabetes and perinatal depressive symptoms [51].

Consequences of GSD for a child.

Studies have shown that the risk of obesity, metabolic syndrome, type 2 diabetes and impaired sensitivity and insulin secretion in the offspring of mothers with GSD is two to eight times higher than in the offspring of mothers without GSD. The main pathogenetic mechanisms underlying the abnormal metabolic risk profile in offspring are unknown, but epigenetic changes caused by exposure to maternal hyperglycemia during intrauterine life are assumed [35,52]

Of particular importance is fetal macrosomia, defined as birth weight ≥ 4000 g, found in 12% of newborns from normal women and from 15 to 45% of newborns from women with GSD. It is believed that the intake of excess glucose to the fetus

after insulin resistance leads to fat deposits, causing macrosomia. For a child, macrosomy increases the risk of shoulder dystocia, collarbone fractures and brachial plexus injury and increases the frequency of hospitalizations to the neonatal intensive care unit [53].

In the study of 298 offspring of mothers with GSD and impaired glucose tolerance, the BMI of offspring of mothers with GSD was significantly higher when analyzed by age. In the offspring of mothers with GSD, risk factors for cardiovascular diseases were positively correlated with age, with the exception of the lipid profile [54].

A recent CANDLE study confirmed that maternal obesity before pregnancy, excessive gestational weight gain and GSD individually and collectively predict rapid growth and obesity at the age of 4 years in offspring, regardless of race [55].

Conclusion

We have conducted a review on gestational diabetes over the past 5-10 years, perhaps it has limitations since there is a huge amount of research on this issue. We found out that the prevalence of gestational diabetes is increasing all over the world and there is a lot of undiagnosed GSD. The pathogenesis of this disease is still ambiguous and requires additional study. Due to the rapid growth of diabetes worldwide, it is necessary to take into account that GSD, according to most studies, generates diabetes in mother and child, which makes a negative contribution to the overall picture of the diabetes pandemic. Large cohort studies and meta-analyses indicate the importance of prevention and timely treatment of this disease due to the dangerous consequences for mothers and their offspring. We found that very few studies on gestational diabetes are conducted in Kazakhstan, although the Consensus reflects special diagnostic criteria that meet international standards. More research is needed because GSD complicates the course of pregnancy and has severe consequences for public health.

Compliance with ethical standards.

The study was approved by the local ethical commission of the Non-Profit Joint-Stock Company Kazakh National Medical University. S.D. Asfendiyarov" (Almaty, Kazakhstan), application No. 1121 dated April 28, 2021.

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