

# GEORGIAN MEDICAL NEWS

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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 ВИНТИ 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 ВИНТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

### WEBSITE

[www.geomednews.com](http://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](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. Корректур авторам не высылаются, 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 computer-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.nlm.nih.gov/bsd/uniform_requirements.html)  
[http://www.icmje.org/urm\\_full.pdf](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 საქურაღებოლ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დაიცვათ 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 შედეგის 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 ფხიხლებში 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.

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## AN INCREASED RISK OF HORMONAL DISORDERS, PRIMARILY DIABETES, IN INDIVIDUALS WITH B -THALASSEMIA MAJOR: A RETROSPECTIVE ANALYSIS

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### Abstract.

**Background:**  $\beta$ -Thalassemia major is an inherited blood condition marked by a serious anemia and a lifetime need for blood transfusions. The effects of  $\beta$ -thalassemia major on endocrine health, notably the risk of diabetes, remain largely unstudied, despite the fact that its haematological components are established. The purpose of this systematic analysis was to examine the incidence of reduced metabolism of glucose in  $\beta$ -thalassemia major.

**Methods:** The articles were under the inclusion requirements, after which the data was retrieved. The main outcome was determined to be every prevalence (P) of DM (diabetes mellitus) in  $\beta$ -thalassemia major. In order to examine the percentage of aberrant glucose metabolism (GM) with individuals among  $\beta$ -thalassemia major, the P with the 95% CI (Confidence Interval) was utilized. In this retrospective investigation, we looked at a cohort of people with  $\beta$ -thalassemia major diagnoses to determine the incidence and risk of hormonal diseases, particularly diabetes. A specialist thalassemia facility treated 315 individuals with  $\beta$ -thalassemia major, and their medical records were examined. Age, gender, age at which a main diagnosis of  $\beta$ -thalassemia was made, the length of transfusion treatment, and concomitant diseases were gathered as part of the demographic and clinical data.

**Result:** Our research, which included 17 studies and 1500 cases altogether, showed that with  $\beta$ -thalassemia major had a considerably greater frequency of diabetes than people in general. With a mean beginning age of 30 years, diabetes was identified in 28% of the research cohort's participants. The combined meta-analysis showed that each year had a rather stable level of DM P in  $\beta$ -thalassemia major. In people with major  $\beta$ -thalassemia, the P of impaired fasting glucose (IFG), DM, and impaired glucose tolerance (IGT) was 17.22% (95% CI: 8.44%-26.02%), (6.57 (95% CI: 5.31%- 7.79%) and 12.47 % (95% CI: 5.97%-18.95%), respectively.

**Conclusion:** Our research suggests that people with  $\beta$ -thalassemia major have a high chance of acquiring diabetes, particularly if they get extended transfusion treatment. For prompt diagnosis and care, early detection of diabetes and other hormonal problems in this group is crucial. In  $\beta$ -thalassemia major, there is a high frequency of endocrine problems, including improper GM. To stop growth and endocrine issues, treatment and preventative measures can be required.

**Key words.**  $\beta$ -thalassemia, diabetes mellitus (DM), transfusion treatment, glucose, and hormonal disorder.

### Introduction.

The most common inherited disease in the world is thalassemia. A wide range of genetic defects linked to decreased hemoglobin chain production make up this disease.

Chronic hemolysis and inefficient erythropoiesis will arise from a deficiency of hemoglobin chains if the body cannot manufacture. In early childhood, when this anemia first manifests and lasts the rest of one's life.

This kind of thalassemia is known as  $\beta$ -thalassemia if it affects the  $\alpha$ -chain of hemoglobin. In contrast,  $\beta$ -thalassemia is caused by a decrease in the production of the  $\beta$ -chain of hemoglobin [1]. The extreme persistent hemolytic anemia that  $\beta$ -thalassemia major patients have necessitates many blood transfusions starting in infancy. Iron chelation therapy (ICT) is used in conjunction with chronic blood transfusion therapy to avoid the negative effects of iron overload, such as cardiac morbidity, liver illness, and endocrine dysfunction [2]. An inherited blood condition known as  $\beta$ -thalassemia major causes inadequate formation of  $\beta$ -globin chains, which causes severe anemia and needs a frequent blood transfusion. Although  $\beta$ -thalassemia's hematological components have received much study, the new data point to a potential link among this condition and hormonal diseases, particularly diabetes [3]. A blood sugar level out of equilibrium is the main characteristic of diabetes, a chronic metabolic condition. The body's capacity to make or properly use the hormone insulin, which controls blood sugar, is compromised in diabetes. Hyperglycemia, or increased blood glucose levels is the result of a variety of negative impacts on different organ systems. Type 1 (T1D) diabetes is distinguished by an autoimmune attack on pancreas cells are those that produce insulin, while type 2 diabetes (T2D) is characterized by insulin resistance is connected to hereditary and lifestyle factors [4]. The severe hereditary blood condition  $\beta$ -thalassemia major presents a wide range of health problems for sufferers. The characteristic of the disease is a weakened ability to produce healthy red blood cells, but new studies have revealed a worrying link among  $\beta$ -thalassemia major and hormonal diseases, particularly diabetes [5]. This research aims to determine that particular treatment approaches, including therapeutic chelation or transfusion regimens, significantly affect the risk of diabetes in people with  $\beta$ -thalassemia major.

In a study [6] a cohort of women across the country at high risk of injury was examined to determine the effects of diabetes and obesity on bone health. They conducted sensitivity analyses using obese non-diabetic individuals and obese non-



diabetic patients, correspondingly, to quantify the individual impact of diabetes and obesity on bone health. The findings should increase vigilance while examining obese and diabetic individuals in clinical practice.

In a study [7] a uric acid research has developed, especially in the investigation of metabolic conditions, it has been found to be linked with various metabolic diseases such as nonalcoholic fatty liver disease, obesity, metabolic syndrome, and diabetes. Through the analysis of the path physiology and clinical trials, the study verified the favorable relationship among DM and uric acid as well as its long-term effects. The study [8] examined the relationships among PCOS and T2D, coronary heart disease (CHD), and they carried out a two-sample Mendelian randomization research. Diabetes and cardiovascular disease have been linked to polycystic ovarian syndrome (PCOS). However, it needs to be clarified whether this connection was causal. The study [9] investigated to discover candidate genes associated with complications of diabetes utilizing candidate gene studies susceptible to false positives, familial linkage analysis suitable for major impact genes, and underpowered genome-wide association studies (GWAS) constrained by sample size. Diabetes was predicted to affect 694 million people by 2040, making it one of the illnesses with the greatest rates of worldwide growth. For those with diabetes, devastating micro vascular and macro vascular consequences cause blindness, renal malfunction, raise mortality rate and generally lower quality of life. In study [10] described a diabetic individuals use a glucometer to assess their blood glucose levels quickly and fairly accurately. The eyeglass biosensors, SwEatch, glucose-sensing patch, breath analysis, etc., are a few of the more sophisticated and least intrusive techniques. Although a great deal of data has been collected and studied on diabetes, the exact biological process by which T2DM is acquired remains unclear. The study [11] determined patients with  $\beta$ -thalassemia major (TM) experience iron-related problems such as short stature, growth slowdown, and growth hormone deficit. Traditional treatments for  $\beta$ -thalassemia ( $\beta$ -thal) include blood transfusions, which increase the anemia and lifespan of patients but also increase the possibility of iron excess in hormonal glands and parenchymal cellular components, which can result in these organs' dysfunction because the body can't get rid of the extra iron naturally. The study [12] described a most genetic diseases in the world are thalassemias, a diverse collection of inheritable illnesses defined by the insufficient synthesis of one or more hemoglobin (Hb) chains. As a result, unstable non-thalassemic Hb chains build up and precipitate, destroying erythroid precursors inside the medullary cavity and causing premature red blood cell (RBC) lysis in the peripheral blood. This systematic research was conducted to investigate the frequency of decreased glucose metabolism in  $\beta$ -thalassemia major patients.

### Materials and Methods.

In this section, we observed that specific treatment strategies, such as transfusion regimens or therapeutic chelation, have a significant impact on the risk of diabetes in individuals with  $\beta$ -thalassemia major. To ensure the validity and consistency of our research, we complied with the guidelines provided by

the Meta-study of Observational Research in Epidemiology (MOOSE).

### Search Techniques.

We set out to investigate an improper growth and maturation GM in people with  $\beta$ -thalassemia major, a genetic blood illness, by conducting an exhaustive and objective evaluation of all published literature on the subject. In order to mitigate any biases and get a comprehensive viewpoint, we purposefully avoided limiting our investigation to a particular geographic area, so enabling us to examine an extensive array of observations and data sources. In order to locate a wide range of pertinent research, we consulted several academic databases that are well-known for their abundance of resources and research papers. We searched through a wide range of literature using Google Scholar, mdpi, Springer link, and Hindawi. The objective of this strategy was to provide a more comprehensive examination of the subject by including diverse research approaches, people, and geographic regions. We followed the principles provided in the Meta-study of Observational Research in Epidemiology (MOOSE) guidelines to guarantee the accuracy and consistency of our study. These standards set the gold standard for systematic reviews and meta-analyses and give our research process a strict structure. We sought to uphold a high standard of gathering and analyzing information along the study by adhering to these guidelines.

### Requirements for inclusion and exclusion.

The crucial inclusion and exclusion of our study is depicted in Figure 1.

### Extracting data and evaluating its quality.

The two authors separately chose the trials and from each included study, they gathered data on the format, criterion of selection, facts or P of impaired GM in  $\beta$ -thalassemia major, initial evaluations, as well as excellence evaluations. We utilized approximated values derived from the Cochrane Handbook in our evaluation to fill in the gaps in the information that it was not possible for us to receive from the principal researchers. Every investigation considered for inclusion had its methodological quality evaluated per standards outlined in published guidelines for observational research. The following items were included on the checklist for evaluating key terms: the method used to collect the data, that the results will be biased, a description of potential confounders, the study's goals, the patient baseline, and statistical information. Five was the final score. Studies were disqualified as being of low quality if their scores were four or more down.

### Statistical Evaluation.

Using SPSS software version 24, the meta-analysis was carried out. For every investigation, Google Scholar was used to determine P with 95% confidence intervals. The Wald method's findings were applied if  $m(1-o) > 5$  or  $m_o > 5$ , where m denotes the total amount as well as o indicates the P in the group. In all other cases ( $m_o \leq 5$  or  $m(1-o) \leq 5$ ), the correct prediction technique's Mid-P was chosen. Using the chi-square and I<sup>2</sup> statistics, heterogeneity was evaluated. It was deemed important at O values  $< 0.05$  for chi-square and  $> 50\%$  for I<sup>2</sup>. We performed an analysis for sensitivity to identify a causes of heterogeneity

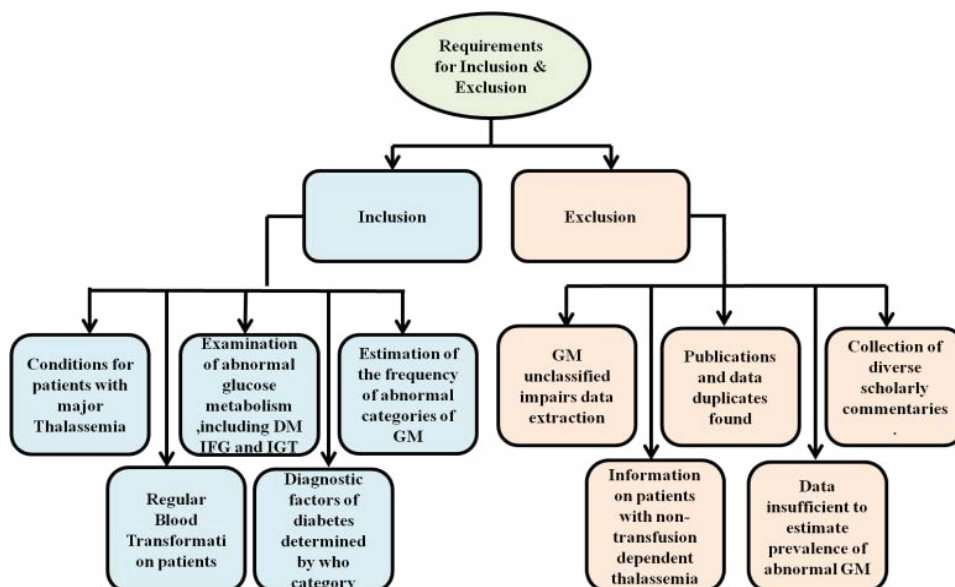


Figure 1. Flow for inclusion and exclusion criterion.

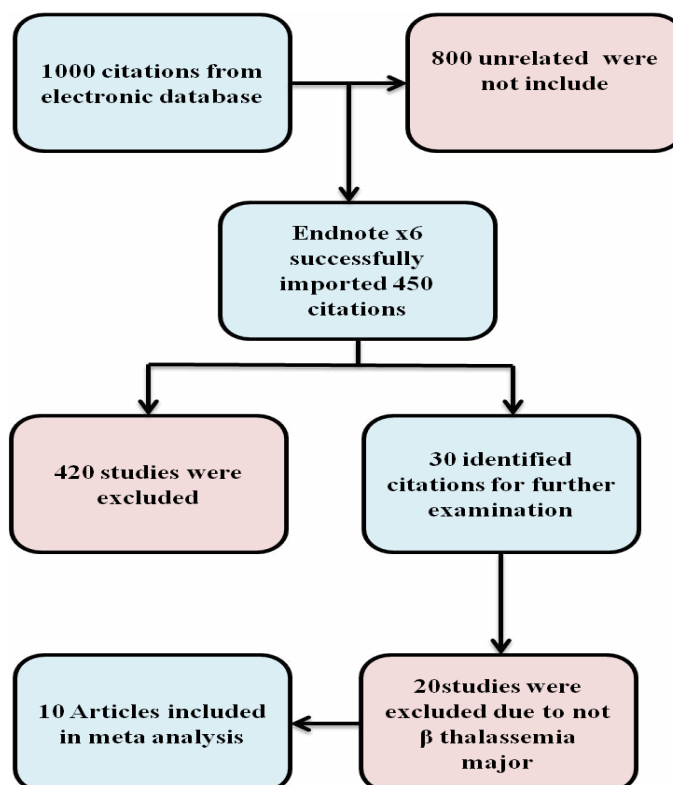


Figure 2. Testing flow chart.

if  $I^2$  was greater than 50%. The variation in blood ferritin levels among the groups with abnormal and normal GM was determined using the standard mean difference (SMD) due to the variability of the assessment unit. The random effects model was used when a significant Q-test with  $O < 0.05$  or  $I^2 > 50\%$  revealed proof of heterogeneity. In all other cases, the fixed-effects approach was used. Because the former incorporates both in study variation and among-study sampling errors in assessing the confidence for the results of a meta-analysis. We used the random-effects model rather than the fixed impacts model in

cases of heterogeneity. The 95% CI of every P was determined to establish the variation in the study result. When the 95% CI excludes 0, an outcome determined is deemed statistically significant. When missing information could not be obtained, values were calculated using techniques based on the frequency of instances of impaired GM in  $\beta$ -thalassemia major. Missing data was obtained from the study authors. The heterogeneity by publication year was further discussed using sensitivity tests and Meta regression evaluation. Figure 2 shows the PRISMA guidelines.

## Findings.

A total of 1000 items were found when we identified for impaired GM and  $\beta$ -thalassemia major in Mdpi, Springer, and Hindawi. We found that some of these researches were unhelpful because they looked at additional illnesses, deficiencies with P, therapies, etc. 450 items were screened and found to be appropriate for abstract reading. A total of 17 studies covering references from 30 full-text papers were included in this meta-analysis. In our investigation, 1500 instances with a significant diagnosis of  $\beta$ -thalassemia were totaled. 10 studies demonstrated the connection between low serum ferritin (SF) and poor GM which is one of the foremost important markers of endocrinopathy in  $\beta$ -thalassemia major. The mean SF level was extensively superior in the impaired GM team as contrasted to the normal glucose metabolism team. Table 1 represents the studies we taken for the analysis.

### DM prevalence (P) in major $\beta$ -thalassemia.

Elevated blood glucose levels are a defining feature of DM, sometimes referred as diabetes. Either T1D or T2D are the causes of this. Numerous health issues, such as renal disease, dementia, eyesight damage, and neuropathy can be brought by diabetes. Its treatment usually entails medication, lifestyle changes, and occasionally insulin therapy. It is a major worldwide health concern. Six studies in total evaluated DM. The publication years were 2020 through 2022. The percentage of people with T1D ranged from 0.00% to 26.68%. Table 2 represents the classification of glucose metabolism in  $\beta$ -thalassemia patients.

The P of DM in people with major  $\beta$ -thalassemia is 6.57%, according to the meta-analysis. A subgroup analysis revealed a P of 5.37% along the Mediterranean Coast. However, Oceania had the highest occurrence rate of 18.19%. The Middle East had the greatest P rate, 7.91%, according to the adjusted subgroup research.

### IFG prevalence in major $\beta$ -thalassemia.

One medical ailment that included in the prediabetes spectrum is impaired fasting glucose (IFG). It is typified by higher-than-average fasting blood glucose levels, which are not high enough to be considered diabetes. A person with IFG is usually diagnosed when their fasting blood glucose level is among 100 and 125 mg/dL. According to the analysis, 17.22% of people with  $\beta$ -thalassemia major had IFG. The P of IFG in the Mediterranean Coast region was 6.53% in a subgroup study. The Middle East had the highest P of 27.89%.

### IGT prevalence in major thalassaemia.

T2D and normal blood sugar levels are separated by a physiological condition called IGT. Elevations in blood glucose levels above normal but not sufficient to qualify as diabetes are its defining characteristics. The analysis revealed that IGT was prevalent in  $\alpha$ -thalassemia major in 12.47% of cases. In a subgroup study, the Mediterranean Coast had the highest frequency of IGT, 15.17%.

Figure 3 and Table 3 show the diabetes P in 2019 by age and gender. An estimated 463 million individuals worldwide or 9.3% of the adult population aged 20 to 79 are forecasted to have diabetes in 2019. It is anticipated that this number will rise to 600 million in 2045 and 578 million in 2030. According to

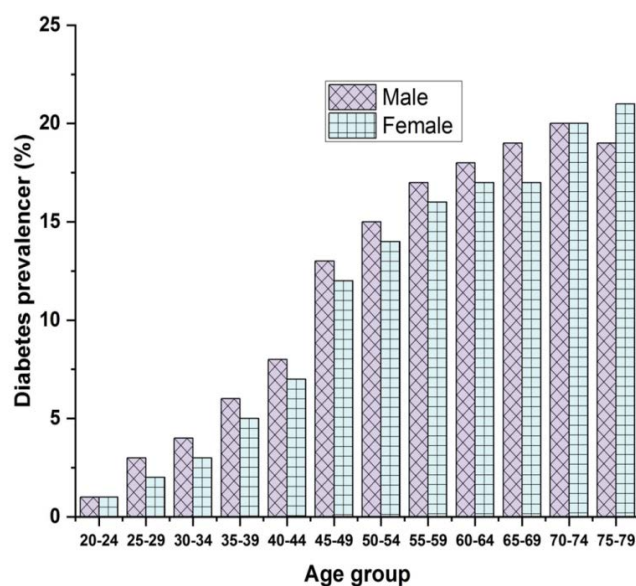


Figure 3. Diabetes prevalence in 2019 by age and gender.

(Source link:

[https://www.google.com/url?sa=i&url=https%3A%2F%2Fwww.sciencedirect.com%2Fscience%2Farticle%2Fpii%2FS0168822719312306&psig=AOvVaw1r4FITsb2iTDNSVHly7RmW&ust=1698384637075000&source=images&cd=vfe&opi=89978449&ved=0CBEQjRxqF-woTCODV1\\_z9koIDFQAAAAAAdAAAAABAD](https://www.google.com/url?sa=i&url=https%3A%2F%2Fwww.sciencedirect.com%2Fscience%2Farticle%2Fpii%2FS0168822719312306&psig=AOvVaw1r4FITsb2iTDNSVHly7RmW&ust=1698384637075000&source=images&cd=vfe&opi=89978449&ved=0CBEQjRxqF-woTCODV1_z9koIDFQAAAAAAdAAAAABAD))

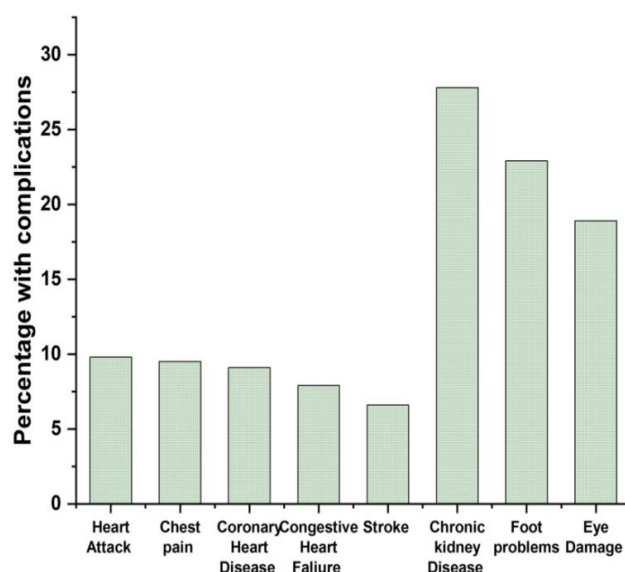


Figure 4. Frequency of T2D's most prevalent diabetes complications.

(Source link: [https://www.researchgate.net/figure/Prevalence-of-diabetes-related-complications-among-people-with-diabetes-National-Health\\_fig2\\_23265341](https://www.researchgate.net/figure/Prevalence-of-diabetes-related-complications-among-people-with-diabetes-National-Health_fig2_23265341))

age group estimates in Figure 3, the P of diabetes in 2019 for women and men is depicted. The P of diabetes rises with age, reaching 19.1% in between the ages of 65 and 79.

The P of the most typical difficulties in diabetes among those with T2D is shown in Figure 4 and Table 4. Compared to macrovascular effects, the P of microvascular difficulties in chronic kidney illness, foot problems, and eye damage is significantly higher. Either episodic complications can be

**Table 1.** Basis of the mentioned studies.

Reference no.	Author	Number	Age	Year	Indicators	Serum ferritin ng/ml
[13]	Pistoia L	70	<10 years	2022	DM/IGT	763.4 ± 887.7
[14]	De Sanctis V	1327	>30 yrs	2020	DM	NR
[15]	Tang CH	2983	13-17 yrs	2021	DM	NR
[16]	Matar BM	48	6-18 yrs	2020	DM	681.26±2537.87
[17]	Hamidi Z	18	2-45 yrs	2019	IGT	NR
[18]	Karimi M	726	2.5-80 yrs	2020	DM	9.32 ± 1.32
[19]	De Sanctis V	25	2 yrs	2021	DM	NR
[20]	Sevimli C	40	23.6 ± 27.4	2022	DM	1247.9 ± 1248.2
[21]	Luo Y	211	4-63 yrs	2019	IGT, DM	300-800
[22]	Yilmaz N	76	28 yrs	2020	IFG, IGT, DM	NR

[Note: NR- not reported, DM- diabetes mellitus, IGT- impaired glucose tolerance, IFG- impaired fasting glucose.]

**Table 2.** Classification of GM in β-thalassemia patients.

Region	Middle East	Europe	Asia	Mediterranean coast	Oceania	America	Total
DM P (%)	7.91	6.06	6.39	5.37	18.19	12.78	6.57
DM 95% CI (%)	5.76-10.6	2.83-9.27	2.76-10.2	3.96-6.78	6.79-29.57	7.25-18.32	5.31-7.79
IGT P (%)	7.15	14.02	9.08	15.17	NR	NR	12.47
IGT 95% CI (%)	0.14-14.16	8.57-19.46	4.98-13.17	3.57-26.77	NR	NR	5.97-18.95
IFG P (%)	27.89	NR	18.28	6.53	NR	NR	17.22
IFG 95% CI (%)	18.51-37.27	NR	5.68-30.92	5.74-7.31	NR	NR	8.44-26.02

**Table 3.** Diabetes prevalence in 2019 by age and gender.

Diabetes prevalence (%)		
Age group	Male	Female
20-24	1	1
25-29	3	2
30-34	4	3
35-39	6	5
40-44	8	7
45-49	13	12
50-54	15	14
55-59	17	16
60-64	18	17
65-69	19	17
70-74	20	20
75-79	19	21

**Table 4.** Frequently occurring diabetic problems associated with T2D.

Diseases	% with complications
Chest pain	9.5
Coronary Heart Disease	9.1
Heart Attack	9.8
Stroke	6.6
Congestive Heart Failure	7.9
Foot problems	22.9
Eye Damage	18.9
Chronic kidney Disease	27.8

managed or repeat frequently or progressive complications typically start out and relatively light but eventually cause more organ damage and a greater, typical eternal loss of capability.

### Discussion.

The β-globin gene, located on chromosome 12 is the cause of the genetic condition known as thalassemia, it is widespread in Southeast Asia and the eastern region. Because of the imbalance among the α and non-α chains of globin caused by mutations, there is less or no globin chain production, which increases erythrocyte fragility through hemolysis. Long-term extravascular hemolysis in thalassemic patients results in increased intestinal absorption of iron and decreased iron bioavailability. This mechanism may cause iron overload and raise the concentration of iron ions when combined with repeated long-term blood transfusions. The most common endocrine diseases were hypogonadotropic, hypogonadism, hypothyroidism, hypoparathyroidism, and impaired glucose metabolism. Patients suffering from thalassemia may display dysfunctions of several organs and pancreatic tissue. Patients may acquire T1D or T2D in a series of chronic malignant cycles since there is no immunologically matched donor pool, and graf-versus-host disease and the sole treatment for thalassemia major is a bone marrow transplant. Iron chelation therapy and conventional long-term blood transfusions are the primary means of maintaining normal hemoglobin concentrations in the body. Furthermore, in patients with thalassemia major

who have hypersplenism, symptomatic splenomegaly, and an elevated blood demand, splenectomy is a therapy option. Because of the therapies, people with  $\beta$ -thalassemia major have much better quality of life. However, an aberrant GM is brought on excessive iron accumulation in the pancreas. A number of factors may contribute to the pathophysiology of abnormal GM: (i) excessive iron deposition-induced islet cell destruction, which lowers synthesis of insulin; (ii) over-oxidation of fatty acids from accumulation of iron, which lowers a measure of the body uses glycogen; and (iii) reduced hepatic ability to penetrate insulin as a result of liver function degradation. Regional variations in glucose metabolism rates is a snapshot of organ and tissue function may be obtained from the distribution of GM, where in specific areas show increased metabolic activity in relation to their energy needs. Decreased metabolism patterns may be linked to neurological diseases like Alzheimer's disease, whereas elevated GM in certain regions may indicate the presence of tumours or inflammation. Abnormalities in these rates might function as diagnostic indications for a number of ailments.

### Conclusion.

A genetic blood disorder called  $\beta$ -thalassemia major is marked by severe anemia and a lifelong requirement for blood transfusions. Though its hemological components are known, the implications of  $\beta$ -thalassemia major on endocrine health, particularly the risk of diabetes are largely unknown. In this study, we examined a cohort of individuals with major diagnoses of  $\beta$ -thalassemia to ascertain the P and risk of hormonal disorders, specifically diabetes. 315 patients with  $\beta$ -thalassemia major were treated at a specialized institution, and their medical records were reviewed. Our study, which comprised 17 studies and 1500 cases overall, revealed that the frequency of diabetes was much higher in individuals with " $\beta$ -thalassemia major" compared to the general public. In the research cohort, which had a mean age at enrollment of 30 years, 28% of the patients had diabetes. The combined meta-analysis, the P of DM in  $\beta$ -thalassemia major remained stable from year to year. Individuals with substantial  $\beta$ -thalassemia had P values of 6.57 (95% CI: 5.31%-7.79%), 17.22% (95% CI: 8.44%-26.02%), and 12.47% (95% CI: 5.97%-18.95%) for DM, IFG, and respectively. There are several restrictions on this analysis. P's pooled analysis revealed a notable degree of heterogeneity. Subgroup examinations involving extra regions were conducted, however the heterogeneity did not significantly diminish. This heterogeneity could result from variations in the quantity of cases or fundamental traits. Secondly, there wasn't enough information available to provide an exhaustive assessment of every area worldwide. The research offers hope for improved treatment and results for people with  $\beta$ -thalassemia major in the future by establishing the path for more knowledge of the intricate link among thalassemia and diabetes.

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