UNIVERSIDADE ESTADUAL PAULISTA
"JÚLIO DE MESQUITA FILHO"
FACULDADE DE MEDICINA

Mariane de Oliveira Menezes

Diferentes estratégias de Rastreamento e Diagnóstico do Diabetes Mellitus Gestacional: estudo de coorte retrospectiva

Strategies for screening and diagnosis of gestational diabetes: a retrospective cohort study

Tese apresentada à Faculdade de Medicina, Universidade Estadual Paulista "Júlio de Mesquita Filho", Câmpus de Botucatu, para obtenção do título de Doutor em Tocoginecologia.

Orientadora: Prof.ª Dr.a Marilza Vieira Cunha Rudge
Coorientadora: Prof.ª Dr.a Cláudia Garcia Magalhães

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FICHA CATALOGRÁFICA ELABORADA PELA SEÇÃO TÉC. AQUIS. TRATAMENTO DA INFORM.
DIVISÃO TÉCNICA DE BIBLIOTECA E DOCUMENTAÇÃO - CÂMPUS DE BOTUCATU - UNESP
BIBLIOTECÁRIA RESPONSÁVEL: ROSEMEIRE APARECIDA VICENTE-CRB 8/5651

Menezes, Mariane de Oliveira.
Diferentes estratégias de rastreamento e diagnóstico do Diabetes mellitus gestacional : estudo de coorte retrospectiva / Mariane de Oliveira Menezes. - Botucatu, 2023

Tese (doutorado) - Universidade Estadual Paulista "Júlio de Mesquita Filho", Faculdade de Medicina de Botucatu
Orientador: Marilza Vieira Cunha Rudge
Coorientador: Cláudia Garcia Magalhães
Capes: 40101150

1. Diabetes gestacional - Diagnóstico. 2. Testes para triagem do soro materno. 3. Estudos de coortes. 4. Glicemia.

Palavras-chave: Diabetes gestacional; Diagnóstico; Glicemia; Testes para Triagem do Soro Materno.

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Tese apresentada à Faculdade de Medicina, Universidade Estadual Paulista "Júlio de Mesquita Filho", Campus de Botucatu, para Exame Geral de Qualificação junto ao Programa de Pós-Graduação em Tocoginecologia

Orientadora: Prof.ª Dr.a Marilza Vieira Cunha Rudge
Corientadora: Prof.ª Dr.a Cláudia Garcia Magalhães

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Botucatu, 01 de agosto de 2023

Dedicatórias

Dedico esta tese a todas as incansáveis pesquisadoras e pesquisadores que dedicam suas vidas ao desenvolvimento de novas abordagens de cuidado baseadas em evidências científicas de qualidade. Estas que mesmo diante de adversidades e da desvalorização da pesquisa em nosso país, continuam trabalhando arduamente. Somos uma comunidade numerosa e nosso trabalho tem um impacto positivo significativo na vida das pessoas. Espero que encontremos maneiras eficazes de comunicar nossas descobertas aos gestores de saúde e de tornar a ciência acessível à população em geral.

Também dedico esta tese às profissionais que se dedicam à atenção à saúde reprodutiva. Seu cuidado é fundamental para promover gestações saudáveis e partos menos traumáticos. Que a atenção, a ciência e o desejo das pessoas atendidas por nós possam caminhar juntos, fornecendo uma base sólida para um cuidado respeitoso.

Por fim, dedico esta conquista ao meu pai e meus avós, que em vida não puderam testemunhar alguém da família chegar tão longe na sua formação. Dois dos meus avós, enfrentando inúmeras dificuldades ao longo da vida e dando prioridade a outras esferas, somente liam e escreviam com muita dificuldade. Meu pai, que iniciou sua educação universitária, mas não chegou a concluí-la.

Agradecimentos

À **Prof.ª Dra. Maíra Libertad**, minha esposa, companheira de vida e aventuras. Você é uma fonte constante de inspiração como pesquisadora. Esteve ao meu lado em todas as etapas desse trabalho, mesmo enquanto nossa vida passava por mudanças e transformações, assim como a própria pesquisa. O projeto nasceu durante nossa mudança de estado e a coleta de dados foi especialmente desafiadora durante os tempos de pandemia, culminando em mais uma mudança de cidade. Ao longo desse período, enfrentamos três gestações – sendo a última a chegada da nossa pequena Maní – enquanto realizávamos a análise de dados, que só foi concluída quando a nossa bebê já estava entre nossos braços. Você é um apoio fundamental que, mesmo diante de diversas adversidades, acreditou que seria possível concluir um projeto significativo com dados relevantes que podem contribuir para a melhoria da saúde de gestantes e bebês.

À **Prof.ª Emérita Marilza Rudge,** você é uma verdadeira inspiração como pesquisadora. Tenho muito orgulho de ter tido a oportunidade de conviver com você e ver seu olhar profundo enquanto traça caminhos possíveis para fortalecer o cuidado a gestantes, bebês e puérperas. Obrigada por me permitir aprender contigo. Sou imensamente grata em ter você como base para a minha formação como pesquisadora. Que venham muitos e muitos projetos para melhoria da saúde materna infantil.

À **Prof.ª Dra. Roxana Knobel,** sua criatividade surpreendente, aliada a outros aspectos da sua inteligência e parceria, foi fundamental para moldar a análise estatística deste estudo. Sou imensamente grata pela sua ajuda e honrada por poder chamá-la de amiga.

À minha mãe **Vera Menezes**, seu apoio durante tantas jornadas da vida é fundamental. É muito gratificante saber que posso contar contigo em momentos complexos e decisões importantes. Te agradeço por tanto amor e dedicação.

Ao apoio da Coordenação de Aperfeiçoamento de Pessoal de Nível Superior – Brasil (**CAPES**) – com a bolsa de auxílio pesquisa pelo Programa de Demanda Social (DS)

Epígrafe

“Without data, you're just another person with an opinion”

W. Edwards Deming

Resumo da Tese

Menezes, M.O. Diferentes estratégias de Rastreamento e Diagnóstico do Diabetes Mellitus Gestacional: estudo de coorte retrospectiva. 2023. Tese (Doutorado) – Faculdade de Medicina de Botucatu, Universidade Estadual Paulista, Brasil.

Introdução: A Diabetes Mellitus Gestacional (DMG) e a Hiperglicemia Gestacional Leve (HGL) são condições que apresentam complicações perinatais graves e representam riscos significativos para o desenvolvimento futuro de Diabetes Mellitus Tipo 2 (DM2) e síndrome metabólica tanto para mães quanto para seus filhos. No entanto, a falta de consenso na definição e no diagnóstico dessas condições resulta em resultados divergentes sobre sua prevalência, dificultando a tomada de decisão dos gestores de saúde em relação ao investimento necessário para o diagnóstico e tratamento adequados. A prevalência de hiperglicemia durante a gestação varia globalmente, mas possui uma média de 16% e pode chegar a mais de 35% em determinados contextos. No Brasil, estima-se que a prevalência de DMG seja de 18% entre todas as gestações, sendo a epidemia de obesidade um fator contribuinte. O diagnóstico preciso da DMG é fundamental em termos de saúde pública, pois possibilita o planejamento e a implementação de medidas preventivas para o DM2 tanto para as mães quanto para seus filhos. Estudos têm mostrado que mulheres com histórico de DMG apresentam maior risco de desenvolver DM2 e enfrentam graves complicações, como mortalidade materna, problemas renais e cardíacos. Além disso, seus filhos têm maior probabilidade de sofrer com mortalidade neonatal precoce, obesidade, hiperglicemia e resistência à insulina. Entretanto, não há um padrão uniforme para o rastreamento e diagnóstico da DMG em todo o mundo.

Justificativa: A diversidade de abordagens destaca a importância de os sistemas de saúde e os tomadores de decisão compreenderem os impactos clínicos de cada estratégia, a fim de garantir um diagnóstico preciso da DMG e um acompanhamento adequado para as mulheres e seus filhos, com o objetivo de controlar o aumento do DM2 e suas complicações na população brasileira, além dos efeitos adversos decorrentes da hiperglicemia gestacional.

Objetivos:

1) A presente análise teve como objetivo investigar a adesão a protocolos vigentes localmente para rastreamento e diagnóstico de DMG em uma coorte retrospectiva de risco obstétrico misto.

2) A presente análise teve como objetivo investigar a incidência de DMG em uma coorte de gestantes de risco obstétrico misto, aplicando retrospectivamente quatro diferentes

critérios diagnósticos aos resultados de exames laboratoriais coletados durante a gestação. Adicionalmente, objetivou-se também investigar diferenças nas características clínicas e demográficas entre subgrupos de gestantes que teriam sido diagnosticadas com DMG se cada critério diagnóstico tivesse sido aplicado no mundo real.

Métodos:

1) Trata-se de uma coorte retrospectiva baseada em revisão de prontuários de partos de risco obstétrico misto de nascidos vivos ocorridos no ano de 2018 no Hospital das Clínicas de Botucatu. Partos ocorridos fora do hospital, cujos prontuários não estivessem disponíveis no sistema hospitalar ou de pacientes com diagnóstico prévio de DM1, DM2 ou Diabetes Mellitus overt foram considerados inelegíveis. A listagem de partos ocorridos no ano de 2018 foi organizada em ordem alfabética do nome da gestante (para evitar qualquer sazonalidade nos resultados) e 660 casos consecutivos foram rastreados para elegibilidade, número estimado necessário para que a amostra contasse com ao menos 246 sujeitos com uma glicemia de jejum antes de 20 semanas e um teste oral de tolerância a glicose (TTOG) 75 gramas de 2 horas durante a gestação. Variáveis sociodemográficas, antecedentes pessoais, fatores de risco para DMG, resultados e datas de exames para rastreamento e diagnóstico de DMG como glicemia de jejum (GJ), TTOG, hemoglobina glicada (A1C) e perfil glicêmico (PG), conforme disponíveis, foram coletados dos prontuários hospitalares. Dados de desfechos maternos e perinatais foram obtidos, porém não integram a presente análise. A adesão a três diferentes protocolos vigentes à época para rastreamento e diagnóstico de DMG (CAB32, MS2017 e Rudge) foi analisada aplicando os algoritmos de cada protocolo aos dados disponíveis na base. As gestantes foram classificadas como ‘com adesão’ a cada protocolo sempre que possuíam exames adequados conforme cada algoritmo. Características sociodemográficas e clínicas da amostra foram comparadas de acordo com a presença de testes mínimos para rastreamento e diagnóstico de DMG no prontuário (GJ e TTOG). Uma análise multivariada foi conduzida para examinar variáveis potencialmente relacionadas à adesão a protocolos de rastreamento e diagnóstico de DMG na amostra.

2) Trata-se de uma coorte retrospectiva baseada em revisão de prontuários de partos de risco obstétrico misto de nascidos vivos ocorridos no ano de 2018 no Hospital das Clínicas da Faculdade de Medicina de Botucatu (UNESP). Partos ocorridos fora do hospital, cujos prontuários não estivessem disponíveis no sistema hospitalar ou de pacientes com diagnóstico prévio de DM1, DM2 ou Diabetes Mellitus overt foram considerados inelegíveis. A listagem de partos ocorridos no ano de 2018 foi organizada em ordem alfabética do nome da gestante (para evitar qualquer sazonalidade nos

resultados) e 660 casos consecutivos foram rastreados para elegibilidade, número estimado necessário para que a amostra contasse com ao menos 246 sujeitos com uma glicemia de jejum antes de 20 semanas e um TTOG 75 gramas de 2 horas durante a gestação. Variáveis sociodemográficas, antecedentes pessoais, fatores de risco para DMG, resultados e datas de exames para rastreamento e diagnóstico de DMG (GJ, TTOG, A1C e PG, conforme disponíveis), diagnóstico de DMG definido pelo profissional pré-natalista e desfechos maternos e perinatais potencialmente associados a DMG foram coletados dos prontuários hospitalares. Quatro diferentes critérios diagnósticos para DMG foram aplicados retrospectivamente aos resultados de exames laboratoriais para rastreamento e diagnóstico de DMG presentes nos prontuários: CAB32, MS2017, ADA23 e Rudge. Cada algoritmo foi utilizado para simular cenários hipotéticos em que todas as gestantes com exames suficientes em seus prontuários (amostra com adesão) tivessem sido adequadamente rastreadas conforme a diretriz correspondente, independentemente do critério efetivamente adotado pelo profissional pré-natalista. Três grupos foram comparados em termos de suas características clínicas e sociodemográficas: i) DMG diagnosticado por qualquer critério, ii) não-DMG com pelo menos um TTOG 75g de 2 horas disponível no prontuário e iii) testes insuficientes para excluir ou confirmar DMG no prontuário. As incidências de DMG em cada cenário hipotético (CAB32, MS2017, ADA23 e Rudge) foram calculadas utilizando como denominador a amostra com adesão à diretriz específica (ou seja, com exames suficientes para aplicar o algoritmo previsto na diretriz). Como desfechos relacionados à DMG foram raros na amostra, a incidência de um desfecho composto potencialmente relacionada à DMG também foi comparada entre os 3 grupos de interesse no estudo: polidramnia, macrossomia, distócia de ombros, hipoglicemia neonatal, icterícia neonatal requerendo fototerapia, admissão em UTI neonatal por qualquer causa excluindo anomalias fetais e síndromes genéticas.

Resultados: 1) Dentro da amostra de 660 prontuários avaliados, foram excluídas duplicatas (gestações gemelares) e diagnósticos prévios de diabetes, resultando em 645 casos elegíveis. A maioria desses casos havia realizado pelo menos um teste de glicemia de jejum (84,3%) e, destes, 46,9% realizaram GTT em qualquer idade gestacional. De toda a amostra elegível, 13% não realizou nenhum teste relacionado à DMG. Quanto às características sociodemográficas e clínicas da amostra, a maioria tinha entre 19 e 34 anos (76,6%), classificada como branca (82,7%) e com pré-natal realizado na atenção primária no serviço público (74,8%). A maioria dos casos iniciou o pré-natal no primeiro trimestre (81,1%) e fez ao menos 6 consulta de pré-natal (91,4%). Na análise bivariada,

as variáveis idade, local de acompanhamento pré-natal, número de consultas pré-natais, presença de hipertensão crônica antes da gravidez ou diagnóstico de hipertensão crônica durante a gravidez atual apresentaram diferenças significativas quando as mulheres que realizaram pelo menos uma GJ e um TTOG foram comparadas àquelas que não possuíam esses exames no prontuário. Foi observada uma maior adesão para o protocolo CAB32 (46,8%). A realização de TTOG durante a gravidez foi observada em 40,9% da amostra, porém apenas 25,9% do total da amostra realizaram o teste no período gestacional recomendado (24-28 semanas). A adesão a qualquer protocolo de rastreamento e diagnóstico de DMG foi observada em 57,1% da amostra. Sobre a idade gestacional em que o TTOG foi realizado, variou de 6 a 43 semanas de gestação (mediana de 27 semanas, intervalo interquartil de 4). Entre aquelas que realizaram o TTOG, 36,7% fizeram o teste fora do período gestacional recomendado (mais comumente após 28 semanas). Na regressão logística multivariada, para todas as diretrizes, o número de consultas pré-natais aumentou a chance de adesão (de 1,10 a 1,19 vezes para cada visita adicional). A hipertensão crônica antes da gravidez foi significativamente associada a uma maior adesão às recomendações para todas as diretrizes, exceto o CAB32 (Odds Ratio [OR] variando de 2,16 para o MoH2017 a 3,15 para Rudge et al).

2) Foram avaliados 660 partos resultando em 645 gestantes elegíveis na amostra. Dos casos incluídos neste estudo, 84,3% realizaram pelo menos um exame de glicemia em jejum. Dentre esses casos 46,8% também realizaram o teste de tolerância à glicose (TTOG) em algum momento durante a gestação. No entanto, é importante ressaltar que cerca de 13% da amostra elegível não passou por nenhum teste relacionado ao diagnóstico de DMG. A DMG foi diagnosticada em 80 gestantes utilizando qualquer um dos quatro critérios em análise e 201 gestantes realizaram pelo menos um TTOG e foram classificadas como não-DMG porque nenhum teste anormal relacionado à DMG foi identificado nos prontuários. Insuficiência de testes para confirmar ou excluir a DMG foi observada em 364 gestantes (56,4%). As seguintes variáveis foram estatisticamente diferentes entre os subgrupos na análise bivariada: idade igual ou superior a 35 anos, local de atendimento pré-natal, mínimo de 6 consultas pré-natais, obesidade/sobrepeso, hipertensão crônica antes da gravidez, história de hipertensão gestacional ou pré-eclâmpsia em uma gestação anterior, história de diabetes gestacional em uma gestação anterior e hipertensão crônica diagnosticada na gravidez atual. A incidência de DMG variou de 5,3% (critérios CAB32) a 22.6% (critérios MoH2017) nos cenários hipotéticos, enquanto a incidência real diagnosticada pelo provedor de cuidados pré-natais foi de

7,1% (independentemente dos critérios diagnósticos utilizados). A alteração no metabolismo da glicose, conforme definido pela ADA23, estava presente em 4,9% da amostra, enquanto a hiperglicemia gestacional leve (Grupo Rudge Ib) foi identificada em 8,5% da amostra conforme as diretrizes de Rudge et al. Vale ressaltar que a maioria dos casos diagnosticados pelos critérios MoH2017 teria sido diagnosticada pela GJ < 20 semanas (isto é, DMG precoce). A incidência considerando qualquer um dos critérios foi de 21,6%.

O diagnóstico perdido representa 10,5% da amostra conforme qualquer uma das diretrizes (apresentavam um teste anormal registrado no prontuário médico, mas não foram diagnosticadas com DMG pelo provedor). O desfecho composto potencialmente relacionado à DMG foi estatisticamente diferente entre os subgrupos, sendo mais comum entre aquelas com DMG de acordo com qualquer critério. Não houve diferença entre os grupos não-DMG e com testes insuficientes para confirmar ou excluir a DMG. Em termos de desfechos individuais relacionados à DMG, diferenças estatisticamente significativas foram observadas apenas para icterícia neonatal que requer fototerapia (DMG segundo qualquer critério 37,5% vs. Não DMG com pelo menos um TTOG 22,9% vs. 25,3% no subgrupo com testes insuficientes para rastrear DMG) e internação em UTI neonatal, excluindo síndromes genéticas e anomalias (23,7% vs. 11,9% vs. 17,9%, respectivamente).

Conclusão: 1) Nossos achados sugerem que a adesão às diretrizes locais disponíveis para rastreamento e diagnóstico de DMG é inadequada em nossa amostra, com uma proporção significativa de mulheres não realizando os testes recomendados para DMG ou realizando-os fora do prazo adequado. Essa observação levanta preocupações em relação à subdiagnóstico de DMG e seus potenciais efeitos prejudiciais. Isso não apenas dificulta o manejo adequado da DMG durante a gravidez, mas também representa riscos de longo prazo tanto para as mulheres quanto para seus filhos devido à DMG não tratada.

2) Nossos achados indicam que a incidência de DMG é altamente dependente dos critérios diagnósticos adotados, mas também da adesão às recomendações de triagem e diagnóstico de DMG no contexto clínico. As diretrizes nacionais atuais para DMG resultariam em uma incidência três vezes maior do que a frequência de DMG diagnosticada pelo provedor de cuidados pré-natais. As mulheres com DMG em nossa amostra eram mais velhas e apresentavam mais comorbidades e fatores de risco do que os casos não DMG ou casos com testes ausentes para excluir ou confirmar DMG.

Palavras-Chaves: *diabetes mellitus* gestacional; diagnóstico; glicemia; testes para triagem do soro materno; estudo de coorte

Thesis Abstract

Menezes, M.O. Strategies for screening and diagnosis of gestational diabetes: a retrospective cohort study. Thesis (Doctorate) - Botucatu Medical School (FMB), São Paulo State University (UNESP), Brazil.

Introduction: Gestational Diabetes Mellitus (GDM) and Mild Gestational Hyperglycemia (MGH) are conditions that present severe perinatal complications and represent significant risks for the future development of Type 2 Diabetes Mellitus (T2DM) and metabolic syndrome for both mothers and their children. However, the lack of consensus in the definition and diagnosis of these conditions results in divergent findings regarding their prevalence, making it challenging for health policymakers to make informed decisions regarding the necessary investment for proper diagnosis and treatment. The prevalence of hyperglycemia during pregnancy varies globally but has an average of 16% and can reach over 35% in certain contexts. In Brazil, it is estimated that the prevalence of GDM is 18% among all pregnancies, with the obesity epidemic being a contributing factor. The accurate diagnosis of GDM is crucial in terms of public health as it enables the planning and implementation of preventive measures for T2DM for both mothers and their children. Studies have shown that women with a history of GDM have a higher risk of developing T2DM and face serious complications such as maternal mortality, renal and cardiovascular diseases. Furthermore, their children are more likely to experience early neonatal mortality, obesity, hyperglycemia, and insulin resistance. However, there is no uniform standard for the screening and diagnosis of GDM worldwide.

Justification: The diversity of approaches highlights the importance of healthcare systems and decision-makers understanding each strategy's clinical impacts to ensure accurate GDM diagnosis and appropriate lifetime follow-up for women and their children. This has the potential to impact the increasing prevalence of T2DM and its complications in the Brazilian population, as well as mitigate the adverse effects resulting from gestational hyperglycemia.

Objectives: 1) The present analysis aimed to investigate adherence to locally established GDM screening and diagnosis protocols in a retrospective cohort of mixed obstetric risk.

2) The present analysis aimed to investigate the incidence of GDM in a cohort of pregnant women with mixed obstetric risk by retrospectively applying four different diagnostic criteria to laboratory test results collected during pregnancy. The study also aimed to investigate differences in clinical and demographic characteristics among subgroups of pregnant women who would have been diagnosed with GDM if each diagnostic criterion had been applied in the real world.

Methods: 1) This is a retrospective cohort based on medical records review from live births with mixed obstetric risk that occurred in 2018 at Hospital das Clínicas de Botucatu. Deliveries that took place outside the hospital, whose medical records were not available in the hospital system, or patients with a previous diagnosis of Type 1 Diabetes Mellitus (DM1), Type 2 Diabetes Mellitus (DM2), or overt Diabetes Mellitus were considered ineligible. The list of deliveries that occurred in 2018 was organized in alphabetical order by the pregnant woman's name (to avoid any seasonality in the results), and 660 consecutive cases were screened for eligibility – an estimated number necessary to have at least 246 subjects with fasting plasma glucose (FPG) before 20 weeks and a 2-hour 75-gram oral glucose tolerance test (GTT) during pregnancy. Sociodemographic variables, personal history, risk factors for GDM, screening and diagnostic test results (FPG, GTT, glycosylated hemoglobin, and glycemic profile) as available were collected from the medical records. Maternal and perinatal outcome data were obtained but were not included in the present analysis. Adherence to three different protocols for GDM screening and diagnosis (CAB32, MS2017, and Rudge) was analyzed by applying the algorithms of each protocol to the available data. Pregnant women were classified as adherent to each protocol if they had appropriate tests according to each algorithm. The sociodemographic and clinical characteristics of the sample were compared based on the presence of minimal tests for GDM screening and diagnosis in the medical records (FPG and GTT). A multivariate analysis was conducted to examine variables potentially related to adherence to GDM screening and diagnostic protocols in the sample.

2) This is a retrospective cohort based on a review of medical records from live births with mixed obstetric risk that occurred in 2018 at the Hospital das Clínicas da Faculdade de Medicina de Botucatu (UNESP). Deliveries that took place outside the hospital, whose medical records were not available in the hospital system, or patients with a previous diagnosis of Type 1 Diabetes Mellitus (DM1), Type 2 Diabetes Mellitus (DM2), or overt Diabetes Mellitus were considered ineligible. The list of deliveries that occurred in 2018 was organized in alphabetical order by the pregnant woman's name (to avoid any

seasonality in the results), and 660 consecutive cases were screened for eligibility – an estimated number necessary to have at least 246 subjects with FPG before 20 weeks and a 2-hour 75-gram oral glucose tolerance test (GTT) during pregnancy. Sociodemographic variables, personal history, risk factors for GDM, screening and diagnostic test results (FPG, GTT, glycosylated hemoglobin, and glycemic profile as available), GDM diagnosis made by the prenatal care provider, and maternal and perinatal outcomes potentially associated with GDM were collected from the medical records. Four different diagnostic criteria for GDM were retrospectively applied to the laboratory test results abstracted from medical records: CAB32, MS2017, ADA23, and Rudge. Each algorithm was used to simulate hypothetical scenarios in which all pregnant women with sufficient tests in their medical records (compliant sample) had been adequately screened according to the corresponding guideline, regardless of the criterion actually adopted by the prenatal care provider. Three groups were compared in terms of their clinical and sociodemographic characteristics: i) GDM diagnosed by any criterion, ii) non-GDM with at least a GTT available in the medical record, and iii) insufficient tests to exclude or confirm GDM in the medical record. The incidences of GDM in each hypothetical scenario (CAB32, MS2017, ADA23, and Rudge) were calculated using the compliant sample to the specific guideline as the denominator (i.e., with sufficient tests to apply the algorithm specified in the guideline). As outcomes related to GDM were rare in the sample, the incidence of a composite outcome potentially related to GDM was also compared among the three groups of interest in the study: polyhydramnios, macrosomia, shoulder dystocia, neonatal hypoglycemia, neonatal jaundice requiring phototherapy, neonatal admission to the NICU for any cause excluding fetal anomalies and genetic syndromes.

Results: 1) Within the 660 evaluated medical records sample, duplicates (twin pregnancies) and previous diabetes diagnoses were excluded, resulting in 645 eligible cases. Most of these cases had undergone at least one FPG test (84.3%), and of those, 46.9% had undergone an oral GTT at any gestational age. Of the entire eligible sample, 13.0% did not undergo any tests related to GDM. Regarding the sociodemographic and clinical characteristics of the sample, the majority were between 19 and 34 years old (76.6%), classified as white (82.7%), and received prenatal care in primary healthcare within the public healthcare system (74.8%). Most cases initiated prenatal care in the first trimester (81.1%) and attended at least 6 prenatal visits (91.4%). In the bivariate analysis, age, location of prenatal care, number of prenatal visits, presence of chronic hypertension before pregnancy or a diagnosis of chronic hypertension during the current pregnancy

showed significant differences when comparing women who underwent at least one FPG and one oral GTT to those who did not have these tests in their medical records. A higher adherence rate was observed for the CAB32 protocol (46.8%). A GTT during pregnancy recorded in the hospital chart was observed in 40.9% of the sample, but only 25.9% of the total sample underwent the test during the recommended gestational period (24-28 weeks). Adherence to any screening and diagnostic guideline for GDM was observed in 57.1% of the sample. Regarding the gestational age at which the GTT was performed, it ranged from 6 to 43 weeks of gestation (median of 27 weeks, interquartile range of 4). Among those who underwent the GTT, 36.7% had the test performed outside the recommended gestational period (most commonly after 28 weeks). In multivariate logistic regression, for all guidelines, the number of prenatal visits increased the likelihood of adherence (ranging from 1.10 to 1.19 times for each additional visit). Chronic hypertension before pregnancy was significantly associated with higher adherence to recommendations for all guidelines, except CAB32 (Odds Ratio [OR] ranging from 2.16 for MoH2017 to 3.15 for Rudge et al.).

2) A total of 660 deliveries were evaluated, resulting in 645 eligible pregnant women in the sample. GDM was diagnosed in 80 pregnant women using any of the four criteria under analysis, and 201 pregnant women underwent at least one GTT and were classified as non-GDM because no abnormal test related to GDM was identified in their medical records. Insufficient testing to confirm or exclude GDM was observed in 364 pregnant women (56.4%). The following variables were statistically different among the subgroups in the bivariate analysis: age equal to or greater than 35 years, location of prenatal care, a minimum of 6 prenatal visits, obesity/overweight, chronic hypertension before pregnancy, history of gestational hypertension or preeclampsia in a previous pregnancy, history of gestational diabetes in a previous pregnancy, and chronic hypertension diagnosed in the current pregnancy. The incidence of GDM varied from 5.3% (CAB32 criteria) to 22.6% (MoH2017 criteria) in the simulated hypothetical scenarios, while the actual incidence diagnosed by prenatal care providers was 7.1% (regardless of the diagnostic criteria used). Abnormal glucose metabolism, as defined by ADA23, was present in 4.9% of the sample, while mild gestational hyperglycemia (Rudge Group Ib) was identified in 8.5% of the sample according to Rudge et al guidelines. Notably, most cases diagnosed by the MoH2017 criteria would have been diagnosed by the FPG test before 20 weeks (i.e., early GDM). The incidence considering any of the criteria was 21.6%. Missed diagnosis accounted for 10.5% of the sample according to any of the guidelines (women who had an abnormal test recorded in the medical records but were

not diagnosed with GDM by the provider). The composite outcome potentially related to GDM was statistically different among the subgroups, being more common among those with GDM according to any criteria. There was no difference between the non-GDM groups and those with insufficient testing to confirm or exclude GDM. In terms of individual outcomes related to GDM, statistically significant differences were observed only for neonatal jaundice requiring phototherapy (GDM according to any criteria 37.5% vs. non-GDM with at least one GTT 22.9% vs. 25.3% in the subgroup with insufficient testing to screen for GDM) and neonatal intensive care unit (NICU) admission, excluding genetic syndromes and anomalies (23.7% vs. 11.9% vs. 17.9%, respectively).

Conclusion: 1) Our findings suggest that compliance with locally available GDM screening and diagnosis guidelines is inadequate in our sample, with a significant proportion of women not undergoing recommended GDM tests or performing tests outside the appropriate timeframe. This observation raises concerns regarding the underdiagnosis of GDM and its potential detrimental effects. It not only hinders the appropriate management of GDM during pregnancy but also poses long-term risks for both women and their offspring due to untreated GDM.

2) Our findings indicate that GDM incidence is highly dependent on the diagnostic criteria adopted, but also the overall compliance to GDM screening and diagnosis recommendations in the clinical setting. The current national GDM guidelines would result in an incidence 3 times higher than the frequency of GDM as diagnosed by the antenatal care provider in the sample. Women with GDM in our sample were older and had more comorbidities and risk factors than non-GDM cases or cases with missing tests to exclude or confirm GDM.

Keywords: gestational diabetes mellitus; diagnosis; blood glucose; tests for maternal serum screening; cohort study

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Artigo 1

Artigo 2

Lista de abreviações

Português e Inglês

Lista de abreviações em Português

CEP	Comitê de Ética em Pesquisa
CIDPN	Centro de Investigação do Diabete Perinatal
DM	diabetes mellitus
DM2	diabetes *mellitus* tipo 2
DMG	diabetes *mellitus* gestacional
DMP	diabetes *mellius* prévia
Dra.	doutora
FEBRASGO	Federação Brasileira das Associações de Ginecologia e Obstetrícia
FMB-UNESP	Faculdade de Medicina de Botucatu de UNESP
GJ	glicemia de jejum
HGG	hiperglicemia gestacional
HGL	hiperglicemia gestacional leve
IMC	índice de massa corporal
MS	Ministério da Saúde
OPAS	Organização Panamericana de Saúde
TCLE	termo de consentimento livre e esclarecido
TTOG75	teste de tolerância oral à glicose com 75g de dextrosol e 3 pontos (jejum, 1 hora e 2 horas)
UNESP	Universidade Estadual Paulista
UTI	Unidade de tratamento intensivo

Lista de abreviações em Inglês

%	Percentage
A1C	glycated hemoglobin
ADA	American Diabetes Association
ANC	antenatal care
BMI	body mass index
DM	diabetes mellitus
FPG	fasting plasma glucose
GDM	Gestational Diabetes Mellitus
GP	glicemic profile
GTT	glucose tolerance test
PDRC	Perinatal Diabetes Research Center

Sumário

Seção 1

Trajetória Acadêmica

Durante minha formação, tive a oportunidade de me envolver em várias experiências de pesquisa desde cedo. No ensino médio, na escola Pueri Domus Jardim, tive acesso a disciplinas inovadoras como o "Núcleo de Estudos e Pesquisas", que tinha como foco identificar um problema de interesse para o grupo e embasar discussões sobre o assunto por meio de uma revisão bibliográfica.

Na graduação em Obstetrícia na Escola de Artes, Ciências e Humanidade da Universidade de São Paulo (EACH-USP 2005-2008), a importância do uso de evidências científicas para fornecer um cuidado de qualidade foi amplamente abordada. Aprendemos a pensar criticamente e a questionar por meio do "Guia para Atenção Efetiva na Gravidez" de Enkin, na época referência para o debate acerca da aplicação de evidências científicas na assistência ao parto. Além disso, tive a oportunidade de participar de uma disciplina de dois módulos chamada "Resolução de Problemas", na qual desenvolvíamos e executávamos projetos de pesquisa a partir de problemas identificados. Um desses projetos resultou em minha primeira apresentação de um trabalho em formato de pôster na "II Conferência Internacional Sobre Humanização do Parto e Nascimento (II CIHPN)" realizada no Rio de Janeiro em 2005.

Foi somente após me formar na graduação que participei efetivamente da publicação de um artigo, auxiliando na coleta de dados e redação. Em seguida, ingressei no mestrado na Faculdade de Saúde Pública (FSP-USP, 2010-2012) para dar meus primeiros passos como pesquisadora. Naquela época, explorei a pesquisa qualitativa com base em etnografia, focando no parto de povos indígenas guarani-mbya. Mantendo um olhar mais amplo sobre meus interesses de estudo, também atuei como monitora na disciplina de "Epidemiologia" para estudantes de Obstetrícia.

Por algum tempo, concentrei-me mais na assistência e no ensino, aprimorando minha leitura das evidências, mas afastando-me da produção delas. No ensino, lecionei na graduação de Obstetrícia da EACH-USP como professora contratada em dois períodos diferentes, além de ter lecionado na pós-graduação de enfermagem obstétrica da Universidade Anhembi Morumbi (UAM).

Em torno de 2018, decidi me reaproximar e trilhar o caminho de me tornar pesquisadora. Conduzimos e publicamos uma revisão sistemática sobre Mulheres Lésbicas e Infecções Sexualmente Transmissíveis (e Vaginose Bacteriana) (Anexo 1). Foi gratificante trabalhar em um projeto sobre um tema muitas vezes invisibilizado, e tive a satisfação de contar com a participação de três mulheres lésbicas na elaboração desse trabalho. No mesmo ano da publicação (em periódico A1 na Medicina III, conforme avaliação QUALIS 2017-2020) iniciei o doutorado, em 2019.

Durante a pandemia, juntei-me a um grupo de profissionais em busca ativa de publicações sobre SARS-CoV-2 e mortalidade materna. Dado o impacto negativo que doenças respiratórias costumam ter nessa população, procurávamos evidências nessa direção. No entanto, a maioria dos primeiros artigos encontrados falava o contrário, ou seja, que não havia um risco aumentado de desfechos negativos aumentados nessa população. Por causa disso, começamos a investigar ativamente os casos de mortalidade materna relacionados à COVID-19 no Brasil, resultando em 10 publicações relevantes sobre o tema (Anexos 2-11 – Sendo anexos 4, 6 e 8 publicados em periódico A1 na Medicina III, conforme avaliação QUALIS 2017-2020)

Durante o doutorado, também estive envolvida em outros projetos que resultaram em mais publicações (Anexo 12-15 – sendo anexo 15 em periódico A2 na Medicina III, conforme avaliação QUALIS 2017-2020). Destaco o artigo sobre a custo-efetividade da inserção de obstetrizes e enfermeiras obstétricas no pré-natal da assistência suplementar (Anexo 15 - em periódico A1 na Medicina III, conforme avaliação QUALIS 2017-2020), que a princípio foi financiado coletivamente e enviado de forma integral à Agência Nacional de Saúde Suplementar (ANS) para apreciação de entrada no rol de procedimentos obrigatórios, resultando em uma resolução normativa que permite consultas com obstetrizes e enfermeiros obstétricos para mulheres que acessam planos de saúde.

Outro ponto importante da produção técnica foi a participação direta no grupo de estudo DIAMATER, liderado pela professora Marilza Vieira Cunha Rudge. A professora tem décadas de conhecimento e pesquisas relacionadas a Diabetes Mellitus Gestacional (DMG) e, junto de um grupo de alunos e professores provenientes de diversas formações e instituições, atualmente dedica-se em particular a investigar a resposta muscular e incontinência urinária relacionadas à patologia. A pesquisa envolve desde estudos teóricos, experimentais e pré-clínicos até estudos clínicos e incluem parcerias internacionais e tem extensa produção sobre o tema, em que participo ativamente desde 2019 como parte integrante do Diamater Study Group (Anexo 16-21) em discussões, planejamento, desenvolvimento e inclusive por momentos na própria coleta de dados.

Nesse período, com muito orgulho, contribuí com a produção de dois capítulos do livro Obstetrícia por Jorge Rezende Filho. A convite da Professora Dra. Melania Maria Ramos Amorim, eu, juntamente com Maíra Libertad Soligo Takemoto, fui autora dos capítulos "Gravidez Prolongada" (Anexo 22) e "Distócia de Ombros" (Anexo 23). Também fui uma das autoras de um capítulo do Manual de Obstetrícia da Associação de Obstetrícia e Ginecologia do Estado de São Paulo (SOGESP, 2021) (Anexo 24) e de um capítulo em um livro sobre luto intitulado "Perdi meu bebê: Uma companhia para atravessar o luto gestacional, perinatal e neonatal" (Anexo 25).

Durante um semestre, realizei estágio docente em campo, acompanhando estudantes de enfermagem no atendimento a gestantes no Centro de Parto Normal do Hospital Estadual de Botucatu. Lecionei aulas de planejamento reprodutivo, pelve materna e estática fetal. Também participei de treinamentos teórico-práticos para residentes em enfermagem obstétrica, abordando temas como exame obstétrico, sutura perineal e resolução de distocia de ombros. Além disso, atuei como membro da banca avaliadora de duas monografias de conclusão da residência de alunas de enfermagem obstétrica. Esses anos foram transformadores, proporcionando uma base sólida para meu desenvolvimento como pesquisadora e aprimoramento na docência.

Seção 2

Contextualização

Diabetes Mellitus Gestacional

Diabetes Mellitus Gestacional (DMG) e Hiperglicemia gestacional leve (HGL) estão associadas com complicações perinatais graves,(1–4) e são fatores de risco relevantes para o desenvolvimento futuro de Diabetes Mellitus Tipo 2 (DM2) e síndrome metabólica tanto para a mãe quanto para seus filhos.(5–10) Um consenso da International Federation of Gynaecology and Obstetrics (FiGO) em 2015 optou por denomina-las em conjunto como hiperglicemia na gestação(11) e o Consenso Brasileiro denominou-as como DMG.(12)

Apesar da gravidade dessa patologia tanto para mãe como para o seu filho a curto e longo prazo, ainda encontram-se publicações em revistas de impacto usando diferentes estratégias diagnósticas e diferentes denominações que levam a resultados controversos de prevalência da doença,(13–17) como consequência, resultados clínicos díspares são disponibilizados para o sistema de saúde o que dificulta a tomada de decisão do gestor em saúde em relação aos investimentos a serem alocados para o diagnóstico e tratamento do DMG.

A prevalência de algum grau de hiperglicemia na gestação (HGG) tem uma média mundial de 16%, estando acima de 35% em alguns contextos, dependendo dos critérios diagnósticos utilizados em cada estimativa, sendo que DMG representa a maior parcela destes casos.(12) Usando teste oral de tolerância a glicose de 75g associado ao perfil glicêmico, no Centro de Investigação do Diabete Perinatal (CIDPN) da Faculdade de Medicina de Botucatu-Unesp, foram encontrados cerca de 20% de distúrbios hiperglicêmicos na gestação.(1)

No Brasil, estima-se que, com os novos critérios diagnósticos propostos através de consenso entre diversas instituições em 2017 (Organização Panamericana de Saúde/OPAS, Ministério da Saúde/MS, Federação Brasileira das Associações de

Ginecologia e Obstetrícia e Sociedade Brasileira de Diabetes/FEBRASGO), a prevalência de DMG seja de 18% de todas as gestações.(12) Além disso, é fato reconhecido globalmente que a prevalência da condição vem aumentando e deve continuar em elevação, em razão da epidemia de obesidade que atinge inúmeros contextos no mundo, incluindo o Brasil.(17)

Deste modo, o diagnóstico adequado de DMG tem impacto direto sobre os desfechos perinatais, mas também relevância destacada do ponto de vista da saúde pública, uma vez que permite planejar e implementar ações para prevenção do DM2 no pós-parto e ao longo da vida da mãe e seus filhos.(8,10) Para compreender a magnitude do impacto dessas ações, estima-se que a prevalência de DM2 na população adulta brasileira tenha dobrado da década de 1980 para a de 2010,(18) sendo que estudo multicêntrico nacional avaliando mais de 15.000 pessoas entre 35 e 74 anos identificou uma prevalência de 19,7%, sendo 50,4% de casos não previamente diagnosticados.(19) Com base nestes números, poderia se estimar que 1 a cada 5 brasileiras venha a desenvolver DM2, sendo que o subdiagnóstico parece ainda ser uma realidade na nossa população. A possibilidade, então, de um diagnóstico acurado de DMG que leve ao acompanhamento em longo prazo dessas mulheres e sua prole é estratégia racional para conter o crescimento do DM2 e suas complicações na população brasileira, para além dos efeitos perinatais da HGG. Em tese defendida em 2018 no Programa de Pós-Graduação em Ginecologia, Obstetrícia e Mastologia PGGOM-FMB-UNESP Arantes M e Rudge MV acompanharam pares de mães e recém-nascidos 5-11 anos pós-parto e detectaram que o DMG prévio aumentou o risco de DM2 nas mães e teve grave repercussão com morte de 12 de 534 mães nesse período sendo 3 por problema renal e 3 por problema cardíaco.(20) Associou-se também a aumento de mortalidade neonatal precoce e de aparecimento

de sinais iniciais de obesidade, hiperglicemia e resistência a insulina nessas crianças de 5-11 anos filhas de mães diabéticas.

Não há, no entanto, um padrão único para rastreamento e diagnóstico do DMG no mundo, havendo variedade de propostas definidas de acordo com o risco basal da população (dados epidemiológicos) e prática clínica corrente em cada contexto. Na realidade brasileira, ainda é bastante disseminado o uso dos critérios propostos pelo Ministério da Saúde em 2012, através de seu Caderno de Atenção Básica (CAB32),(21) uma vez que este regula a prática na atenção primária, nível do sistema de saúde que alcança a maioria da população. Em 2017, no entanto, uma reunião de especialistas com a participação da Organização Panamericana de Saúde (OPAS), Ministério da Saúde (MS), Federação Brasileira das Associações de Ginecologia e Obstetrícia (FEBRASGO) e Sociedade Brasileira de Diabetes (SBD), propôs novas diretrizes, baseadas em dois cenários: viabilidade financeira e disponibilidade técnica total (propondo a realização de glicemia de jejum no primeiro trimestre e TTOG75 no segundo trimestre, com detecção esperada de 100% dos casos) e viabilidade financeira e disponibilidade técnica parcial (baseada apenas na realização de glicemia de jejum, com detecção esperada de 86% dos casos).(12)

Em serviços específicos, em particular de nível secundário ou terciário e serviços universitários ou no âmbito da saúde suplementar, são adotados ainda os critérios propostos pela American Diabetes Association (ADA) em 2016 e suas atualizações mais recentes, incluindo a versão publicada em 2023.(22) No CIDPN da Faculdade de Medicina da UNESP em Botucatu (FMB-UNESP), utilizam-se os critérios da ADA 2016 em associação com o perfil glicêmico realizado entre 24 e 28 semanas, para detectar os casos de hiperglicemia gestacional leve. Deste modo, no Brasil e no mundo há grande variação nas propostas de rastreamento e diagnóstico,

sendo relevante para o sistema de saúde e os tomadores de decisão compreender os impactos clínicos de cada proposta.

6 Objetivos

6.1 Artigos

Os resultados desta Tese estão apresentados em 2 artigos de acordo o respectivo objetivo:

1 - *“Adherence to screening and diagnostic guidelines for gestational diabetes mellitus: a retrospective cohort"*

Objetivo: A presente análise teve como objetivo investigar a adesão a protocolos vigentes localmente para rastreamento e diagnóstico de DMG em uma coorte retrospectiva de gestantes de risco obstétrico misto.

2 - *“Incidence of gestational diabetes mellitus according to different diagnostic criteria: a retrospective cohort"*

Objetivo: A presente análise teve como objetivo investigar a incidência de DMG em uma coorte de gestantes de risco obstétrico misto, aplicando retrospectivamente quatro diferentes critérios diagnósticos aos resultados de exames laboratoriais coletados durante a gestação. Adicionalmente, objetivou-se também investigar diferenças nas características clínicas e demográficas entre subgrupos de gestantes que teriam sido diagnosticadas com DMG se cada critério diagnóstico tivesse sido aplicado no mundo real.

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Seção 3
Artigos

Artigo 1

Artigo Original redigido para publicação na revista *Cadernos de Saúde Pública* para a qual será submetido.

Qualis A1 MED III (Sucupira Qualis Capes 2017-2020) – FI: 3.371 (2022-2023) https://cadernos.ensp.fiocruz.br/csp/

"Adherence to screening and diagnostic guidelines for gestational diabetes mellitus: a retrospective cohort"

INTRODUCTION

Gestational diabetes mellitus (GDM) is a pregnancy common complication, characterized by glucose intolerance that typically develops during the late second trimester.(1) It is associated with adverse maternal and perinatal outcomes, including an increased risk of cesarean section, preeclampsia, macrosomia, neonatal hypoglycemia, and long-term metabolic complications for both the mother and the offspring.(2–5) Early identification and appropriate management of GDM are essential to optimize maternal and neonatal health outcomes and also prevent lifetime complications that may impair people's quality of life and burden the healthcare system.

Appropriate use of standardized screening and diagnostic protocols plays a crucial role in the identification and management of GDM. Guidelines from several organizations recommend different approaches, leading to variations in clinical practice worldwide and much uncertainty about the best diagnostic pathway to be implemented.(6–11) These variations can significantly impact the identification and subsequent management of GDM cases.

In this context, adherence to established screening and diagnostic protocols is critical. However, studies assessing adherence to these protocols are limited,(12,13) and there is a need to evaluate their implementation and impact on clinical outcomes. In Brazil, updated GDM screening and diagnosis recommendations were issued by a conjoint group of organizations in 2017 (Pan American Health Organization/PAHO, Ministry of Health/MS, Brazilian Federation of Gynecology and Obstetrics Associations, and Brazilian Diabetes Society/FEBRASGO), proposing early diagnosis based on first-

trimester fasting plasma glucose (FPG).(9) However, the previous 2012 Brazilian Ministry of Health Antenatal Care Guidelines for Primary Health Care Facilities (CAB32)(8) are still widely used, since updates in the specific context of primary health care have not been issued. Thus, understanding the level of adherence to screening and diagnostic protocols for GDM is crucial for optimizing healthcare practices and improving patient outcomes in Brazil. The present study aimed to investigate compliance to locally available GDM screening and diagnosis guidelines in a retrospective cohort of mixed-risk pregnant women. We hypothesized that there is a poor adherence to these guidelines likely resulting in reduced GDM diagnosis and management.

METHODS

This retrospective cohort study enrolled subjects who gave birth to a live born at the Clinical Hospital of Botucatu during 2018. The Hospital Perinatal Diabetes Research Center (PDRC) provides antenatal care (ANC) for high-risk pregnancies and intrapartum and postpartum care for both low and high-risk pregnant women referred by primary care services from over 20 cities in the region, as well as is responsible for inpatient admissions to manage both GDM and type 1 and 2 Diabetes Mellitus (DM). Most tests for GDM diagnosis as fasting plasma glucose (FPG), glycated hemoglobin (A1C), glucose tolerance test (GTT), and glycemic profile (GP) from patients attended at the PDRC are processed by the Hospital laboratory using standardized methods.

Subjects were deemed eligible if their birth occurred at the hospital and their medical chart was available in the hospital system. Subjects with a previous diagnosis of Type 1 or 2 DM or overt DM during early pregnancy were excluded. We intended to identify at least 246 subjects with an FPG before 20 weeks and a 75g 2 hours GTT, based on a sample size calculation to estimate a population parameter (frequency of GDM diagnosis) assuming a 20% frequency of GDM diagnosis previously described for the Hospital (1) and a 95% confidence interval of 15% to 25%. To identify those cases, 660 consecutive participants were included.

Ethical approval was obtained from local ethics committees on August 7, 2019, with approval number 17333619.3.0000.5411, and a waiver of informed consent was requested and granted due to the study’s retrospective nature. Data was abstracted

from the electronic medical record system that includes information about the admission for birth (from both the parturient and the baby), but also about the antenatal care (ANC) received, including laboratory tests. Medical charts were reviewed by two authors (Mariane de Oliveira Menezes-MOM and Maíra Libertad Soligo Takemoto-MLST) and the following variables were retrieved and included in the study database: city of origin, age, level of education, ethnicity, parity, maternal height, maternal weight, body mass index, number of visits to ANC, gestational age of ANC initiation, ANC setting (primary care, high risk, private care or none), previous diseases and risk factors (chronic hypertension before pregnancy, gestational hypertension/preeclampsia or gestational diabetes in previous pregnancy, smoking), laboratory tests for GDM screening and diagnosis, hypertensive disorders of pregnancy during the current pregnancy and GDM diagnosis. Variables concerning maternal and perinatal outcomes were collected but were not included in the present analysis.

GDM screening and diagnosis protocols and tests

The following GDM-related diagnostic tests results and dates were abstracted from inpatient medical charts and ANC records (both available in the Hospital data system): Fasting Plasma Glucose up to 20 weeks of pregnancy; A1C (the first available test during pregnancy if more than one was available); 2-hour 75 g glucose OGTT; a glycemic profile (GP) consisting of serial plasma glucose every 2 hours (from 8 am to 6 pm) following a standardized 2840 calories diet divided into 5 meals. For the GP, normal values adopted by the PDRC following Rudge et al(14–16) were 90 mg/dL for fasting and 130 mg/dL postprandial.

Three different protocols for GDM diagnosis were considered in the present analysis: Brazilian Ministry of Health 2012 Low-Risk Antenatal Care Guidelines (CAB32),(8) Brazilian Ministry of Health 2017 GDM Screening and Diagnosis Guidelines (MoH2017),(9) and the Rudge protocol.(14–16) They are summarized in Figure 1. CAB32 was selected due to its widespread use in the context of primary care in Brazil and MoH2017 because it had been recently published when the sample pregnancies occurred and is the current official Brazilian guideline. Rudge recommendations to combine GP and OGTT for GDM diagnosis emerged from studies conducted in the study site and they are adopted by the high-risk pregnancy PDRC outpatient clinic.

The information about the specific protocol for GDM diagnosis adopted by the ANC provider was not available on medical charts, hence we applied the three diagnosis algorithms to the data abstracted during data collection to assess potential compliance to each guideline.

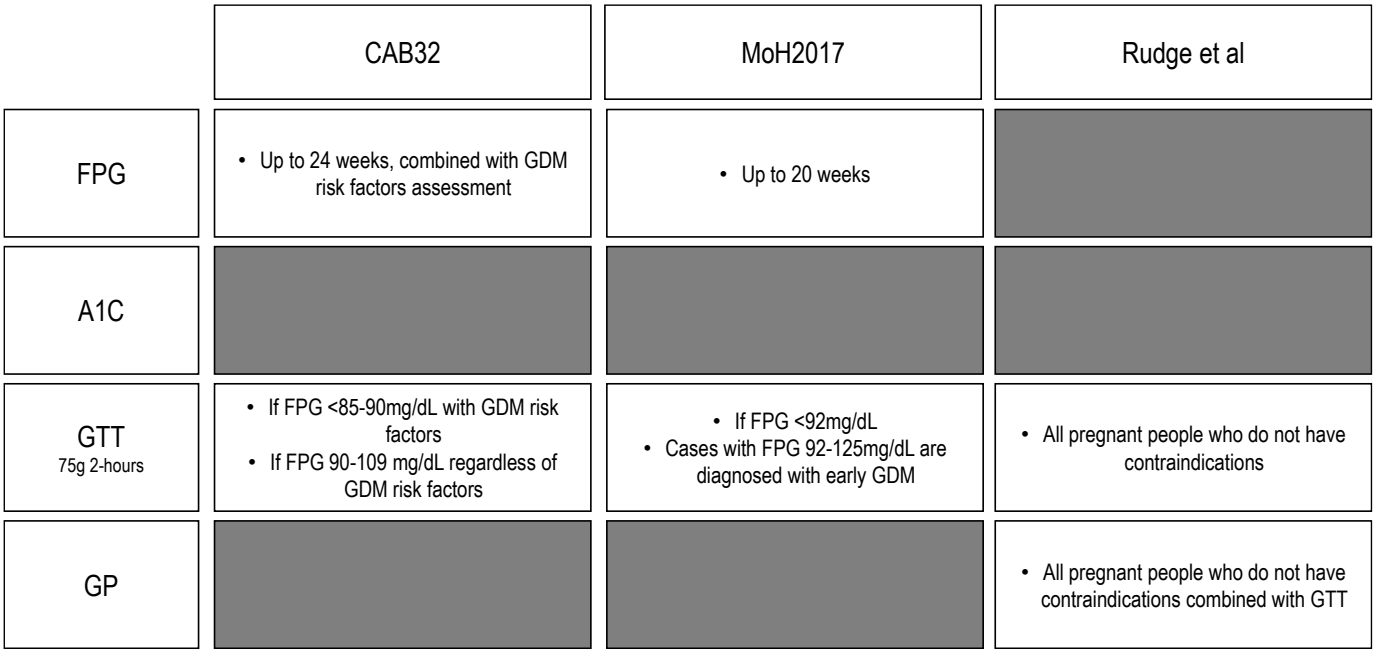

Figure 1. Criteria for compliance for each of the examined GDM screening and diagnosis guidelines

A1C, glycated hemoglobin; CAB32, Brazilian Ministry of Health 2012 Antenatal Care Guidelines for Primary Health Care Facilities; FPG, fasting plasma glucose; GDM, Gestational Diabetes Mellitus; GP, glycemic profile; GTT, 2-hours oral 75g glucose tolerance test; MoH2017, Brazilian Ministry of Health GDM Screening and Diagnosis Guideline

Statistical analysis

Subjects were classified as compliant or non-compliant to the three GDM screening and diagnosis guidelines considered in this analysis (CAB32, MoH2017, and Rudge) based on the compliance to the screening and diagnosis algorithm presented in each protocol. The criteria for compliance were nevertheless flexible with the gestational age in which the GTT and GP were collected due to the significant discrepancy between guideline recommendations and the observed data in the sample. Gestational age for FPG and A1C was strictly followed as per each guideline. Descriptive statistics were used to present the proportion of compliance to the full guideline and different components of the screening and diagnosis algorithms. Sociodemographic and clinical characteristics were compared between subgroups defined by having received

minimum GDM diagnostic tests (ann FPG before 20 weeks and a 2-hour 75g OGTT) using the chi-squared test. FPG and GTT were defined as the minimum GDM screening and diagnosis tests for the subgroup analysis both because they are the most common tests in most GDM guidelines and because they are recommended by the Brazilian most updated protocol in effect at the time of data collection (MoH2017). Multivariate logistic regression analyses were performed to estimate the association between exposure variables and compliance to each GDM diagnosis guideline. Variables with $p<0.10$ in the univariate analysis were initially included in the model and a stepwise backward approach was used for variables selection (removing terms with $p \geq 0.1$ and adding those with $p < 0.05$). Results were presented with odds ratios (OR) and their 95% confidence intervals (CI). Statistical analysis was done using STATA 16/MP 16.1 and a level of significance of $p<0.05$.

RESULTS

Within the screened sample of 660 medical records, duplicates due to twin pregnancies and pre-existing diabetes diagnoses were excluded, resulting in 645 eligible cases. As shown in Figure 2, most of these cases had undergone at least one FPG (84.3%), while 13% of the sample did not undergo any GDM-related tests.

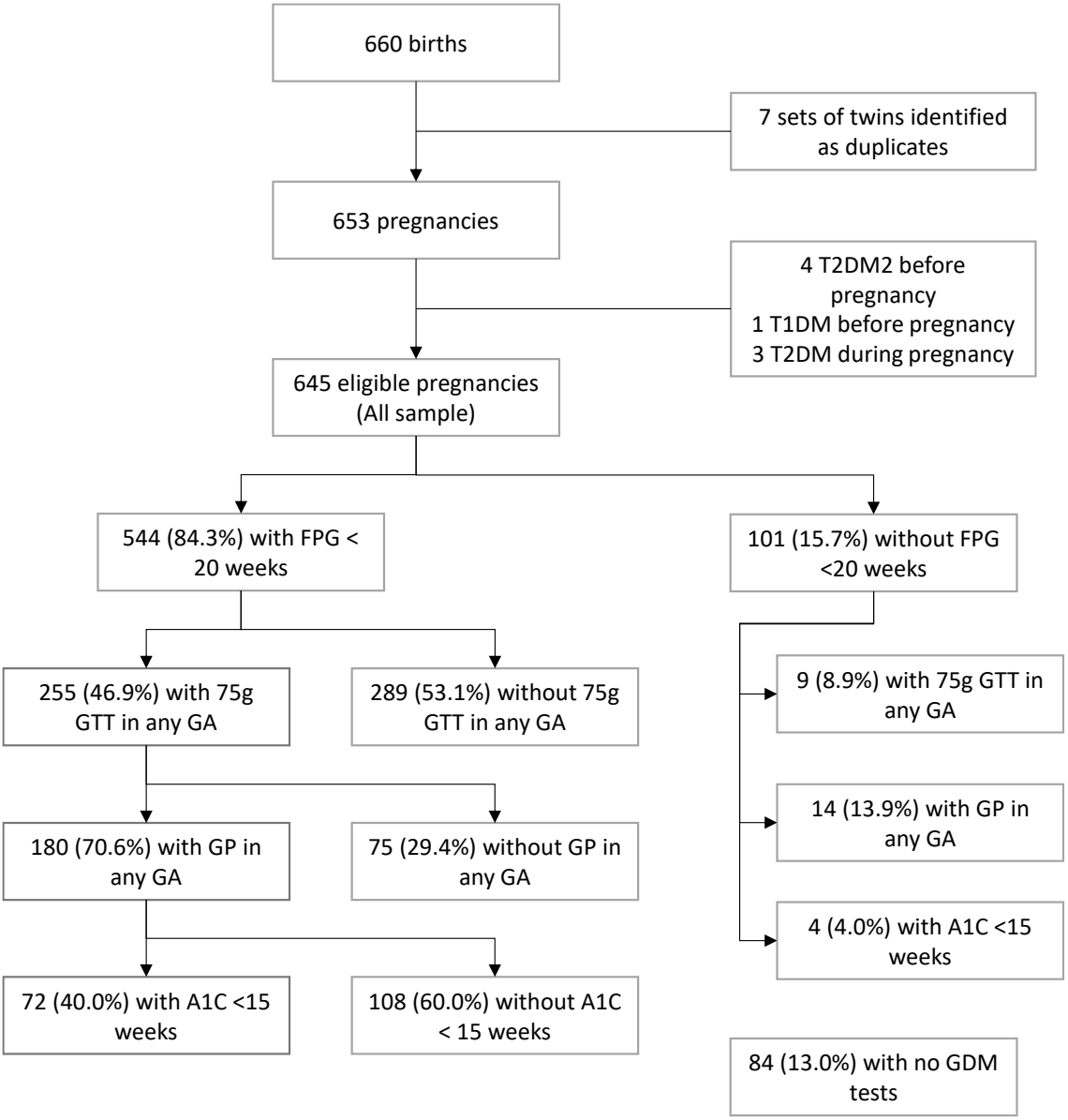

Figure 2. Study flowchart

A1C, glycated hemoglobin; FPG, fasting plasma glucose; GA, gestational age; GP, glycemic profile; GTT, 2-hours oral 75g glucose tolerance test; T2DM, Type 2 Diabetes Mellitus; T1DM, Type 1 Diabetes Mellitus

Table 1 shows the sociodemographic and clinical characteristics of the sample and the bivariate analysis performed to investigate between-subgroup differences. The variables age, antenatal care setting, number of antenatal care visits, having chronic hypertension before pregnancy, or being diagnosed with chronic hypertension during the current pregnancy were significantly different between women who had undergone an FPG and a GTT.

Table 1. Sample characteristics according to compliance to minimum GDM screening and diagnosis tests

	All sample (n=645)		FPG + GTT (n=255)		No FPG and/or GTT (n=390)		p-value*
	N	%	N	%	n	%	
Age							
<19 years	67	10.3	17	6.7	50	12.8	**<0.001**
19-34 years	494	76.6	194	76.1	300	76.9	
35+ years	84	13.0	44	17.3	40	10.3	
Ethnicity/skin color							
Black/brown	106	16.4	38	14.9	68	17.4	0.586
White	533	82.7	216	84.7	317	81.3	
Yellow	2	0.3	0	0.0	2	0.5	
Not reported	4	0.6	1	0.4	3	0.8	
Antenatal care setting (n=642)							
Primary care public service	480	74.8	148	58.0	332	85.8	**<0.001**
High risk public service	153	23.8	104	40.8	49	12.7	
Private practice	6	0.9	3	1.2	3	0.8	
No antenatal care	3	0.5	0	0.0	3	0.8	
Antenatal care initiation in 1st trimester (n=603)							
Yes	489	81.1	200	83.0	289	79.8	0.333
No	114	18.9	41	17.0	73	20.2	
Minimum of 6 antenatal appointments (n=581)							
Yes	531	91.4	225	96.1	306	88.2	**0.001**
No	50	8.6	9	3.9	41	11.8	
Obesity (vs. non-obesity) (n=558)	168	30.1	84	35.6	84	26.1	**0.016**
Nulliparity	218	33.8	80	31.4	138	35.4	0.292
History of abortion	136	21.1	59	23.1	77	19.7	0.302
Chronic hypertension before pregnancy	46	7.1	28	11.0	18	4.5	**0.002**
Hypertensive disorders of pregnancy in previous pregnancy	47	7.2	23	9.0	24	6.0	0.171
Previous gestational diabetes mellitus	9	1.4	6	2.4	3	0.8	0.094
Smoking	72	11.0	29	11.4	43	10.8	0.891
Weight gain in this pregnancy (n=536)							
Excessive	299	55.8	137	59.3	162	53.1	0.153
Non-excessive	237	44.2	94	40.7	143	46.9	
Chronic hypertension diagnosed in this pregnancy	15	2.3	10	3.9	5	1.3	**0.030**
Gestational hypertension in this pregnancy	88	13.6	33	12.9	55	14.1	0.674

Preeclampsia in this pregnancy	85	13.2	33	12.9	52	13.3	0.886

*Pearson's chi-squared test

The highest adherence was observed for CAB32 (46.8%), as shown in Table 2. Having at least one GTT during pregnancy was observed in 40.9% of the sample, but only 25.9% had the test in the recommended gestational age window (24-28 weeks). Compliance to any GDM screening and diagnosis protocol was observed for 57.the 1% of the sample.

Table 2. Compliance to different GDM screening and diagnosis guidelines (n=645)

	All sample		
	n	%	95% CI
Compliance to Ministry of Health CAB32 protocol	**302**	**46.8**	**42.9-50.7**
FPG before 20 weeks	544	84.3	81.3-87.1
Risk factors for GDM* (n=544)	483	74.9	71.3-78.2
FPG < 85-90 mg/dL without risk factors (n=544)	125	23.0	19.5-26.7
FPG < 85-90 mg/dL with risk factors (n=544)	365	67.1	63.0-71.0
FPG 90-109 mg/dL (n=544)	52	9.6	7.2-12.4
FPG ≥ 110 mg/dL (n=544)	2	0.4	0.04-1.3
75g GTT 24-28 weeks being eligible (n=544)	136	21.1	18.0-24.4
75g GTT in any GA being eligible (n=544)	215	33.3	29.7-37.1
75g GTT in any GA when already had GDM according to a previous test	1	0.2	0.0-0.8
Compliance to Ministry of Health 2017 protocol - Full technical and financial feasibility	**250**	**38.8**	**35.0-42.6**
FPG before 20 weeks	544	84.3	81.3-87.1
FPG < 92 mg/dL (n=544)	501	92.1	89.5-94.2
FPG 92-125 mg/dL (n=544)	43	7.9	5.8-10.5
75g GTT 24-28 weeks being eligible (n=544)	147	22.8	19.6-26.2
75g GTT in any GA being eligible (n=544)	231	35.8	32.1-39.6
75g GTT in any GA when already had GDM according to a previous test	24	3.7	2.4-5.5
Compliance to Rudge protocol	**188**	**29.1**	**25.7-32.8**
GP 24-28 weeks if eligible (n=645)	116	18.0	15.1-21.2
GP in any GA if eligible (n=645)	222	34.4	30.7-38.2
GP + 75g GTT 24-28 weeks if eligible	23	3.6	2.2-5.3
GP + 75g GTT in any GA if eligible	188	29.1	25.7-32.8
75g GTT with 24-28 weeks (regardless of other tests)	**167**	**25.9**	**22.5-29.4**
75g GTT in any GA (regardless of other tests)	**264**	**40.9**	**37.1-44.8**
Compliance to any GDM screening and diagnosis protocol	**368**	**57.1**	**53.1-60.9**
No GDM screening/diagnosis tests	**84**	**13.0**	**9.7-14.9**

*The following factors were considered: Age of 35 years or older; overweight, obesity, or excessive weight gain during this pregnancy; short stature; adverse obstetric history or previous gestational diabetes mellitus (GDM).

Figure 3 presents the variation in the gestational age in which the GTT was performed, ranging from 6 to 43 weeks of gestation (median 27 weeks, interquartile range 4). Among those who had a GTT recorded in the medical charts, 36.7% had the test performed outside the recommended gestational age (most commonly after 28 weeks).

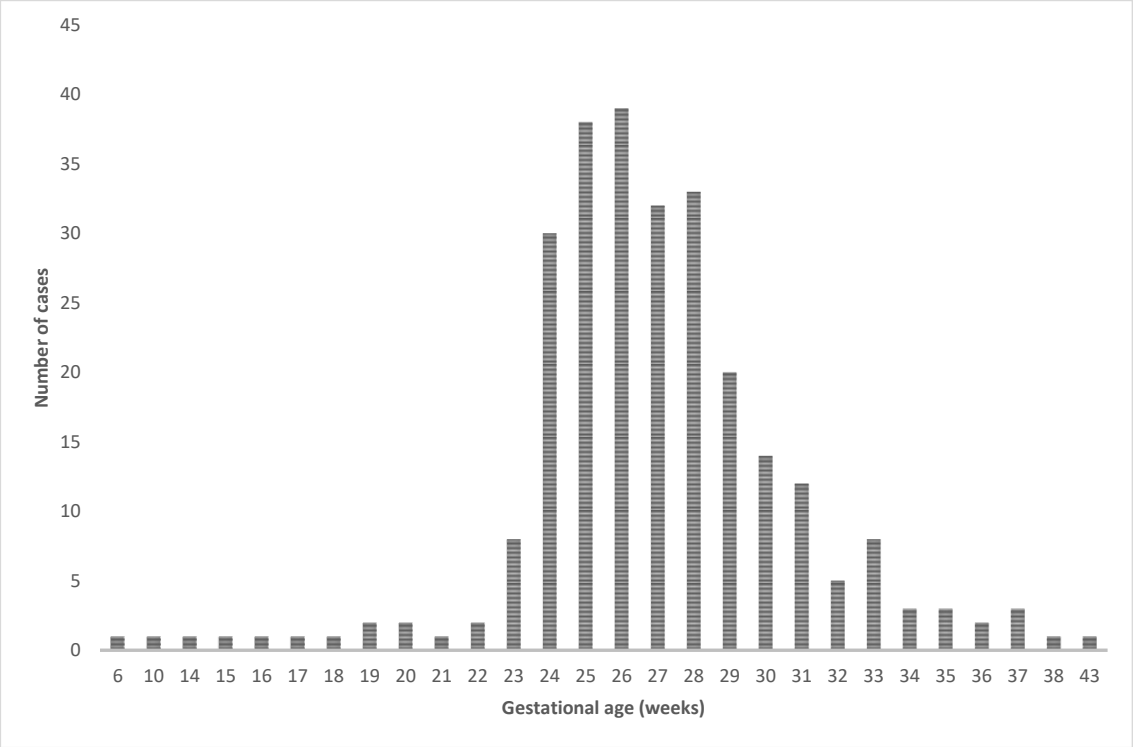

Figure 3. Gestational age in which oral GTT was collected

Table 3 presents the results of the multivariate logistic regression for compliance by guideline. For all guidelines, the number of antenatal visits increases the chance of adherence (from 1.10 to 1.19 times for each additional visit). Chronic hypertension before pregnancy was significantly associated with increased odds of adherence to GDM screening and diagnosis recommendations for all guidelines except CAB32 (Odds Ratio[OR] ranging from 2.16 for MoH2017 to 3.15 for Rudge et al).

Table 3. Multivariate analysis logistic regression analysis for compliance to GDM screening and diagnosis protocols for specified variables

GDM diagnosis protocol	Exposure variables retained in the final model	Odds Ratio	95% Confidence Interval
CAB32	Obesity	1.39	0.95-2.04
	Number of ANC visits	1.10	1.03-1.18
MoH2017	Chronic hypertension before pregnancy	2.16	1.10-4.25
	Number of ANC visits	1.15	1.08-1.23
Rudge et al	Obesity	1.65	1.08-2.53

	Chronic hypertension before pregnancy	3.15	1.54-6.43
	Number of ANC visits	1.19	1.10-1.29
	Gestational age at first ANC visit	1.03	0.99-1.07
Any of the three protocols	Chronic hypertension before pregnancy	2.18	1.04-4.54
	Number of ANC visits	1.16	1.08-1.23
At least a 2-hour 75g GTT	Obesity	1.51	1.01-2.27
	Chronic hypertension before pregnancy	2.37	1.15-4.89
	Number of ANC visits	1.16	1.08-1.24

DISCUSSION

Our findings indicate that compliance to GDM screening and diagnosis guidelines remains a significant concern, both from the standpoint of individual clinical outcomes and from a public health perspective. Our study examined the adherence to these recommendations and found a surprisingly low adherence rate. Sufficient tests to apply the diagnostic algorithm recommended by the updated Brazilian Ministry of Health guidelines issued in 2017 (the year before the data collection period) were available to less than 40.0% of the sample. Only 57% of the sample could be classified as being compliant to any of the GDM screening and diagnosis guidelines locally available at the time sample pregnancies and births occurred, while 13.0% of the sample had no GDM-related tests recorded in medical charts. Adherence to recommended GDM tests was associated with an increased number of antenatal visits and having chronic hypertension for most investigated scenarios.

This finding is consistent with previous studies that have also reported poor compliance to GDM screening and diagnosis recommendations.(12,13) Agbozo et al 2022(13) examined compliance to recommended appointments for GDM testing in Ghana. The proportion of pregnant women who completed FPG, 1-hour, and 2-hour GTT was 54.6%, 54.3%, and 53.2%, respectively. The observed frequencies are lower than our findings for FPG and higher for GTT. Factors positively associated with compliance to recommended appointments in Agbozo et al sample were maternal age above 35 years, secondary education, formal sector employment and having same-sex children. Murphy et al(12) investigated compliance to NICE risk-based screening for GDM in a cohort of 2432 women. Among those, 27% had at least one risk factor for GDM as described in NICE guidance from which only 60.8% were adequately screened. At the same time, 14.6% of women had no GDM risk factors according to NICE, and underwent an oral GTT. The authors also identified that ethnicity was the most

commonly missed risk factor and that GTT was collected in the recommended gestational age window for 56.6% of cases.

Interestingly, our study identified factors that were associated with an increased chance of adherence to the recommended GDM diagnostic tests. Pregnant women with chronic hypertension, obesity and who attended more antenatal care visits seem more likely to undergo appropriate testing, even though those findings were not consistent across all hypothetical scenarios. These observations align with existing literature that highlights the increased risk of GDM in higher BMI populations.(17–19) However, there are conflicting recommendations from different guidelines about whether chronic hypertension should be considered a risk factor for GDM,(8,10,20,21) even though it is a well-established risk factor for type 2 DM(10) and is listed as a risk factor for GDM in the most recent Brazilian guideline.(9) The association between chronic hypertension and obesity with higher adherence to GDM screening guidelines may suggest that antenatal care providers may be more aware of these risk factors and thus more motivated to follow the recommended testing protocols. Nevertheless, it is not possible to rule out that these women are referred early in pregnancy to high-risk healthcare facilities (particularly those with chronic hypertension) and that care providers in such settings may be more used to GDM testing guidelines due to their daily clinical practice with higher risk populations.

Furthermore, we found that the number of antenatal care visits attended by pregnant women had a positive association with adherence to GDM screening and diagnosis guidelines. This finding suggests that the provision of regular and adequate prenatal care plays a crucial role in promoting compliance to GDM testing. Previous studies have reported several barriers to GDM screening and diagnosis from both the care provider and patients' perspectives.(22–25) Even though these barriers assessed in the available literature varies depending on the study and specific contexts, it seems reasonable to affirm that factors related to a better quality of antenatal care provided by the health care system are markedly relevant to improve GDM testing and diagnosis both in lower and higher resource settings.

Our study has some limitations that warrant consideration. Due to its retrospective nature, we cannot exclude the risk of information bias. The accuracy and completeness of medical records may vary, potentially leading to misclassification of guideline non-compliance or missing data on exposure variables. Additionally, despite our attempts

to control for confounding variables, unknown confounders may still affect retrospective studies. Our analysis was limited by the variables available in the medical charts. For example, it is likely that characteristics of the antenatal care setting where women received care play a role in the observed adherence, but these aspects could not be explored by the study's hospital-based approach. In terms of study strengths, our analysis included a large sample size of mixed-risk pregnant women with a high coverage of antenatal care visits and most of them performed antenatal tests in the hospital laboratory, decreasing the likelihood of missing information about GDM test results (a crucial variable to address adherence to guidelines outcomes). Despite these limitations, our findings contribute to the overall understanding of GDM screening and diagnosis patterns within the public healthcare system in Brazil. They also highlight the need for strategies to improve adherence to national recommendations. Future prospective studies on GDM screening and diagnosis practices in real-world clinical settings could explore additional variables potentially linked to compliance with GDM guidelines, such as barriers to access healthcare for women and the knowledge and attitudes of antenatal care providers regarding GDM screening and diagnosis.

In conclusion, our findings suggest that compliance with locally available GDM screening and diagnosis guidelines is inadequate in our sample, with a significant proportion of women not undergoing recommended GDM tests or performing tests outside the appropriate timeframe. This observation raises concerns regarding the underdiagnosis of GDM and its potential detrimental effects. It not only hinders the appropriate management of GDM during pregnancy but also poses long-term risks for both women and their offspring due to untreated GDM.

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Artigo 2

Artigo original elaborado de acordo com as normas de publicação da revista BMC Pregnancy and Childbirth para a qual será submetido.

Qualis A1 Med III – FI: 3,007 https://bmcpregnancychildbirth.biomedcentral.com/

"Incidence of gestational diabetes mellitus according to different diagnostic criteria: a retrospective cohort"

INTRODUCTION

Gestational diabetes mellitus (GDM) is a common metabolic disorder that occurs during pregnancy and is characterized by glucose intolerance.(1) It poses significant health risks for both the mother and the offspring, including complications during childbirth, maternal and neonatal morbidity, and long-term metabolic consequences.(2–5) The prevalence of GDM varies worldwide with reports ranging from 2.0%-32.0%, depending on multiple factors such as ethnicity, maternal age, obesity, and family history of diabetes, as well as diagnostic criteria.(6–9)

Accurate diagnosis and appropriate management of GDM are essential for optimizing maternal and neonatal health outcomes, in the short-term and long-term settings. However, there is a lack of consensus regarding the diagnostic criteria for GDM, which leads to variations in its reported prevalence. Several organizations and guidelines propose different diagnostic criteria, such as those set by the International Association of Diabetes and Pregnancy Study Groups (IADPSG), the American Diabetes Association (ADA), and the World Health Organization (WHO)(1,3,10,11) These variations in diagnostic criteria make it challenging to determine the true prevalence of GDM and may have implications for clinical practice and resource allocation. Also, uncertainty remains about the impact of those different diagnostic criteria on perinatal outcomes and if more intensive strategies lead to increased benefits.(12)

Understanding the incidence of GDM according to different diagnostic criteria is fundamental for effective healthcare planning and the development of appropriate screening and management strategies. Additionally, there is solid evidence supporting an increased risk of long-term adverse metabolic and cardiovascular outcomes among those with a previous GDM diagnosis.(13–15) Thus, undiagnosed cases can be

considered lost opportunities to implement preventive strategies to impact people's overall lifetime health and also the consequences of such metabolic and cardiovascular disorders for the public health. By examining the incidence derived from different criteria, healthcare providers and policymakers can make informed decisions regarding screening practices and resource allocation. Thus, the present study aimed to investigate GDM incidence in a cohort of mixed-risk pregnant women by retrospectively applying four different diagnostic criteria to GDM test results as abstracted from medical records. We also aimed to investigate differences in sociodemographic and clinical characteristics to explore how they vary between subgroups of women that would have been diagnosed with GDM if each criterion had been applied in the real world.

METHODS

This retrospective single-center cohort study enrolled subjects who gave birth to a live born at the Clinical Hospital of Botucatu in 2018. Details on methods and participants were published elsewhere. In brief, births that occurred at the hospital with medical records available in the hospital system were deemed eligible. A previous diagnosis of Type 1 or 2 Diabetes Mellitus (DM) or overt DM during early pregnancy was the sole exclusion criterion. Ethical approval was obtained from the Institutional Review Board on August 7, 2019, with approval number 17333619.3.0000.5411 including a waiver of informed consent due to the retrospective nature of data. The following variables were included in the present analysis: age, level of education, ethnicity, parity, smoking status, body mass index, gestational weight gain, number of prenatal care visits, gestational age of prenatal care onset, setting of the prenatal care received (primary care, high risk, private care or none), GDM risk factors (chronic hypertension before pregnancy, gestational hypertension or preeclampsia or gestational diabetes in previous pregnancy, hypertensive disorders of pregnancy during the current pregnancy), laboratory tests for GDM screening and diagnosis, and a GDM diagnosis as determined by the antenatal care (ANC) provider (regardless of the diagnostic criteria used).

GDM screening and diagnosis protocols and tests

Results from Fasting Plasma Glucose (FPG) up to 20 weeks of pregnancy, glycated hemoglobin (A1C, the first available test during pregnancy if more than one was available), 2-hour 75 g glucose tolerance test (GTT), and a glycemic profile (GP, consisting of serial plasma glucose every 2 hours from 8 am to 6 pm following a standardized 2840 calories diet divided into 5 meals) were abstracted from medical records when available. Most laboratory tests performed by the study sample were processed in the Hospital laboratory using standardized procedures. Four different GDM diagnosis criteria were retrospectively applied to laboratory test results as defined in the following GDM screening and diagnosis guidelines: Brazilian Ministry of Health 2012 Low-Risk Antenatal Care Guidelines (CAB32),(16) Brazilian Ministry of Health 2017 GDM Screening and Diagnosis Guidelines (MoH2017),(17) American Diabetes Association 2023 GDM Screening and Diagnosis Recommendations (ADA23),(1) and the Rudge protocol(18–20) (Figure 1). Each guideline was used to explore hypothetical scenarios where all women with sufficient tests available in their medical charts (the guideline-compliant subsample) would have been screened using the guideline algorithm, despite the criteria actually adopted by the prenatal care provider.

	CAB32	MoH2017	Rudge et al	ADA23
FPG	• If>110mg/dL, repeat the test immediately and if >110mg/dL diagnose GDM	• Early GDM if 92-125mg/dL	• Not considered for screening or diagnosis on the guideline	• Early AGM if 110–125mg/dL
A1C	• Not considered for screening or diagnosis on the guideline	• Not considered for screening or diagnosis on the guideline	• Not considered for screening or diagnosis on the guideline	• Early AGM if 5.9–6.4%
GTT 75g 2-hours	• GDM if FPG > 110mg/dl and/or 2h > 140mg/dl	• GDM if at least one of the following: FPG 92-125mg/dL, 1-hour ≥ 180mg/dL, 2h 153-199 mg/dL	• GDM if at least one of the following: FPG 92-125mg/dL, 1-hour ≥ 180mg/dL, 2-hour ≥ 153mg/dL	• GDM if at least one of the following: FPG 92-125mg/dL, 1-hour ≥ 180mg/dL, 2-hour ≥ 153mg/dL
GP	• Not considered for screening or diagnosis on the guideline	• Not considered for screening or diagnosis on the guideline	• MGH if FPG ≥ 90mg/dL or post prandial glucose ≥ 130mg/dL with normal GTT values	• Not considered for screening or diagnosis on the guideline

Figure 1. Criteria for GDM diagnosis in each guideline

A1C, glycated hemoglobin; ADA23, American Diabetes Association Classification and Diagnosis of Diabetes: Standards of Care in Diabetes; AGM, abnormal glucose metabolism; CAB32, Brazilian Ministry of Health 2012 Antenatal Care Guidelines for Primary Health Care Facilities; FPG, fasting

plasma glucose; GDM, Gestational Diabetes Mellitus; GP, glycemic profile; GTT, 2-hours oral 75g glucose tolerance test; MGH, Mild Gestational Hyperglycemia; MoH2017, Brazilian Ministry of Health GDM Screening and Diagnosis Guideline

Statistical analysis

Data were explored as means and standard deviations for continuous variables and proportions for categorical variables. A bivariate comparison of sociodemographic and clinical characteristics was made between three groups according to GDM status: GDM diagnosed by any criteria, non-GDM with at least a 2-hour 75g OGTT available in the medical chart, the remaining sample with insufficient tests to exclude or diagnose GDM. GDM incidence was estimated using four hypothetical scenarios (CAB32, MoH2017, ADA23 and Rudge) using as numerator the number of diagnoses that would be made if each guideline algorithm had been applied and as denominator the subgroup with sufficient data to apply the algorithm (guideline compliant subgroups). As GDM-related outcomes were rare in the sample, we also explore differences in the frequency of a composite outcome combining potentially GDM-related events: polyhydramnios, macrosomia, shoulder dystocia, neonatal hypoglycemia, neonatal jaundice requiring phototherapy, or admission to neonatal ICU due to any causes excluding genetic syndromes or malformation. Statistical analysis was done using STATA 16/MP 16.1 and a level of significance of $p<0.05$.

RESULTS

Figure 1 depicts the study flowchart. 660 births were screened for eligibility resulting in 645 pregnant people in the sample, which were classified into four guideline compliance subsamples. Compliance to GDM screening and diagnosis guidelines in the sample was overall inadequate, as previously reported. In the sample, 84.3% had at least one FPG before 20 weeks and of those, 46.9% had undergone an oral GTT at any gestational age. 13.0% had no GDM-related tests.

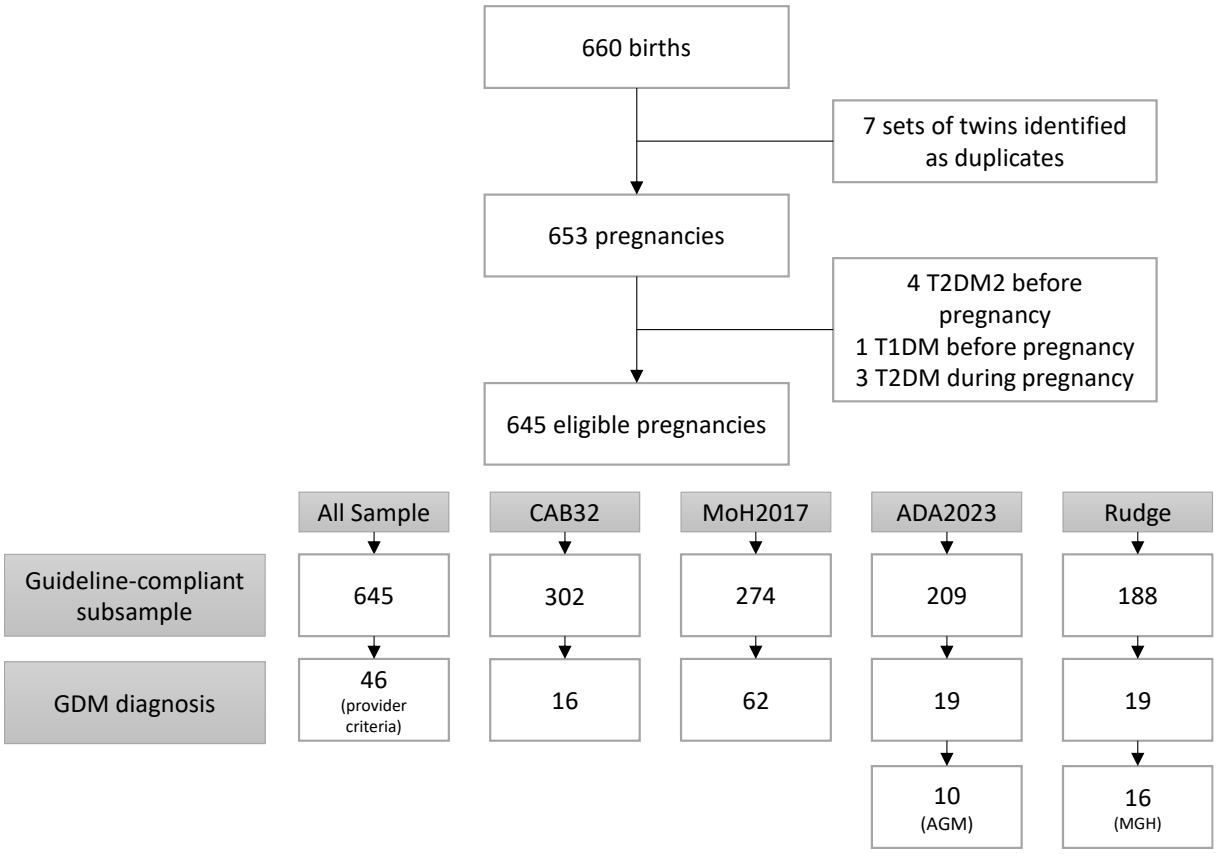

Figure 2. Study flowchart

ADA2023, American Diabetes Association Classification and Diagnosis of Diabetes: Standards of Care in Diabetes; AGM, abnormal glucose metabolism; CAB32, Brazilian Ministry of Health 2012 Antenatal Care Guidelines for Primary Health Care Facilities; GDM, Gestational Diabetes Mellitus; MGH, Mild Gestational Hyperglycemia; MoH2017, Brazilian Ministry of Health GDM Screening and Diagnosis Guideline; T2DM, Type 2 Diabetes Mellitus; T1DM, Type 1 Diabetes Mellitus

Table 1 presents the sample characteristics by the subgroup of interest based on the GDM status. GDM was diagnosed in 80 subjects, while 201 subjects had at least one GTT and were classified as non-GDM because no abnormal GDM-related tests were identified in medical charts. Insufficient tests to either confirm or exclude GDM were observed in 364 pregnant women (56.4%). The following variables were statistically different between subgroups in the bivariate analysis: age 35+ years, antenatal care setting, a minimum of 6 antenatal care visits, obesity/overweight, chronic hypertension before pregnancy, history of gestational hypertension or preeclampsia in a previous pregnancy, history of gestational diabetes in a previous pregnancy, and chronic hypertension diagnosed in the current pregnancy.

Table 1. Sample characteristics according to GDM diagnosis according to different criteria

	All sample (n=645)		GDM by any criteria (n=80)		Non-GDM with at least GTT (n=201)		Insufficient tests to screen for GDM (n=364)		p-value*
	n	%	n	%	n	%	n	%	
Age 35+ years	84	13.0	18	22.5	31	15.4	35	9.62	**0.004**
Ethnicity/skin color									
Black/brown	106	16.5	11	13.7	31	15.4	64	17.6	
White	533	83.1	68	85.0	169	84.1	296	81.3	0.929
Yellow	2	0.3	0	0.0	0	0.0	2	0.6	
Not reported	4	0.6	1	1.2	1	0.5	2	0.5	
Antenatal care setting (n=642)									
Primary care public service	480	74.8	26	32.5	134	66.7	320	88.6	
High risk public service	153	23.8	53	66.2	65	32.3	35	9.7	**<0.001**
Private practice	6	0.9	1	1.2	2	1.0	3	0.8	
No antenatal care	3	0.5	0	0.0	0	0.0	3	0.8	
Antenatal care initiation in 1st trimester (n=603)	489	81.1	61	80.3	157	82.6	271	80.4	0.807
Minimum of 6 antenatal appointments (n=581)	531	91.4	73	98.6	173	95.0	285	87.7	**0.001**
Obesity/overweight (n=558)	312	55.9	57	73.1	98	53.5	157	52.9	**0.004**
Nulliparity	218	33.8	19	23.7	69	34.3	130	35.7	0.120
History of abortion	136	21.1	23	28.7	42	20.9	71	19.5	0.185
Chronic hypertension before pregnancy	46	7.1	14	17.5	17	8.5	15	4.1	**<0.001**
Hypertensive disorders of pregnancy in previous pregnancy	47	7.3	11	13.7	16	8.0	20	5.5	**0.033**
Previous gestational diabetes mellitus	9	1.4	4	5.0	3	1.5	2	0.6	**0.009**
Smoking	72	11.0	13	16.2	20	9.9	39	10.7	0.292
Excessive weight gain in this pregnancy (n=536)	299	55.8	41	53.9	105	59.3	153	54.1	0.511
Chronic hypertension diagnosed in this pregnancy	15	2.3	6	7.5	5	2.5	4	1.1	**0.003**
Gestational hypertension in this pregnancy	88	13.6	13	16.2	23	11.4	52	14.3	0.493
Preeclampsia in this pregnancy	85	13.2	13	16.2	22	10.9	50	13.7	0.442

*Pearson's chi-squared test

Table 2 presents the incidence of GDM, abnormal glucose metabolism, and mild gestational hyperglycemia according to each diagnostic criteria, considering the compliant sample for each guideline. The GDM incidence ranged from 5.3% (CAB32 criteria) to 22.6% (MoH2017 criteria) in the hypothetical scenarios, while the actual incidence as diagnosed by the antenatal care provider was 7.1% (regardless of the diagnostic criteria used). Abnormal glucose metabolism as defined by ADA23 was

present in 4.8% of the ADA23-compliant sample, while mild gestational hyperglycemia (Rudge Ib Group) was identified in 8.5% of the Rudge et al compliant sample. It is worth mentioning that most cases diagnosed by MoH2017 criteria would have been diagnosed by the FPG < 20 weeks (e.g., early GDM). The prevalence considering any of the criteria was 21.6%. Missed diagnoses represent 10.5% of the sample compliant with any of the guidelines (had an abnormal test reported in the medical chart but were not diagnosed with GDM by the provider).

Table 2. Gestational diabetes mellitus, abnormal metabolism of glucose and mild gestational hyperglycemia diagnosis according to different criteria

	N	%	95% CI
Antenatal care provider criteria for GDM (All sample, n=645)	46	7.1	5.2-9.3
Had FPG 92-125 mg/dL up to 20 weeks (n=46)	20	46.5	31.2-62.3
Had at least one 75g GTT abnormal value in any GA (n=46)	25	54.3	39.0-69.1
Had abnormal GP in any GA (n=46)	15	32.6	19.5-48.0
It was not possible to identify the GDM diagnostic criteria used (n=46)	7	15.2	6.3-28.9
Classified as Rudge Ib group by the antenatal care provider (All sample, n=645)	6	0.9	3.4-2.0
Ministry of Health CAB32 criteria (CAB32 compliant sample, n=302)	16	5.3	3.0-8.5
Had 75g GTT fast value ≥ 110 mg/dL	0	0.0	-
Had 75g GTT 2-hour value ≥ 140 mg/dL	16	100.0	-
Ministry of Health 2017 criteria (MH2017 compliant subsample, n=274)	62	22.6	17.8-28.0
FPG 92-105 mg/dL criteria	43	69.3	56.3-80.4
75g GTT criteria	19	30.7	19.6-43.6
ADA 2023 criteria (ADA23 compliant subsample, n=209)			
Abnormal glucose metabolism	10	4.8	2.3-8.6
75g GTT criteria	19	9.3	5.7-14.1
Rudge criteria* (Rudge compliant subsample, n=188)	35	18.6	13.3-24.9
Mild gestational hyperglycemia (MGH, Rudge Ib group)	16	8.5	4.9-13.4
GDM	19	10.1	6.2-15.3
GDM by any criteria (compliant to any protocol sample, n=371)	80	21.6	17.5-26.1
Missed GDM diagnosis (compliant to any protocol sample, n=371)	39	10.5	7.6-14.1

*GDM prevalence for Rudge et al was calculated by summing GDM cases plus mild gestational hyperglycemia

The composite outcome potentially related to GDM was statistically different between subgroups, being most common among those with GDM by any criteria (Table 3). There was no difference between non-GDM and insufficient tests to confirm or exclude GDM groups. In terms of individual GDM-related outcomes, statistically significant differences were observed only for neonatal jaundice requiring phototherapy (37.5% vs. 22.9% vs. 25.3%) and admission to neonatal ICU excluding genetic syndromes and

anomalies (23.7% vs. 11.9% vs. 17.9%).

Table 3. Outcomes potentially related to GDM in the sample.

	GDM by any criteria (n=80)		Non-GDM with at least GTT (n=201)		Insufficient tests to screen for GDM (n=364)		p-value
	N	%	n	%	n	%	
Composite outcome	48	60.0	84	41.8	152	41.8	**0.009**
Macrosomia	12	15.0	21	10.4	27	7.4	0.085
Polyhydramnios	3	3.7	6	3.0	4	1.10	0.155
Shoulder dystocia	0	0.0	4	2.0	1	0.3	0.059
Neonatal hypoglycemia	3	3.8	13	6.5	22	6.1	0.683
Neonatal jaundice requiring phototherapy	30	37.5	46	22.9	92	25.3	**0.037**
Admission to neonatal ICU excluding genetic syndromes and anomalies	19	23.7	24	11.9	65	17.9	**0.039**

DISCUSSION

Our data revealed significant variation in the incidence of GDM depending on the screening and diagnostic guidelines employed. The estimated incidence using the four diagnostic criteria widely varied from 5.3% to 22.6%, whereas the real-world frequency of GDM in our sample was 7.1%. These findings align with those described in the literature, which indicates a global prevalence of gestational hyperglycemia (GH) at an average of 16%, reaching levels above 35% in certain contexts depending on the diagnostic criteria used as well as sample characteristics.(18) A previous retrospective study conducted at our institution(19-20) reported an approximate incidence of hyperglycemic disorders in pregnancy of 20%, compatible with the higher estimates from our analysis.

In a study conducted in sub-Saharan Africa, applying different screening and diagnostic protocols for GDM, prevalence ranging from 3.8% to 8.6% were found, with the highest point estimates observed when following the IADPSG protocol.(21) A systematic review of 64 studies demonstrated a wide range of GDM prevalence depending on the diagnostic criteria used, varying from 0% to 41.9%. Similarly, a meta-analysis indicated that the utilization of the IADPSG criteria resulted in significantly higher rates of GDM diagnosis.(22) A Canadian scoping review on the trends of protocol recommendations for GDM screening and diagnosis showed a fourfold

increase in the prevalence of GDM over the past two decades. This increase is attributed to clinical and epidemiological changes (such as obesity, maternal age, and ethnic diversity) as well as changes in diagnostic criteria. The data revealed a rise in GDM prevalence from approximately 3.7-6.5% to 7-16%.(24) A study conducted in South India compared the prevalence of GDM and the risk of certain adverse outcomes using the National Institute for Health and Care Excellence (NICE) and the International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria. The authors diagnosed GDM in 11.6% and 25.1% of pregnant women, respectively. Furthermore, there was little agreement between the two diagnostic criteria, and pregnant women who tested positive according to IADPSG but negative according to NICE had a higher incidence of negative outcomes potentially associated with GDM.(25) In the Latin America setting, an incidence of 7.6% was reported in a study conducted in Argentina.(23) A Brazilian study compared two fasting plasma glucose cutoff points for the diagnosis of GDM. Using a cutoff point of FPG ≥95 mg/dL, the diagnosis was made in 8.7% of cases, whereas when the cutoff was changed to ≥92 mg/dL, the diagnosis increased to 16.7%.(9)

The lack of consensus in the literature and also among healthcare providers and health system managers regarding GDM diagnostic criteria results in pregnant women being susceptible to both under- and overdiagnosis.(10,12) This uncertainty about the actual GDM incidence may directly affect the availability of therapeutic resources within the healthcare system, as well as increase the odds of adverse outcomes. On one hand, the absence of a diagnosis can deprive a group of pregnant women with diabetes of necessary treatment, leading to increased risks for both the mother and the fetus during pregnancy and in the future.(13-14) Furthermore, potentially preventable adverse outcomes can place an additional burden on healthcare costs. On the other hand, excessive diagnoses can result in unnecessary treatment expenses and escalation in the level of care, categorizing the pregnant woman as high-risk and subjecting her to more interventions and potential iatrogenesis. The absence of a well-established criterion based on solid evidence detrimentally affects individual health but also the ability of healthcare professionals to improve the care they provide for people.(4)

Our analysis also explored a composite outcome potentially associated with GDM, which was as expected more frequent in the GDM group. Despite the fact that it was

not possible to observe differences between the non-GDM group and the group with insufficient tests, it is worth mentioning that the two individual outcomes (neonatal jaundice requiring phototherapy and admission to the neonatal intensive care unit) with statistically significant differences were more common among women with insufficient tests. The association between these outcomes and gestational hyperglycemia was well described in the foundational HAPO study,(2) thus our findings raise concerns about potentially missed cases that were left untreated. As our study was not powered to address less frequent outcomes, this finding needs to be interpreted with caution.

Our study has some limitations that need to be highlighted. Due to its retrospective nature, our analysis was limited by the variables currently available in the institution's electronic medical record system. This may have impaired our ability to explore relevant confounders, particularly GDM risk factors related to previous pregnancies or family history (such as the history of macrosomia, previous GDM, GDM or T2DM history in first- and second-degree relatives, etc.). Additionally, it is not possible to exclude that some women in our sample did undergo GDM tests that were not processed in the hospital laboratory nor registered by care providers in the medical chart, thus potentially reducing the guideline-compliant samples and overestimating the incidence by decreasing the population at-risk. Nevertheless, we believe that the magnitude of such bias is likely small, once our institution provides laboratory services for several cities in the region, particularly the GTT and GP, which are centrally collected and processed. The potentially GDM-related outcomes were rare in our sample and this analysis may have been negatively affected by the small sample size of GDM cases. However, all outcomes were related to events occurring in our institution and well-documented in the medical charts, reducing the likelihood of information bias (ultrasound assessment of fetal growth and amniotic fluid volume, intrapartum care, and neonatal care). Further studies are needed to investigate GDM incidence using different criteria commonly adopted in Brazil using a prospective approach, thus addressing these limitations. Also, GDM screening and diagnosis strategies still need to be cautiously investigated in the context of pragmatic randomized clinical trials to better describe safety and effectiveness in the real-world clinical setting, as well as the cost-effectiveness of different tests and thresholds.

In conclusion, our findings indicate that GDM incidence is highly dependent on the diagnostic criteria adopted, but also the overall compliance to GDM screening and

diagnosis recommendations in the clinical setting. The current national GDM guidelines would result in an incidence 3 times higher than the frequency of GDM as diagnosed by the antenatal care provider in the sample. Women with GDM in our sample were older and had more comorbidities and risk factors than non-GDM cases or cases with missing tests to exclude or confirm GDM.

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Seção 4

Perspectivas Acadêmicas e Científicas

Em termos de perspectivas acadêmicas e científicas, pretendo continuar buscando aperfeiçoamento e especialização nas áreas de assistência, docência e pesquisa em Obstetrícia. Pretendo dar seguimento às atividades de pesquisa acadêmica em projeto de Pós-Doutorado que ofereça continuidade ao processo de produção de conhecimento iniciado no âmbito do Doutorado, expandindo os achados de forma socialmente comprometida, com vistas a contribuir para a garantia de acesso a cuidado seguro da gestação ao pós-parto. Pretendo ainda fortalecer minha produção científica, mantendo o ritmo atual de publicação de artigos científicos relacionados aos projetos de pesquisa em que estou atualmente envolvida. Espero ainda poder contribuir para a formação de novos profissionais e para consolidação da carreira acadêmica de pesquisadores iniciantes dentro da área de Obstetrícia, atuando na docência e na orientação e coorientação de projetos de pesquisa. Tenho especial interesse na docência para a formação de novas parteiras profissionais (obstetrizes e enfermeiras obstetras), bem como em atuar em iniciativas de formação permanente para essas categorias profissionais. Em última análise, espero que minha trajetória acadêmica e científica possa contribuir em alguma medida para a promoção da saúde reprodutiva de mulheres e pessoas com útero.

Seção 5

Diamater Study Group

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Dra. Gabriela Marini Prata
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Ms. Bruna Bologna Catinelli
Ms. Fabiana Vieira Duarte de Souza Reis
Ms. Rafael Guilen de Oliveira
Ms. Sarah Maria Barneze Costa
Ms. Mariane de Oliveira Menezes
Ms. Nilton José dos Santo
Ms. Isabella Otenio de Lourenço
Ms. Jéssica Maróstica de Sá
Ms. Raissa Escandiusi Avramidis
Ms Guilherme Thomaz de Aquino Nava
Ms Talita Costa Domingues
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Jose Vitor Freitas Melo (*in memoriam)*
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Apoio à Pesquisa
Rita de Cássia Athanázio
Cinthia Scolastico Cecilio

Seção 6

Anexos

Anexo 1

CSP CADERNOS DE SAÚDE PÚBLICA
REPORTS IN PUBLIC HEALTH

REVISÃO
REVIEW

Prevalence of sexually transmitted infections and bacterial vaginosis among lesbian women: systematic review and recommendations to improve care

Prevalência de infecções sexualmente transmissíveis e vaginose bacteriana em mulheres lésbicas: revisão sistemática e recomendações para melhoria do cuidado

Prevalencia de infecciones sexualmente transmisibles y vaginosis bacteriana entre mujeres lesbianas: revisión sistemática y recomendaciones para mejorar el cuidado

Maira Libertad Soligo Takemoto [1]
Mariane de Oliveira Menezes [1]
Carla Betina Andreucci Polido [2]
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Jessica Fernandes Cirelli [6]
Roxana Knobel [7]

doi: 10.1590/0102-311X00118118

Anexo 2

THE JOURNAL OF MATERNAL-FETAL & NEONATAL MEDICINE
https://doi.org/10.1080/14767058.2020.1786056

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ORIGINAL ARTICLE

Maternal mortality and COVID-19

Maira L. S. Takemoto[a], Mariane O. Menezes[a], Carla B. Andreucci[b], Roxana Knobel[c], Liduína A. R. Sousa[d], Leila Katz[c], Eduardo B. Fonseca[f], Claudia G. Magalhães[a], Wanderson K. Oliveira[g], Jorge Rezende-Filho[h], Adriana S. O. Melo[i] and Melania M. R. Amorim[e]

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ABSTRACT

Objective: The aim of this study was to collect and analyze data from different sources to have a general overview of COVID-19-related maternal deaths in Brazil, as well as to compare data with worldwide reports.

Study design: We systematically searched data about COVID-19 maternal deaths from the Brazilian Ministry of Health surveillance system, State Departments of Health epidemiological reports, and media coverage. Data about timing of symptom onset and death (pregnancy or postpartum), gestational age, mode of birth, maternal age, comorbidities and/or risk factors, date of death, and place of death were retrieved when available.

Results: We identified 20 COVID-19-related maternal deaths, age range 20–43 years. Symptoms

ARTICLE HISTORY
Received 1 June 2020
Revised 9 June 2020
Accepted 18 June 2020

KEYWORDS
COVID-19; coronavirus; severe acute respiratory syndrome coronavirus 2; pregnancy; postpartum period; maternal mortality

Anexo 3

International Journal of GYNECOLOGY & OBSTETRICS

BRIEF COMMUNICATION | Free Access

The tragedy of COVID-19 in Brazil: 124 maternal deaths and counting

Maira L. S. Takemoto, Mariane de O. Menezes, Carla B. Andreucci, Marcos Nakamura-Pereira, Melania M.R. Amorim, Leila Katz, Roxana Knobel

First published: 09 July 2020 | https://doi.org/10.1002/ijgo.13300 | Citations: 122

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Abstract

At the time of writing 124 pregnant or postpartum women in Brazil have died due to COVID-19 (representing a mortality rate of 12.7%), a figure that currently surpasses the total number of COVID-19-related maternal deaths reported throughout the rest of the world.

Volume 151, Issue 1
October 2020
Pages 154-156
This article also appears in:
Covid-19 Virtual Issue
Free-to-view Collection

Anexo 4

Disproportionate Impact of Coronavirus Disease 2019 (COVID-19) Among Pregnant and Postpartum Black Women in Brazil Through Structural Racism Lens

To the Editor—Tai and collaborators [1] raised important questions about the potential biomedical factors and social determinants that play a role in the observed racial disparities on coronavirus disease 2019 (COVID-19) outcomes in the United States. Evidence of such challenges during the pandemic. We searched the Brazilian Acute Respiratory Distress Syndrome Surveillance System for COVID-19 cases among pregnant or postpartum women with complete data on ethnicity until 14 July 2020 (n = 1860), then selected records of White and Black women (n = 669; Table 1).

In our sample, there were similar mean ages and morbidity profiles between Black women and White women, but Black women were hospitalized in worse conditions (higher prevalence of dyspnea and lower O_2 saturation) and had higher were not significantly different between Black and White women. Therefore, it is reasonable to rely predominantly on social determinants of health to interpret our findings. In Brazil, this implies recognizing both racism and sexism as structural determinants that shape worse living and working conditions, as well as a lack of access to health care and a lack of opportunities within the Black population, particularly Black women [7]. By focusing on this group, specifically during pregnancy and the postpartum period, we direct our lens to the most vulnerable

Table 1. Case Characteristics

	Black, n = 134		White, n = 535		
	n/N	%	n/N	%	*P* Value[a]
Age, mean (SD)	30.6 (7.0)		30.3 (6.6)		>.05
Comorbidity or risk factors					
Cardiovascular disease[b]	22/134	16.4	67/535	12.5	>.05
Diabetes[c]	19/134	14.2	57/535	10.6	>.05
Obesity	12/134	8.9	37/535	6.9	>.05
Any comorbidity	45/134	33.6	160/535	29.9	>.05
Symptoms at admission					
Dyspnea	85/124	68.5	260/474	54.8	<.001
Respiratory distress	69/120	57.5	238/463	51.40	>.05
SpO2 <95%	56/118	47.5	137/446	30.7	<.001
ICU admission	37/134	27.6	104/535	19.4	<.001
Mechanical ventilation	20/134	14.9	39/535	7.3	<.001
Death[d]	17/100	17.0	38/423	8.9	<.001

Data are from Black and White maternal COVID-19 ARDS cases in Brazil (n = 669).

Abbreviations: ARDS, Acute Respiratory Distress Syndrome; COVID-19, coronavirus disease 2019; ICU, intensive care unit; SD, standard deviation; SpO2, oxygen saturation.

[a]Chi-square test.

[b]Includes both heart diseases and hypertension, whether chronic or gestational.

[c]Includes both gestational and pregestational diabetes.

[d]Among women with a recorded outcome in the database.

individuals in our society, who constitute the base of the power pyramid [8].

Our findings showed that maternal mortality in Black women due to COVID-19 was almost 2 times higher than that observed for White women. This adds to previous observations from the United States and United Kingdom that Black and other ethnic minority groups are struggling to survive pregnancy and the postpartum period with COVID-19 [9, 10]. However, they also highlight the need to move forward with tackling social determinants of health outside hospitals, including by implementing social

of Coronavirus Disease 2019 (COVID-19) and Pregnancy.

Disclaimer. The funder had no role in the study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Financial support. This work was supported by the Fund for Support to Teaching, Research and Outreach Activities (FAEPEX) from Universidade Estadual de Campinas.

Potential conflicts of interest. The authors: No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.

Mariana de Oliveira Menezes,[1]
Carla Betina Andreucci,[1] Marcos Nakamura-Pereira,[1] Roxana Knobel,[1] Leila Katz,[1] Heloisa de Oliveira Salgado,[1] Melania Maria Ramos de Amorim,[1] and Meira L. S. Takemoto[2,3]

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Anexo 5

Comment > J Matern Fetal Neonatal Med. 2022 Oct;35(19):3831-3832.
doi: 10.1080/14767058.2020.1838482. Epub 2020 Nov 1.

Letter to the editor regarding the article: COVID-19 and maternal, fetal and neonatal mortality: a systematic review

Marcos Nakamura-Pereira [1], Maíra Libertad Soligo Takemoto [2], Roxana Knobel [3], Mariane de Oliveira Menezes [2], Carla Betina Andreucci [4]

Affiliations + expand

PMID: 33135518 DOI: 10.1080/14767058.2020.1838482

No abstract available

Comment in

Response to "Letter to the editor regarding the article: COVID-19 and maternal, fetal and neonatal mortality: a systematic review".
Hessami K.
J Matern Fetal Neonatal Med. 2022 Dec;35(23):4506. doi: 10.1080/14767058.2020.1852214. Epub 2020 Nov 29.
PMID: 33249952 No abstract available

Anexo 6

CSP CADERNOS DE SAÚDE PÚBLICA
REPORTS IN PUBLIC HEALTH

ESPAÇO TEMÁTICO: COVID-19 – CONTRIBUIÇÕES DA SAÚDE COLETIVA
THEMATIC SECTION: COVID-19 – PUBLIC HEALTH CONTRIBUTIONS

Testagem universal de COVID-19 na população obstétrica: impactos para a saúde pública

Universal COVID-19 testing in the obstetric population: impacts on public health

Detección universal de COVID-19 en la población obstétrica: impactos en la salud pública

Mariane de Oliveira Menezes [1]
Carla Betina Andreucci [2]
Marcos Nakamura-Pereira [3]
Roxana Knobel [4]
Cláudia Garcia Magalhães [1]
Maíra Libertad Soligo Takemoto [1]

doi: 10.1590/0102-311X00164820

Em 11 de março de 2020, a Organização Mundial da Saúde (OMS) declarou a COVID-19 como

[1] *Faculdade de Medicina de Botucatu, Universidade*

Anexo 7

Int J Gynaecol Obstet. 2020 Dec;151(3):415-423. doi: 10.1002/ijgo.13407. Epub 2020 Oct 24.

Risk factors for adverse outcomes among pregnant and postpartum women with acute respiratory distress syndrome due to COVID-19 in Brazil

Mariane O Menezes [1], Maíra L S Takemoto [1], Marcos Nakamura-Pereira [2], Leila Katz [3], Melania M R Amorim [3], Heloisa O Salgado [4], Adriana Melo [5], Carmen S G Diniz [6], Liduina A R de Sousa [7], Claudia G Magalhaes [1], Roxana Knobel [8], Carla B Andreucci [9]; Brazilian Group of Studies for COVID-19, Pregnancy

Affiliations + expand

PMID: 33011966 PMCID: PMC9087686 DOI: 10.1002/ijgo.13407

Free PMC article

Abstract

Objective: To evaluate whether clinical and social risk factors are associated with negative outcomes for COVID-19 disease among Brazilian pregnant and postpartum women.

Methods: A secondary analysis was conducted of the official Acute Respiratory Syndrome Surveillance System database. Pregnant and postpartum women diagnosed with COVID-19 ARDS until July 14, 2020, were included. Adverse outcomes were a composite endpoint of either death,

Anexo 8

BJOG. 2020 Dec;127(13):1618-1626. doi: 10.1111/1471-0528.16470. Epub 2020 Sep 14.

Clinical characteristics and risk factors for mortality in obstetric patients with severe COVID-19 in Brazil: a surveillance database analysis

Mls Takemoto [1], M O Menezes [1], C B Andreucci [2], R Knobel [3], L Sousa [4], L Katz [5], E B Fonseca [6], M Nakamura-Pereira [7], C G Magalhães [8], Csg Diniz [9], Aso Melo [10], Mmr Amorim [5]; Brazilian Group for Studies of COVID-19 and Pregnancy

Affiliations + expand

PMID: 32799381 PMCID: PMC7461482 DOI: 10.1111/1471-0528.16470

Free PMC article

Abstract

Objective: To describe clinical characteristics of pregnant and postpartum women with severe COVID-19 in Brazil and to examine risk factors for mortality.

Design: Cross-sectional study based on secondary surveillance database analysis.

Setting: Nationwide Brazil.

Population or sample: 978 Brazilian pregnant and postpartum women notified as COVID-19 Acute

Anexo 9

Int J Gynaecol Obstet. 2020 Oct;151(1):148-150. doi: 10.1002/ijgo.13328. Epub 2020 Aug 9.

Worldwide maternal deaths due to COVID-19: A brief review

Marcos Nakamura-Pereira [1], Carla Betina Andreucci [2], Mariane de Oliveira Menezes [3], Roxana Knobel [4], Maíra Libertad Soligo Takemoto [3]

Affiliations + expand

PMID: 32706925 PMCID: PMC9087603 DOI: 10.1002/ijgo.13328

Free PMC article

Abstract

160 maternal deaths due to COVID-19 have been reported worldwide, most of them in middle-income countries, representing a barrier to reducing maternal mortality.

Keywords: COVID-19; Health services accessibility; Health status indicators; Maternal death; Maternal mortality.

Conflict of interest statement

The authors have no conflicts of interest.

Anexo 10

Int J Gynaecol Obstet. 2021 Oct;155(1):101-109. doi: 10.1002/ijgo.13811. Epub 2021 Jul 18.

COVID-19-related deaths among women of reproductive age in Brazil: The burden of postpartum

Roxana Knobel [1], Maíra L S Takemoto [2], Marcos Nakamura-Pereira [3], Mariane O Menezes [2], Vicente K Borges [4], Leila Katz [5], Melania M R Amorim [5], Carla B Andreucci [6]

Affiliations + expand

PMID: 34213771 PMCID: PMC9087613 DOI: 10.1002/ijgo.13811

Free PMC article

Abstract

Objective: To compare risk of death due to COVID-19 among pregnant, postpartum, and non-pregnant women of reproductive age in Brazil, using the severe acute respiratory syndrome surveillance system (SARS-SS).

Methods: A secondary analysis was performed of the Brazilian official SARS-SS, with data retrieved up to August 17, 2020. Cases were stratified by pregnancy status, risk factors or co-morbidities, and outcome (death or recovery). Multiple logistic regression was employed to examine associations between independent variables and risk of death.

Results: A total of 24 805 cases were included, with 3129 deaths (12.6%), including 271 maternal

Anexo 11

Int J Gynaecol Obstet. 2021 May;153(2):360-362. doi: 10.1002/ijgo.13643. Epub 2021 Mar 8.

The impact of the COVID-19 pandemic on maternal mortality in Brazil: 523 maternal deaths by acute respiratory distress syndrome potentially associated with SARS-CoV-2

Marcos Nakamura-Pereira [1], Roxana Knobel [2], Mariane O Menezes [3], Carla B Andreucci [4], Maíra L S Takemoto [3]

Affiliations + expand

PMID: 33570755 PMCID: PMC9087565 DOI: 10.1002/ijgo.13643

Free PMC article

Abstract

During the study period, 523 pregnant or postpartum women died in Brazil due to confirmed COVID-19 or undetermined etiology. This results in a projected COVID-19 MMR of 17.5/100 000 or potentially even higher.

Keywords: COVID-19; maternal death; maternal mortality.

Conflict of interest statement

Anexo 12

Cesarean-section Rates in Brazil from 2014 to 2016: Cross-sectional Analysis Using the Robson Classification

Taxas de cesariana no Brasil de 2014 a 2016: Análise transversal utilizando a classificação de Robson

Roxana Knobel[1] Thiago Jose Pinheiro Lopes[1] Mariane de Oliveira Menezes[2]
Carla Betina Andreucci[3] Juliana Toledo Gieburowski[1] Maira Libertad Soligo Takemoto[1]

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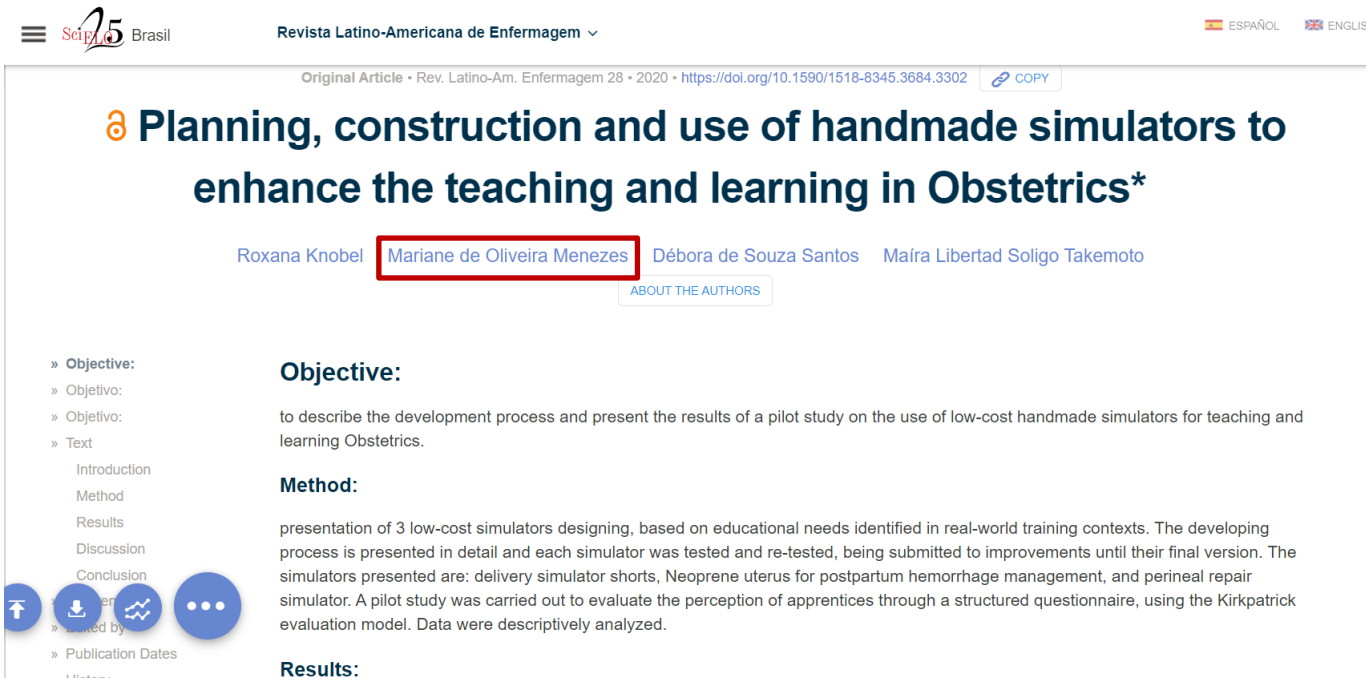
Rev Bras Ginecol Obstet 2020;42(9):522–528.

Abstract

Objective To obtain cesarean-section (CS) rates according to the Robson Group Classification in five different regions of Brazil.

Methods A descriptive epidemiological study using data from secondary birth records from the Computer Science Department of the Brazilian Unified Health System (Datasus, in Portuguese) between January 1st, 2014, and December 31st, 2016, including all live births in Brazil.

Anexo 13



SciELO Brasil

Revista Latino-Americana de Enfermagem

ESPAÑOL ENGLIS

Original Article • Rev. Latino-Am. Enfermagem 28 • 2020 • https://doi.org/10.1590/1518-8345.3684.3302 COPY

Planning, construction and use of handmade simulators to enhance the teaching and learning in Obstetrics*

Roxana Knobel Mariane de Oliveira Menezes Débora de Souza Santos Maíra Libertad Soligo Takemoto

ABOUT THE AUTHORS

» Objective:
» Objetivo:
» Objetivo:
» Text
Introduction
Method
Results
Discussion
Conclusion
» Publication Dates

Objective:

to describe the development process and present the results of a pilot study on the use of low-cost handmade simulators for teaching and learning Obstetrics.

Method:

presentation of 3 low-cost simulators designing, based on educational needs identified in real-world training contexts. The developing process is presented in detail and each simulator was tested and re-tested, being submitted to improvements until their final version. The simulators presented are: delivery simulator shorts, Neoprene uterus for postpartum hemorrhage management, and perineal repair simulator. A pilot study was carried out to evaluate the perception of apprentices through a structured questionnaire, using the Kirkpatrick evaluation model. Data were descriptively analyzed.

Results:

Anexo 14


Journal of Obstetrics and Gynaecology ▶ List of Issues ▶ Volume 41, Issue 7 ▶ Concerning the article 'aromatherapy int ....
Concerning the article 'aromatherapy intervention on anxiety and pain during first stage labour in nulliparous women: a systematic review and meta-analysis'
Lara Caline Santos Lira, Melania Maria Amorim, Alexandre Delgado, Mariane de Oliveira Menezes & Maíra Libertad Soligo Takemoto
Page 1180 | Published online: 16 Jan 2021
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Journal of Obstetrics and Gynaecology, 41(7), p. 1180
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Anexo 15

CSP CADERNOS DE SAÚDE PÚBLICA
REPORTS IN PUBLIC HEALTH

ARTIGO
ARTICLE

Pré-natal de gestantes de risco habitual por enfermeira obstetra e obstetriz: custo-efetividade sob a perspectiva do Sistema de Saúde Suplementar

Prenatal care for normal-risk pregnant women by obstetric nurses and midwives: cost-effectiveness from the perspective of the Supplementary Health System in Brazil

Período prenatal de gestantes de riesgo habitual con enfermera obstetra y partera: costo-efectividad desde la perspectiva del Sistema de Salud Suplementario

Mariane de Oliveira Menezes [1]
Roxana Knobel [2]
Carla Betina Andreucci [3]
Claudia Garcia Magalhães [1]
Melania Maria Ramos Amorim [4]
Leila Katz [4]
Maíra Libertad Soligo Takemoto [1]

doi: 10.1590/0102-311X00076320

Anexo 16

International Urogynecology Journal (2022) 33:3203–3211
https://doi.org/10.1007/s00192-022-05245-y

ORIGINAL ARTICLE

Relaxin-2 during pregnancy according to glycemia, continence status, and pelvic floor muscle function

Caroline Baldini Prudencio[1] · Sthefanie Kenickel Nunes[1] · Fabiane Affonso Pinheiro[1] · Carlos Isaias Sartorão Filho[1] · Flávia Ignácio Antônio[2] · Guilherme Thomaz de Aquino Nava[3] · Marilza Vieira Cunha Rudge[1] · Angélica Mércia Pascon Barbosa[1,2] Diamater Study Group

Received: 16 November 2021 / Accepted: 5 May 2022 / Published online: 3 June 2022

Abstract

Introduction and hypothesis To investigate relaxin-2 concentration comparing gestational diabetes mellitus (GDM) and non-GDM patients during pregnancy according to urinary incontinence (UI) and pelvic function status.

Methods This is a cross-sectional study evaluating 282 pregnant women from 24 weeks of gestation. The participants were divided into two groups, non-GDM and GDM, according to American Diabetes Association's diabetes mellitus gestational threshold. In addition, according to subanalysis, both groups were subdivided according to the presence of pregnancy-specific urinary incontinence: non-GDM continent, non-GDM incontinent, GDM continent, and GDM incontinent. All participants filled in questionnaires on clinical, obstetric, and urinary continence status (International Consultation on Incontinence Questionnaire-Short Form, ICIQ-SF, and Incontinence Severity Index, ISI), followed by pelvic floor muscle evaluation by the PERFECT scheme in which strength, endurance, and speed of contractions were evaluated.

Results Serum relaxin-2 concentrations were significantly lower in pregnant women with pregnancy-specific urinary incontinence in both non-GDM and GDM patients, but GDM showed the lowest concentration. In addition, the stratification of the groups according to pelvic floor muscle strength showed that pregnant patients with GDM and modified Oxford scale 0–2 had significantly lower levels than those who were non-GDM and GDM with Modified Oxford Scale 3–5. Relaxin-2 level was much lower in GDM incontinent pregnant women with MOS 0–2 compared to the other three groups.

Conclusions Lower relaxin-2 concentration was associated with the presence of pregnancy-specific urinary incontinence, but the combination of GDM, pregnancy-specific urinary incontinence, and lower levels of pelvic floor strength led to lower levels of relaxin-2 compared to the other three groups.

Keywords Gestational diabetes · Obstetrics · Pelvic floor · Pregnancy · Relaxin-2

Introduction

Urinary incontinence (UI) is a silent but prevalent event [1]. Pregnancy-specific urinary incontinence (PSUI) is a term we propose to describe the urinary incontinence that appears during pregnancy. The pathophysiology is multifactorial, and many gaps in the literature have not yet been clarified, including the inclusion in a scientific glossary. The first-line treatment for UI is pelvic floor muscle (PFM) training [2]; therefore, PFM function is one of the main points of interest, and all other possible conditions that modify its function and/or morphology should be investigated. Gestational diabetes mellitus (GDM) can damage muscular tissue, causing atrophy, thinning, disorganization, and co-localization of fast

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The literature is very restricted concerning the link between PFM function and hormonal status in general; during pregnancy it is apparently absent. We chose MOS because it has high interrater reliability (r = 0.947; $p < 0.001$). Laycock et al. [27] our analysis were based on the scale stratified into 0–2 and 3–5, with 0–2 indicating women who cannot perform a contraction resulting a movement against the pubic bone associated with cranial movement and those (3–5) who are able to do so. The relaxin-2 levels were even lower if we stratified the sample according to GDM pregnant women who scored MOS = 0–2 compared with GDM women with MOS = 3–5 and with the non-GDM group. When the GDM group was stratified by continence status, the GDM-PSUI had significantly lower relaxin-2 levels compared to the other three groups.

Fibrosis is considered an important factor in lower urinary tract dysfunctions [28] if we consider that there is some plausibility to support that GDM-PSUI patients may have intense connective tissue and morphological muscle alterations [3, 29]. This could lead us to consider further investigations on the influence of lower relaxin levels, especially in this group. This seems promising, as a recent study in an animal model has shown relaxin-2's potential for fibrosis reversal and increased detrusor force generation in the bladder [28].

The strengths of this study were approaching converging subjects (GDM, PSUI, and PFM function) together, using 3 points on the OGTT-75g to classify groups, using a high-quality relaxin kit for dosing, selecting pregnant women and assessing them during gestational weeks in which relaxin is expected to be stable [30], and having participants with similar characteristics concerning obstetric history among the groups. Regarding limitations, since this study is an observational study, causality cannot be determined. It would be interesting for future studies to use earlier dosages at different time points, and we suggest other authors consider including an objective tool for PFM function assessment.

Conclusion

Our findings showed that lower relaxin-2 concentration is associated with the presence of pregnancy-specific urinary incontinence in GDM and non-GDM groups but it is especially notable in the GDM-PSUI group. In addition, pregnant women with GDM who had lower PFM strength (MOS = 0–2), regardless of continence status, had lower relaxin-2 levels compared to GDM pregnant women with better PFM strength (MOS = 3–5). Considering also the continence status, the GDM-PSUI group with lower PFM strength (MOS = 0–2) presented even lower levels of relaxin-2 than the non-GDM-C, non-GDM-PSUI, and GDM-C groups.

Research implications

Contrasting physiological actions on the extracellular matrix affected the subjects of this article; while diabetes leads to a fibrosis process, relaxin leads to an anti-fibrotic process. Further studies are needed to investigate the influence over time and determine the strength of the connection between lower levels of relaxin on PFM impairment and fibrosis in the GDM population, especially in GDM-PSUI patients. As relaxin is a favorable hormone used to improve fibrotic conditions, it may be a useful new therapeutic tool for preventive and therapeutic strategies, requiring further investigation in the future.

Acknowledgments The authors would like to thank the pregnant women who participated in this study.

Diamater Study Group

Calderon IMP, Souza FP, Berghmans B, de Bie R, Thabane L, Junginger B, Graeff CFO, Magalhães CG, Costa RA, Lima SAM, Kron-Rodrigues MR, Felisbino S, Barbosa W, Campos FJ, Bossolan G, Corrente JE, Nunes HRC Abbade J, Rossignoli PS, Pedroni CR, Atallah AN, Di Bella ZIKJ, Uchoa SMM, Hungaro MA, Mareco EA, Sakalem ME, Martinho N, Hallur LSR, Reyes DRA, Alves FCB, Marcondes JPC, Quiroz SBCV, Pascon T, Catinelli BB, Reis FVDS, Oliveira RG, Barneze S, Enriquez EMA, Takano L, Carr AM, Magyori ABM, Iamundo LF, Carvalho CNF, Jacomin M, Avramidis RE, Silva AJB, Orlandi MIG, Dangió TD, Bassin HCM, Melo JVF, Takemoto MLS, Menezes MD, Caldeirão TD, Santos NJ, Lourenço IO, Marostica de Sa J, Caruso IP, Rasmussen LT, Garcia GA, Pascon C, Bussaneli DG, Nogueira VKC, Rudge CVC, Piculo F, Prata GM, Barbosa VP.

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Funding Funding received: Supported by Sao Paulo Research Foundation protocol number 2016/01743-5 and 2021/10665-6. Coordenação de Aperfeiçoamento de Pessoal de Nível Superior, CAPES/DS. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Declarations

Conflicts of interest None.

Anexo 17

frontiers | Frontiers in Endocrinology

TYPE Original Research
PUBLISHED 06 October 2022
DOI 10.3389/fendo.2022.958909

OPEN ACCESS

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SPECIALTY SECTION
This article was submitted to Clinical Diabetes, a section of the journal Frontiers in Endocrinology

RECEIVED 01 June 2022
ACCEPTED 31 August 2022
PUBLISHED 06 October 2022

CITATION
Prudencio CB, Nunes SK, Pinheiro FA, Sartorão Filho CI, Nava GTA, Salomoni SE, Pedroni CR, Rudge MVC, Barbosa AMP and Diamater Study Group (2022) Gestational diabetes is associated with alteration on pelvic floor muscle activation pattern during pregnancy and postpartum: Prospective cohort using electromyography assessment. *Front. Endocrinol.* 13:958909. doi: 10.3389/fendo.2022.958909

Gestational diabetes is associated with alteration on pelvic floor muscle activation pattern during pregnancy and postpartum: Prospective cohort using electromyography assessment

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Background and objective: Gestational diabetes mellitus (GDM) is a comorbidity which may cause acute and lifelong disorders to mother and child. Alterations in muscular and connective tissues have been associated with GDM in translation studies, characterizing gestational diabetic myopathy. Pregnancy-specific urinary incontinence and sexual disabilities, disorders that depend on the pelvic floor muscle (PFM) integrity, are also associated with GDM both during and after pregnancy. The aim was to compare PFM activation patterns between GDM and non-GDM women from 24–30 gestational weeks to 18–24 months postpartum during a standard clinical test during gestation and postpartum.

Methods: We conducted a prospective three-time-point cohort study from gestation (24–30 weeks—T1, and 36–38 weeks—T2) to 18–24 months postpartum (T3). PFM electromyography was recorded in primigravida or primiparous women with one previous elective c-section with or without the diagnosis of GDM according to the American Diabetes Association criteria. A careful explanation of the muscle anatomy and functionality of the PFM was given to participants before EMG assessment. The outcome measures were PFM activation patterns assessed during pregnancy and postpartum, comparing intra and between groups. PFM activation patterns were assessed

Education/SD (Coordenação de Aperfeiçoamento de Pessoal de Nível Superior, CAPES/DS). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Acknowledgments

We would like to give our great appreciation to the pregnant women who participated in this study.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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Rudge MVC, Barbosa, AMP, Calderon IMP, Souza FP, Berghmans B, Thabane L, Junginger B, Graeff CFO, Magalhães CG, Costa RA, Lima SAM, Kron-Rodrigues MR, Felisbino S, Barbosa W, Campos FJ, Bossolan G, Corrente JE, Nunes HRC Abbade J, Rossignoli PS, Pedroni CR, Atallah AN, Di Bella ZIKJ, Uchoa SMM, Hungaro MA, Mareco EA, Sakalem ME, Martinho N, Hallur LSR, Reyes DRA, Alves FCB, Marcondes JPC, Prudencio CB, Pinheiro FA, Sartorão Filho CI, Quiroz SBCV, Pascon T, Nunes SK, Catinelli BB, Reis FVDS, Oliveira RG, Barneze S, Enriquez EMA, Takano L, Carr AM, Magyori ABM, Iamundo LF, Carvalho CNF, Jacomin M, Avramidis RE, Silva AJB, Orlandi MIG, Dangió TD, Bassin HCM, Melo JVF, Takemoto MLS, Menezes MD, Caldeirão TD, Santos NJ, Lourenço IO, Marostica de Sá J, Caruso IP, Rasmussen LT, Garcia GA, Nava GTA, Pascon C, Bussaneli DG, Nogueira VKC, Rudge CVC, Piculo F, Prata GM, Barbosa VP.

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Received: 21 June 2021 | Accepted: 15 March 2022

DOI: 10.1002/nau.24927

CLINICAL ARTICLE

Neurourology Urodynamics | SUFU | WILEY

Pelvic floor muscle dysfunction at 3D transperineal ultrasound in maternal exposure to gestational diabetes mellitus: A prospective cohort study during pregnancy

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Funding information
Fundação de Amparo à Pesquisa do Estado de São Paulo, Grant/Award Numbers: FAPESP-2016/01743-5, 2021/10665-6

Abstract

Aim: This study aimed to assess, for the first time, the dynamic morphometry of pelvic floor muscles (PFM) using three-dimensional transperineal ultrasound (3D-TPUS) and its progression at two-time points of gestation between women with and without gestational diabetes mellitus (GDM), and whether the PFM dysfunction is connected to GDM.

Methods: The study comprised 83 consecutive pregnant women with ($n = 38$) and without ($n = 45$) GDM screened at 24–30 and 38–40 weeks of gestation. 3D-TPUS and a mobility test were used to quantify PFM dynamic morphometry during maximum contraction and the Valsalva maneuver.

Results: When compared to the control group, GDM women had no significant variations in all levator hiatal dimensions at 24–30 weeks of gestation. Meanwhile, women with GDM experienced an increase in levator hiatal area (LHa) ($p < 0.000$) during PFM contraction and enlargement in LHa ($p < 0.001$) during Valsalva maneuver ($p = 0.010$) at 38–40 weeks of gestation.

Fabiane A. Pinheiro, Carlos I. Sartorão Filho, Marilza V. C. Rudge, and Angélica M. P. Barbosa contributed equally to this study.

Fabiane A. Pinheiro and Carlos I. Sartorão Filho are co-first authors.

Caroline B. Prudencio, Sthefanie K. Nunes, Tawana Pascon, Ragavendra L. S. Hallur, Luis Takano, Eusébio M. A. Enriquez, Bruna B. Catinelli, Aline M. Carr, and Baerbel Junginger contributed equally to this study.

Marilza V. C. Rudge and Angélica M. P. Barbosa are last authors of this study.

expected the participants to perform an intense PFM relaxation that replicated what was expected during delivery, but as previously reported in the literature, even with good clinical guidance, some participants may perform a co-activation of LA in response to the intraabdominal pressure increase.[31] Because the GDM diagnosis lasted until the conclusion of the pregnancy, we were able to investigate the hyperglycemic effects. The examiner who analyzed the ultrasound datasets and images was blinded and the results were reviewed by a second investigator. Furthermore, because the strategy was based on earlier investigations of pregnant diabetes women and rodents, this study had translational qualities. To validate the relevance of these findings, all pregnant women should have been evaluated before gestation to confirm that there was no prior GDM interference, and postpartum follow-up of the participants may clarify the long-term influence of GDM on PFM function. Despite the study's strengths, several limitations should be noted. The initial maternal examination was chosen as a baseline at 24–30 weeks of gestation. Finally, the findings of this study should be viewed as prospective biomarkers of PS-UI in GDM women to validate gestational diabetic myopathy as a likely etiology of the condition.

5 | CONCLUSION

The current findings contribute to our knowledge of the role of GDM in changes to PFM functioning. Finally, our longitudinal PFM dynamic 3D-TPUS study of GDM women reveals three key structural muscle deficits in the third trimester of GDM women. Our data indicate that maternal GDM exposure may lead to a loss of PFM functioning, as measured by decreased PFM contractility, distensibility, and mobility compared to non-GDM women. Furthermore, as these muscles move to a lower functional muscle near the end of pregnancy, GDM may decompensate the PFM maternal adaption for normal delivery. Given these data, it is appropriate to identify GDM as a risk factor for PFMD in pregnancy, one of the PFD. Long-term follow-ups are required to determine if these women would develop atypical and persistent PFD, and if so, whether it will be directed in the opposite way as previously mentioned, or even postponed.

ACKNOWLEDGMENTS

This study was supported by Sao Paulo Research Foundation (FAPESP-2016/01743-5 and 2021/10665-6). The authors would like to thank all participants that help them to better understand pelvic floor muscle dysfunction in gestational diabetes mellitus women at two-time points of gestation. They would also like to thank José V. F. Melo for participating in this study until the end of his life.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

ETHICS STATEMENT

This was a study approved by the Institutional Ethical Committee of Botucatu Medical School of Sao Paulo State University (Protocol: 1.716.895). All participants consented to participate in the study by signing the written informed consent.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author, Angélica M. P. Barbosa, upon reasonable request.

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Anexo 19

Rudge *et al. BMC Pregnancy and Childbirth* (2020) 20:117
https://doi.org/10.1186/s12884-020-2749-x

BMC Pregnancy and Childbirth

STUDY PROTOCOL Open Access

Study protocol to investigate biomolecular muscle profile as predictors of long-term urinary incontinence in women with gestational diabetes mellitus

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Abstract

Background: Pelvic floor muscles (PFM) and rectus abdominis muscles (RAM) of pregnant diabetic rats exhibit atrophy, co-localization of fast and slow fibers and an increased collagen type I/III ratio. However, the role of similar PFM or RAM hyperglycemic-related myopathy in women with gestational diabetes mellitus (GDM) remains poorly investigated. This study aims to assess the frequency of pelvic floor muscle disorders and pregnancy-specific urinary incontinence (PS-UI) 12 months after the Cesarean (C) section in women with GDM. Specifically, differences in PFM/RAM hyperglycemic myopathy will be evaluated.

Methods: The Diamater is an ongoing cohort study of four groups of 59 pregnant women each from the Perinatal Diabetes Research Centre (PDRC), Botucatu Medical School (FMB)-UNESP (São Paulo State University), Brazil. Diagnosis of GDM and PS-UI will be made at 24–26 weeks, with a follow-up at 34–38 weeks of gestation. Inclusion in the study will occur at the time of C-section, and patients will be followed at 24–48 h, 6 weeks and 6 and 12 months postpartum. Study groups will be classified as (1) GDM plus PS-UI; (2) GDM without PS-UI; (3) Non-GDM plus PS-UI; and (4) Non-GDM without PS-UI. We will analyze relationships between GDM, PS-UI and hyperglycemic myopathy at 12 months after C-section. The mediator variables to be evaluated include digital palpation, vaginal squeeze pressure, 3D pelvic floor ultrasound, and 3D RAM ultrasound. RAM samples obtained during C-section will be analyzed for ex-vivo contractility, morphological, molecular and OMICS profiles to further characterize the hyperglycemic myopathy. Additional variables to be evaluated include maternal age, socioeconomic status, educational level, ethnicity, body mass index, weight gain during pregnancy, quality of glycemic control and insulin therapy.

Discussion: To our knowledge, this will be the first study to provide data on the prevalence of PS-UI and RAM and PFM physical and biomolecular muscle profiles after C-section in mothers with GDM. The longitudinal design allows for the assessment of cause-effect relationships between GDM, PS-UI, and PFMs and RAMs myopathy. The findings may reveal previously undetermined consequences of GDM.

Keywords: Gestational diabetes mellitus, Hyperglycemic myopathy, Pelvic floor muscles, Rectus abdominis muscles, Urinary incontinence, Proteomics, Collagen, Electromyography, Transmission electron microscopy

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risk of long-term UI in GDM mothers. An enhanced understanding of the impact of modifiable risk factors can lead to protocols to reduce the rates of UI and associated health care costs, improve the quality of life of affected women and contribute to the global eradication of UI after GDM exposure. It will also enable clinicians to deal more effectively with individual women after their pregnancy and facilitate the transition of the Brazilian Health System from a curative to a preventive strategy [65].

Conclusion

In conclusion, Diamater is an ongoing study recruiting GDM pregnant women at a prenatal care outpatient clinic to investigate the relationship between GDM plus PS-UI with the occurrence of symptomatic UI plus PFMD 1 year after C-section and assess whether this relation can be explained by hyperglycaemic myopathy. It offers the unique opportunity to establish well-powered biomarker research in a new triad composed of GDM + PS-UI+ hyperglycemic myopathy as a predictor of long-term UI and PFMD. This approach allows for future innovative treatment proposals.

Supplementary information

Supplementary information accompanies this paper at https://doi.org/10.1186/s12884-020-2749-x.

Additional file 1. Specific protocols for clinical assessment and laboratory analysis of PFM and RAM.

Abbreviations

ANOVA: One-way analysis of variance; CCL7: Chemokine C-C motif ligand 7; CRF: Case Report Forms; C-section: Cesarean section; DIAMATER: Diabetes and Maternity; ECM: Extracellular Matrix; EMG: Electromyography; EMGs: Surface electromyograms; GAGs: Glycosaminoglycans; GDM: Gestational Diabetes Mellitus; HPLC: High-Performance Liquid Chromatography; ICIQ-SF: International Consultation on Incontinence Questionnaire-Urinary Incontinence-Short Form; IRB: The Institutional Review Board; ISI: Incontinence Severity Index; OGTT: Oral Glucose Tolerance Test; OPLS: Orthogonal partial least squares; PCR: Polymerase chain reaction; PDRC: The Perinatal Diabetes Research Centre; PFM: Pelvic Floor Muscles; PLS: Partial least squares; PS-UI: Pregnancy Specific Urinary Incontinence; PTH: Parathyroid Hormone; RAM: Rectus Abdominis Muscles; RNA: Ribonucleic acid; SENIAM: Surface Electromyography for the Non-Invasive Assessment of Muscles; T2DM: Type 2 Diabetes Mellitus; UI: Urinary Incontinence; UNESP: Universidade Estadual Paulista Júlio de Mesquita Filho

Acknowledgments

We would like to thank the Perinatal Diabetes Research Center (PDRC) -Botucatu Medical School-UNESP, Brazil. We gratefully acknowledge the substantial contribution of all women who participated/participating in the Diamater study.

The Diamater Study Group: Rudge MV, Barbosa AMP, Calderon IMP, Souza FP, Abbade JF, Hallur LSR, Piculo F, Marini G, Vesentini G, Thabane L, Palma MS, Graeff CFO, Arni RK, Herculano RD, Salvadori DF, Mateus S, Dal Pai Silva M, Magalhães CG, Costa RA, Lima SAM, FelisbinoSL, Barbosa W, Atallah A, Girão MJB, Di Bella Z, Uchoa SM, Payão S, Hijas A, Berghman B, De Bie R, Sobrevia L, Junginger B, Alves FCB, Rossignoli PS, Prudencio CB, Orlandi MIG, Gonçalves MI, Nunes SK, Catinelli BB, Quiroz S, Sarmento BV, Pinheiro FA, Sartorão CI, Lucas RR, Reyes DRA, Quiroz SBCV, Enriquez EMA, Oliveira RG, Floriano JF, Marcondes JPC, Barneze S, Dangió TD, Pascon T, Rossignoli P, Freitas JV, Takano L, Reis F, Caldeirão TD, Fernandes JN, Carr AM, Gaitero MVC, Corrente JE, Nunes HRC, Candido AF, Sarmento, Costa SMB, Dangió TD, Pascon T, Melo JVF, Takano L, Reis FVDS, Caldeirão TD, Carr AM, Garcia GA, Rebaudeti CB, Bussin HCM, Suyama KS, Damasceno LN, Takemoto MLS, Menezes MD, Bussaneli DG, Nogueira VKC, Lima PR, Lourenço IO, Marostica de Sá J, Magini RA, Caruso IP, Rasmussen LT, Prata GM, Piculo F, Vesentini G, Arantes MA, Ferraz GAR, Camargo LP, Kron MR, Corrente JE, Nunes HRC.

Authors' contributions

MVCR and AMPB conceived the study concept, developed the funding proposal, applied for funding, and initiated the writing of the protocol paper. JFA and LT were responsible for the critical review of the final draft. SSW and RLSH were responsible for clarifying manuscript content and word usage for an English language audience. MVCR is the principal investigator (PI) and the grant holder of the CNPq -Brazil (PQ-1C). AMPB, IMPC and FPS are Co-PI of the Project, and IMPC is grant holder of CNPq-Brazil (PQ-1D). MVCR, AMPB, IMPC, and FPS initiated the study design. MVCR, AMPB, RLSH, and JP wrote the protocol for research ethics committee and conceptual model. AMPB, IMPC, JFA, RLSH, and JEC develop the statistical analysis plan and will contribute to the interpretation of data. MVRC, SFP, JFA, RLSH, JPM, FP, GM, GV, LT, IMPC, SSW, and AMPB drafted and revised the manuscript after feedback from all authors. All authors contributed to the refinement of the present manuscript and approved the final version of the manuscript.

Funding

This study is funded by the São Paulo Research Foundation-FAPESP, São Paulo, Brazil in a 5 year (01-04-2017 to 31-03-2022) project grant (No: FAPESP 2016/01743–5), a government funding agency with the aim of providing grants, funds, and programs to support research, education, and innovation. The funding agency had no role in the design of this study and will not have any role during the collection, analysis, interpretation of data, in writing the manuscript or in decision to submit results. Postdoctoral fellowships and undergraduate scholarships for the Diamater project are supported by the São Paulo Research Foundation-FAPESP, São Paulo, Brazil, under the grant No: FAPESP 2016 / 01743–5.

Availability of data and materials

This is an ongoing study, and data sharing does not apply to this article. No data were generated or analyzed during the current study. Protocol related information can be obtained from the corresponding author (Marilza V.C. Rudge) upon request.

Ethics approval and consent to participate

Institutional Research Bureau (IRB) of Botucatu Medical School-UNESP approved the study, on 2nd December 2017 (R17.036/NL60484.100.17). Written informed consent will be obtained from all subjects, and the procedures used in the study are in accordance with the guidelines of the Helsinki Declaration on human experimentation.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

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PLOS ONE

RESEARCH ARTICLE

Alterations in the structural characteristics of rectus abdominis muscles caused by diabetes and pregnancy: A comparative study of the rat model and women

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OPEN ACCESS

Citation: Vesentini G, Barbosa AMP, Damasceno DC, Marini G, Piculo F, Matheus SMM, et al. (2020) Alterations in the structural characteristics of rectus abdominis muscles caused by diabetes and pregnancy: A comparative study of the rat model and women. PLoS ONE 15(4): e0231096. https://doi.org/10.1371/journal.pone.0231096

Editor: Lingjun Li, National University Singapore Yong Loo Lin School of Medicine, SINGAPORE

Received: September 24, 2019

Accepted: March 16, 2020

Published: April 3, 2020

Data Availability Statement: All data is available at http://hdl.handle.net/11449/190666.

Funding: The financial support provided by the Brazilian Public Health System (SUS) supported the treatment of all pregnant women. The authors gratefully acknowledge funding by São Paulo Research Foundation (FAPESP) (Grant No: #2016/09710-9 and #2016/01743-5). GV received a FAPESP scholarship (Grant No: #2014/26852-6).

Abstract

Background and objective

In the present study, we compared the effect of diabetic pregnancy on the rectus abdominis muscle (RAM) in humans and rats. We hypothesized that our animal model could provide valuable information about alterations in the RAM of women with Gestational Diabetes (GDM).

Method

Newborns female rats (n = 10/group) were administered streptozotocin (100 mg/kg body weight) subcutaneously and were mated on reaching adulthood, to develop the mild hyperglycemic pregnant (MHP) rat model. At the end of pregnancy, the mothers were sacrificed, and the RAM tissue was collected. Pregnant women without GDM (non-GDM group; n = 10) and those diagnosed with GDM (GDM group; n = 8) and undergoing treatment were recruited, and RAM samples were obtained at C-section. The RAM architecture and the distribution of the fast and slow fibers and collagen were studied by immunohistochemistry.

Results

No statistically significant differences in the maternal and fetal characters were observed between the groups in both rats and women. However, significant changes in RAM

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Anexo 21

DIABETES RESEARCH AND CLINICAL PRACTICE 166 (2020) 108315

Contents available at ScienceDirect

Diabetes Research and Clinical Practice

journal homepage: www.elsevier.com/locate/diabres

Deleterious effects of gestational diabetes mellitus on the characteristics of the rectus abdominis muscle associated with pregnancy-specific urinary incontinence

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ARTICLE INFO

Article history:
Received 7 February 2020
Received in revised form
5 June 2020
Accepted 7 July 2020
Available online 15 July 2020

Keywords:
Pregnancy-specific urinary incontinence
Urinary incontinence
Gestational diabetes mellitus
Skeletal muscle

ABSTRACT

Aims: To evaluate the effects of gestational diabetes mellitus (GDM) on the structural characteristics of the rectus abdominis muscle (RAM) and its indirect effects on pregnancy-specific urinary incontinence (PSUI).

Methods: A total of 92 pregnant women were divided into four groups, according to their clinical conditions: non-GDM continent, non-GDM associated PSUI, GDM continent and GDM associated PSUI. The muscle morphometry (histochemistry and immunohistochemistry) for the fiber types and collagen fiber distribution, the ultrastructural analysis (transmission electron microscopy), the protein expression of fiber types and calcium signaling (Western blotting), and the content of types I and III collagen fiber (ELISA) in RAM collected at delivery were assessed.

Results: The GDM groups presented a significantly increased number of slow fibers and slow-twitch oxidative fiber expression; decreased fiber area, number of fast fibers, and area of collagen; an increase in central nuclei; ultrastructural alterations with focal lesion areas such as myeloid structures, sarcomere disorganization, and mitochondrial alteration. The

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https://doi.org/10.1016/j.diabres.2020.108315

tions have been closely linked with the recruitment of the abdominal muscles [40,71–73].

There were some limitations to the present study. First, the size of the groups varied, given the difficulty in finding GDM women without PSUI. Second, the patients included in this study were not all primigravida, which may have influenced the results. Third, the RAM suffers from substantial strain (e.g., diastasis) during gestation. Diastasis recti abdominis is defined as a separation between the edges of the RAM at the linea alba [74] However, these limitations do not invalidate our results, as they also contribute to advancing knowledge in the field of urogynecology.

In conclusion, our results confirm that RAM is a plastic tissue that adapts its size and morphology in response to external and internal stimuli (here represented by GDM). GDM-related changes in muscular morphology may lead to the development of PSUI in pregnant women. Future studies are clearly needed to confirm RAM myopathy as a key factor of GDM-associated PSUI. In addition, this study may be a basis for the development of new therapies for pathologies with loss of muscle mass, diabetic myopathy, muscle atrophy, and consequently UI. Another relevant aspect of these findings is the identification of biomarkers that can be used as a diagnosis and prognosis allowing the implementation of early interventions and proper management of the patients, mitigating the deleterious impacts of GDM on the muscles.

Acknowledgments

The authors wish to thank the patients who donated their RAM tissue within the context of this study. The authors are also grateful to all medical staff at the Maternity of University Hospital Botucatu Medical School UNESP for excellent patient care.

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Funding sources

The study was supported by the human resources and infrastructure of the PDRC Botucatu Medical School UNESP. The financial maintenance provided by the Brazilian Public Health System (SUS) supported the treatment of all pregnant women attended at PDRC. The study was also supported by the São Paulo Research Foundation (FAPESP) grants #2016/09710-9 and #2014/26852-6.

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PLOS ONE

REGISTERED REPORT PROTOCOL

Effectiveness of the pelvic floor muscle training on muscular dysfunction and pregnancy specific urinary incontinence in pregnant women with gestational diabetes mellitus: A systematic review protocol

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Citation: Barbosa AMP, Enriquez EMA, Rodrigues MRK, Prudencio CB, Atallah ÁN, Reyes DRA, et al. (2020) Effectiveness of the pelvic floor muscle training on muscular dysfunction and pregnancy specific urinary incontinence in pregnant women with gestational diabetes mellitus: A systematic review protocol. PLoS ONE 15(12): e0241962. https://doi.org/10.1371/journal.pone.0241962

Editor: Frank T. Spradley, University of Mississippi Medical Center, UNITED STATES

Received: April 20, 2020

Accepted: October 9, 2020

Published: December 7, 2020

Peer Review History: PLOS recognizes the benefits of transparency in the peer review process; therefore, we enable the publication of all of the content of peer review and author responses alongside final, published articles. The editorial history of this article is available here: https://doi.org/10.1371/journal.pone.0241962

Abstract

Background

There is ample evidence that gestational diabetes mellitus has a direct influence on urinary incontinence and pelvic floor muscles. There are no standardized pelvic floor muscle exercise programs in the literature for the physiotherapy and differ in the type of exercise, intensity, type and duration of application, and the frequency and duration of treatment sessions. The aim of this systematic review will be to investigate that Pelvic Floor Muscle Training can prevent and/or decrease the pregnancy specific urinary incontinence in women with gestational diabetes mellitus or gestational hyperglycemia.

Methods

We will perform a systematic review according to the Cochrane methodology of Randomized Controlled Trials. An overall search strategy will be developed and adapted for Embase, MEDLINE, LILACS, and CENTRAL databases, with the date of consultation until

In this way we may obtain robust and conclusive evidence whether or not there is evidence to support clinical practice, in addition to promote high quality studies on the subject.

Supporting information

S1 File. PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: Recommended items to address in a systematic review protocol*.
(DOC)

S2 File. PROSPERO international prospective register of systematic reviews.
(PDF)

Acknowledgments

We thank the Diamater Study Group for making valuable comments.

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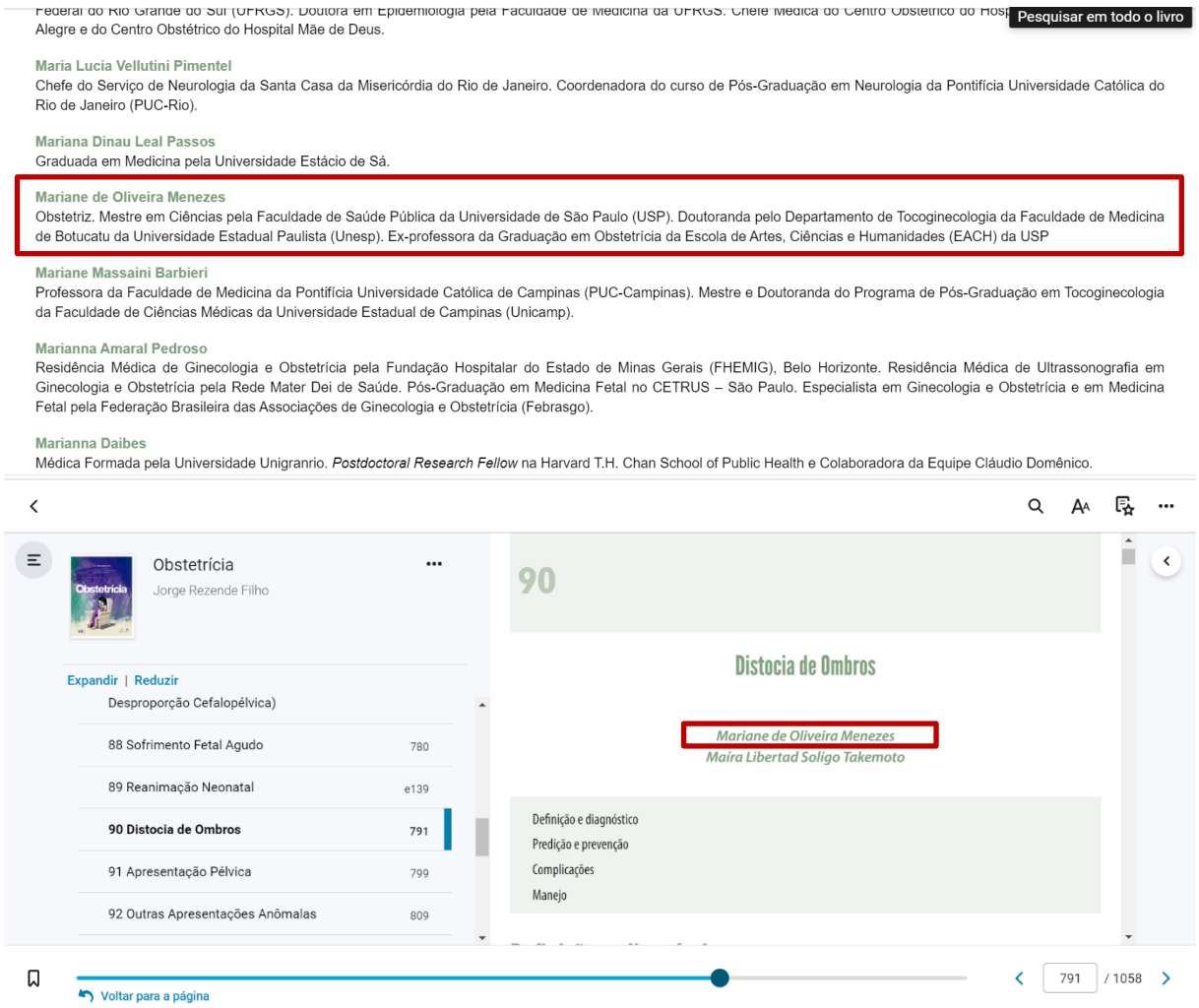
Anexo 23

TAKEMOTO, M. L. S. ; MENEZES, MARIANE O. . Gravidez Prolongada. In: Jorge Rezende Filho. (Org.). Obstetrícia. 14ed.Barueri: Guanabara Koogan, 2022, v. , p. 454-458.

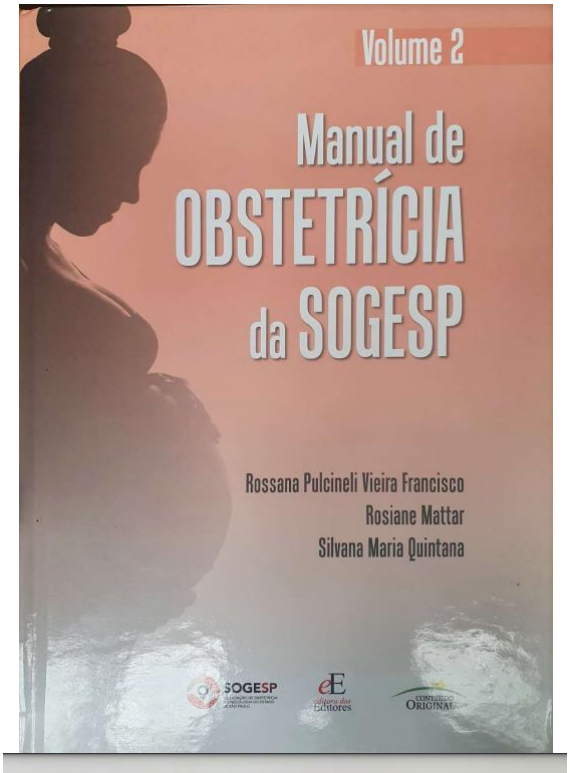
Anexo 24

MENEZES, MARIANE O.; TAKEMOTO, M. L. S. . Distócia de Ombros. In: Jorge Rezende Filho. (Org.). Obstetrícia. 14ed.Barueri: Guanabara Koogan, 2022, v. , p. 791-798.



Anexo 25

TAKEMOTO, M. L. S. ; MENEZES, M. O. ; KNOBEL, R. . Correção das apresentações não usuais utilizando Spinning Babies®. In: Rossana Pulcineli Vieira Francisco; Rosiane Mattar; Silvana Maria Quintana. (Org.). Manual de Obstetrícia da SOGESP. 1ed.São Paulo: Editora dos Editores Eireli, 2021, v. 2, p. 319-327.



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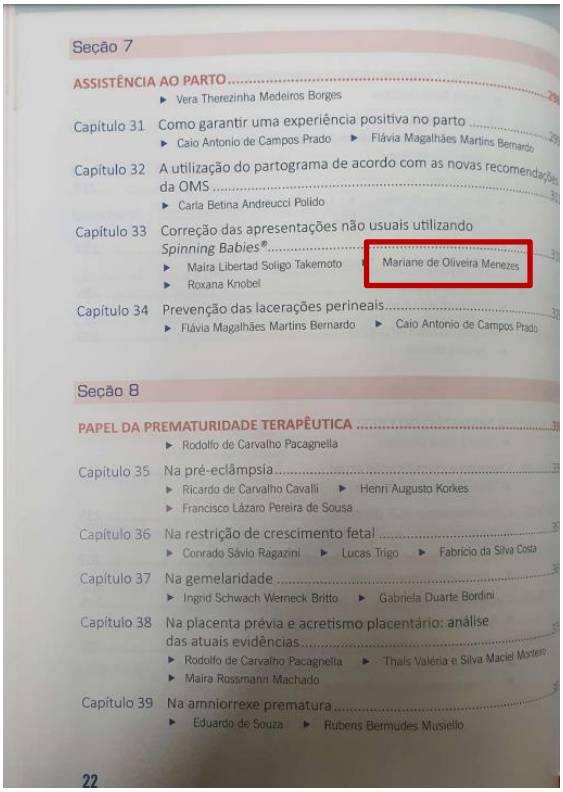

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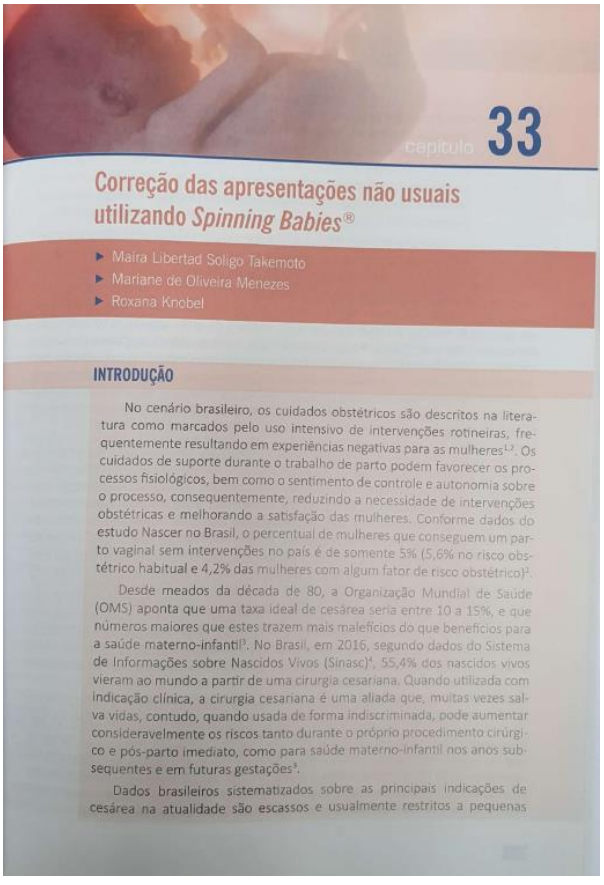

capítulo 33

Correção das apresentações não usuais utilizando *Spinning Babies®*

▸ Maira Libertad Soligo Takemoto
▸ Mariane de Oliveira Menezes
▸ Roxana Knobel

INTRODUÇÃO

No cenário brasileiro, os cuidados obstétricos são descritos na literatura como marcados pelo uso intensivo de intervenções rotineiras, frequentemente resultando em experiências negativas para as mulheres[1,2]. Os cuidados de suporte durante o trabalho de parto podem favorecer os processos fisiológicos, bem como o sentimento de controle e autonomia sobre o processo, consequentemente, reduzindo a necessidade de intervenções obstétricas e melhorando a satisfação das mulheres. Conforme dados do estudo Nascer no Brasil, o percentual de mulheres que conseguem um parto vaginal sem intervenções no país é de somente 5% (5,6% no risco obstétrico habitual e 4,2% das mulheres com algum fator de risco obstétrico)[2].

Desde meados da década de 80, a Organização Mundial de Saúde (OMS) aponta que uma taxa ideal de cesárea seria entre 10 a 15%, e que números maiores que estes trazem mais malefícios do que benefícios para a saúde materno-infantil[3]. No Brasil, em 2016, segundo dados do Sistema de Informações sobre Nascidos Vivos (Sinasc)[4], 55,4% dos nascidos vivos vieram ao mundo a partir de uma cirurgia cesariana. Quando utilizada com indicação clínica, a cirurgia cesariana é uma aliada que, muitas vezes salva vidas, contudo, quando usada de forma indiscriminada, pode aumentar consideravelmente os riscos tanto durante o próprio procedimento cirúrgico e pós-parto imediato, como para saúde materno-infantil nos anos subsequentes e em futuras gestações[5].

Dados brasileiros sistematizados sobre as principais indicações de cesárea na atualidade são escassos e usualmente restritos a pequenas

Anexo 26

ANGRIMANI, D. ; TAKEMOTO, MAIRA L. S. ; MENEZES, MARIANE O. O luto no limbo. In: Damiana Angrimani. (Org.). Perdi meu bebê: Uma companhia para atravessar o luto gestacional, perinatal e neonatal. 1aed.São Paulo: Instituto do Luto Parental, 2022, v. 1, p. 39-46.