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CHARLES M'POCA CHARLES

IMPACTO DA PANDEMIA DA COVID-19 NA SAÚDE SEXUAL E REPRODUTIVA EM MOÇAMBIQUE E NO BRASIL: UMA AVALIAÇÃO EPIDEMIOLÓGICA NA PERSPECTIVA DAS METAS DOS OBJETIVOS DE DESENVOLVIMENTO SUSTENTÁVEL

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Tese apresentada à Faculdade de Ciências Médicas da Universidade Estadual de Campinas como parte dos requisitos exigidos para a obtenção do título de Doutor em Ciências da Saúde na área de Saúde Materna e Perinatal.

ORIENTADOR: PROF. DR. RODOLFO DE CARVALHO PACAGNELLA

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Aos meus Mestres, que minuciosamente lapidaram a minha singela trajetória acadêmica.

&

A minha mãe Delfina Eduardo Pinho (em memória) e a minha esposa Aline Charles, pelo amor incondicional que me fortalece a cada amanhecer.

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EPÍGRAFE

A sensação do ser humano perante uma conquista não é a plenitude, mas sim o anseio por algo maior e mais palatável.

(Harari 2015)

RESUMO

Introdução: A pandemia da COVID-19 sobrecarregou os sistemas de saúde, especialmente em áreas com recursos limitados, afetando severamente os Serviços de Saúde Sexual e Reprodutiva e resultando na redução ou interrupção de serviços essenciais, aumentando a vulnerabilidade das mulheres em idade reprodutiva. Isso contribuiu para um aumento no risco de gestações não planejadas, complicações de aborto e piores desfechos maternos e neonatais, comprometendo os esforços globais para reduzir a mortalidade materna e alcançar metas dos Objetivos de Desenvolvimento Sustentável (ODS). No entanto, a implementação de medidas não farmacêuticas e a vacinação contra a COVID-19 foram cruciais para mitigar a propagação da doença e reduzir suas consequências graves, incluindo em gestantes e puérperas. O surgimento de variantes mais transmissíveis da SARS-COV-2 apresenta novos desafios na compreensão da infecção nessas populações e no impacto contínuo da pandemia na saúde sexual e reprodutiva. **Objetivo**: O estudo proposto visa avaliar os aspectos epidemiológicos do impacto da pandemia da COVID-19 na Saúde Sexual e Reprodutiva em Moçambique e no Brasil. Para alcançar esse objetivo, foram definidos os seguintes objetivos específicos: conscientizar sobre a necessidade de redução dos impactos da COVID-19 na saúde materna e perinatal em países de baixa e média renda; avaliar o impacto da COVID-19 nas vendas de métodos contraceptivos modernos no Brasil; avaliar o conhecimento e aceitabilidade de doses adicionais da vacina contra a COVID-19 em um grupo de mulheres brasileiras em idade reprodutiva (gestantes e não gestantes) e homens; estimar a prevalência da COVID-19 e o impacto da infecção por SARS-CoV-2 nos desfechos maternos em Moçambique; analisar o impacto indireto da pandemia de COVID-19 no número de nascimentos vivos e partos prematuros no Brasil; e avaliar o impacto das variantes de preocupação nos desfechos maternos graves na população obstétrica brasileira. **Material e Métodos:** Utilizamos uma abordagem multifacetada para atingir nossos objetivos. Isso incluiu a redação de um artigo instigando ação e uma carta ao editor para formar redes colaborativas de estudos sobre COVID-19 na gestação em países de baixa e média renda, incentivando a cooperação entre eles. Além disso, realizamos uma análise temporal das vendas mensais de métodos contraceptivos de curta e longa duração no Brasil, identificando variações significativas mensais superiores a 5%. Conduzimos um estudo transversal para avaliar os preditores de aceitação e hesitação em relação às doses adicionais da vacina COVID-19 entre gestantes, mulheres não grávidas em idade reprodutiva e parceiros no Brasil, usando análises bivariadas e multivariadas. Também realizamos um estudo de coorte prospectivo para avaliar os desfechos maternos em uma população obstétrica exposta e não exposta a infecção pelo SARS-CoV-2, em Maputo, Moçambique. Utilizando dados do Sistema de Informação sobre Nascidos Vivos (SINASC) do Brasil, conduzimos um estudo populacional com técnicas de aprendizado de máquina e escores de propensão para estimar a prevalência de parto prematuro antes e durante a pandemia da COVID-19. Por fim, realizamos um estudo ecológico comparativo das características sociodemográficas e clínicas dos participantes durante os períodos de predominância das variantes Ômicron, Delta e Gama no Brasil, estimando as chances de desfechos maternos graves nessas regiões por meio de análises bivariadas e multivariadas. **Resultados:** Dois artigos foram publicados, um de comunicação breve e outro de comentário, destacando a importância da colaboração entre países de baixa e média renda nas pesquisas sobre COVID-19 para fornecer evidências robustas sobre o impacto da pandemia na saúde materna e perinatal. Observou-se um aumento não significativo nas vendas de anticoncepcionais em 2020 em

comparação com 2019, com uma média mensal variando de 12,8 a 13,0 milhões de unidades. Houve aumento nas vendas de anticoncepcionais injetáveis entre fevereiro e maio de 2020, e de pílulas de contracepção de emergência entre junho e julho de 2020. O SIU LNG e o Implante hormonal apresentaram três padrões distintos de vendas. As grávidas mostraram-se mais hesitantes em relação ao reforço da vacina contra a COVID-19 do que as não grávidas, assim como os parceiros do sexo masculino. Fatores associados à redução da aceitação da vacina incluíram baixa renda familiar, religião evangélica e preocupações com segurança e importância percebida da vacina. A prevalência de COVID-19 foi de 9,2%, sendo metade das gestantes sintomáticas. Vulnerabilidades à infecção incluíram falta de companheiro, gravidez e consumo de álcool. Não houve diferenças significativas nos resultados entre grupos positivos e negativos para COVID-19. As taxas de parto prematuro aumentaram durante a pandemia, especialmente no Sul, enquanto a região Norte registrou uma redução significativa. A variante Ômicron foi associada a um menor risco de internação em UTI e morte materna em comparação com as variantes Gamma e Delta. A presença de sintomas (febre, dispneia e baixa saturação de oxigênio) na admissão aumentaram o risco de internação em UTI e morte materna durante o período de predominância da variante Omicron. **Conclusão**: As vendas de anticoncepcionais modernos variaram em 2020, destacando-se o aumento do implante de DIU-LNG/ENG no setor privado, sugerindo desigualdades no acesso à contracepção. Grávidas enfrentam obstáculos para aceitar a vacina de reforço da COVID-19, influenciados por fatores como renda, crenças e preocupações com segurança. Desinformação afeta negativamente essa população vulnerável. Mulheres grávidas e puérperas têm maior risco de contrair COVID-19, mesmo assintomáticas, especialmente aquelas sem parceiro e que consomem álcool. Testes universais e acompanhamento são essenciais. O aconselhamento durante a gravidez sobre medidas preventivas da COVID-19 é vital, mas mais pesquisas são necessárias. Nossa análise revela disparidades regionais crescentes no número de partos prematuros no Brasil durante a pandemia. A variante Ômicron está associada a um menor risco de desfechos maternos graves, mas mulheres grávidas e pós-parto sintomáticas ainda enfrentam riscos, especialmente se apresentam tosse, febre ou dispneia na admissão.

Palavras-chave: morbidade materna grave; prematuridade; variantes do SARS-CoV-2; vacinas; métodos contraceptivos; Objetivos de Desenvolvimento Sustentável; países de baixa e média renda.

ABSTRACT

Introduction: The COVID-19 pandemic has put immense pressure on health systems, especially in areas with limited resources, resulting in a significant impact on sexual and reproductive health services. This has led to a higher risk of negative maternal and neonatal outcomes, hindering global efforts to reduce maternal mortality and achieve sustainable development goals. However, implementing non-pharmaceutical measures and administering COVID-19 vaccines have been essential in limiting the spread of the disease and reducing its severe effects, particularly among pregnant and postpartum women. The emergence of more contagious variants of SARS-COV-2 presents new challenges in comprehending the infection's effects on these populations and the pandemic's ongoing impact on sexual and reproductive health. **Objective:** This study aims to evaluate the impact of COVID-19 on Sexual and Reproductive Health in Mozambique and Brazil. The study objectives include raising awareness about reducing COVID-19 impacts on maternal and perinatal health in low and middle income countries, assessing the impact of COVID-19 on contraceptive sales in Brazil, evaluating the knowledge and acceptability of additional COVID-19 vaccine doses on reproductive-aged Brazilians and partners, estimating COVID-19 prevalence and impact on maternal outcomes in Mozambique, analysing indirect impacts of the pandemic on preterm births in Brazil, and evaluating the impact of SARS-CoV-2 variants of concerns (VOCs) on maternal outcomes in the Brazilian obstetric population. **Material and Methods**: We have adopted a comprehensive approach to achieve our goals, which includes various research studies. We have written an article to urge action and a letter to the editor to encourage collaboration between studies on COVID-19 during pregnancy in low- and middle-income countries. Besides, we conducted a temporal analysis of monthly sales of short- and long-acting contraceptive methods in Brazil, identifying significant monthly variations greater than 5%. We also conducted a cross-sectional study to evaluate predictors of acceptance and hesitancy toward additional COVID-19 vaccine doses among pregnant women, non-pregnant people of reproductive age, and partners in Brazil, using bivariate and multivariate analyses. We conducted a prospective cohort study to evaluate maternal outcomes in an obstetric population in Maputo, Mozambique. Using data from Brazil's Live Birth Information System (SINASC), we conducted a population-based study using machine learning techniques and propensity scores to estimate the prevalence of preterm birth before and during the COVID-19 pandemic. Finally, we conducted a comparative ecological study of the sociodemographic and clinical characteristics of the participants during periods of predominance of the Omicron, Delta and Gamma variants in Brazil, estimating the chances of severe maternal outcomes in these regions through bivariate and multivariate analyses. **Results:** Two articles were published - one a brief communication and the other a commentary - emphasizing the importance of collaboration between low- and middle-income countries in research on COVID-19. They also highlighted the need for robust evidence on how the pandemic affects maternal and perinatal health. A non-significant increase in contraceptive sales was observed in 2020 compared to 2019, with a monthly average of 12.8 to 13.0 million units. There was an increase in sales of injectable contraceptives between February and May 2020, and of emergency contraception pills between June and July 2020. Sales of IUD/hormonal implants showed three distinct patterns. Pregnant women and their male partners were more hesitant about getting a COVID-19 vaccine booster than non-pregnant women. Factors associated with reduced vaccine acceptance included low family income, evangelical religion, and concerns about the safety and perceived importance of the vaccine. Among pregnant women, the prevalence of COVID-19 was

9.2%, with half being symptomatic. Vulnerabilities to infection included lack of a partner, pregnancy, and alcohol consumption. There were no significant differences in outcomes between COVID-19 positive and negative groups. Preterm birth rates increased during the pandemic, especially in the South, while the North region recorded a significant reduction. The Omicron variant was associated with a lower risk of ICU admission and maternal death compared to the Gamma and Delta variants. Symptoms on admission increased the risk of ICU admission and maternal death during the period of the predominance of the Omicron variant. **Conclusion**: In 2020, sales of modern contraceptives varied. However, pregnant women are facing challenges with the acceptance of COVID-19 booster vaccines due to misinformation. This misinformation can negatively impact this vulnerable group. Additionally, pregnant and postpartum women are at a higher risk of contracting COVID-19, so it is important to have universal testing and follow-up procedures in place. Our analysis shows an increasing regional disparity in the frequency of preterm births in Brazil during the pandemic. The Omicron variant is associated with a lower risk of severe maternal outcomes. Nevertheless, symptomatic pregnant and postpartum women still have a significant risk of severe outcomes.

Keywords: severe maternal morbidity; preterm birth; SARS-CoV-2 variants; vaccine; contraceptive methods; Sustainable Development Goals; low and middle-income countries.

LISTA DE ABREVIATURAS E SIGLAS

AIDS - Acquired immunodeficiency syndrome

AOC - Contraceptivos Orais Combinados

CAISM - Centro de Atenção Integral à Saúde da Mulher

CAPES – Coordenação de Aperfeiçoamento de Pessoal de Nível Superior do Brasil

CE - Contracepção de Emergência

CEMICAMP - Centro de Pesquisas em Saúde Reprodutiva de Campinas

CNBS - Comité Nacional de Bioética para Saúde

COVID-19 - Coronavirus Disease

CPAV – Condições Potencialmente Ameaçadora da Vida

DATASUS - Departamento de Informática do Sistema Único de Saúde

DIU - Dispositivo Intrauterino

FNI – Fundo Nacional de Investigação de Moçambique

GISAID – The Global Initiative on Sharing Avian Influenza Data

H1N1 – *Swine influenza A vírus*

HCM - Hospital Central de Maputo

HIV – Human Immunodeficiency Virus

HRP – Human Reproduction Programme

IC – Intervalo de Confiança

IDH - Índice de Desenvolvimento Humano

INS - Instituto Nacional de Saúde de Moçambique

LARC - Long-acting reversible contraceptives method

LNG - Levonorgestrel

MISAU - Ministério da Saúde de Moçambique

MMR - Maternal Mortality Ratio

MMWG - Maternal Morbidity Working Group

ODM – Objetivos do Desenvolvimento do Milênio

ODS - Objetivos de Desenvolvimento Sustentável

OMS – Organização Mundial da Saúde

OR – *Odds Ratio*

PNUD - United Nations Development Programme

POP - Pílulas exclusivamente de progestágeno

PSW - Propensity Score Weighting

REDCap - Research Electronic Data Capture

RR - Risco Relativo

RT-qPCR - Real-Time Quantitative Reverse Transcription Polymerase Chain Reaction

SARC - Short-acting reversible contraceptives method

SARS-CoV-2 - Severe Acute Respiratory Syndrome Coronavirus 2

SIU – Sistema Intrauterino

SIVEP-Gripe - Sistema de Informações da Vigilância Epidemiológica da Gripe

SNS - Sistema Nacional de Saúde

SRAG - Síndrome Respiratória Aguda Grave

SSR - Saúde Sexual e Reprodutiva

SUS - Sistema Único de Saúde

TALE - Termo de Assentimento Livre e Esclarecido

TCLE - Termo de Consentimento Livre e Esclarecido

UEM – Universidade Eduardo Mondlane

UNFPA - United Nations Population Fund

UNICAMP - Universidade Estadual de Campinas

UNICEF - United Nations Children's Fund

UTI - Unidade de Terapia Intensiva

VOC - *Variants of Concern*

WOICE - WHO Maternal Morbidity tool

SUMÁRIO

1. INTRODUÇÃO

A mortalidade e morbidade materna constituem um importante problema de saúde pública, principalmente em países de baixa e média renda. Os Objetivos de Desenvolvimento do Milênio (2000 a 2015) estabeleceram como principal meta, no objetivo 5, uma redução da mortalidade materna e mortalidade por causas relacionadas a gestação em três quartos e alcançar um acesso universal os serviços de saúde sexual e reprodutiva. (1) Apesar da provisão dos serviços de saúde sexual e reprodutiva ser fundamental para o indivíduo e para o desenvolvimento social e econômico da sociedade e nações, o acesso universal a esses cuidados ainda apresenta enormes desafios. (2)

Dados da literatura sugerem redução significativa da razão da mortalidade materna e avanços significativos na provisão dos serviços de saúde sexual e reprodutiva (SSR). No período em análise, 1990 a 2015, observou-se uma redução da mortalidade materna em 43,9% (34,0–48,7). (3) A redução da mortalidade materna não foi igualitária, observou-se uma variação macro e microrregional. (3) A maior proporção de redução da mortalidade materna foi observada em países da África subsaariana, em cerca de 44.6%, 546 (511-652) mortes para cada 100 000 nascidos vivos, uma redução anual de 2,4 (1,6 – 2,8) nesta região africana. A América Latina teve uma redução da razão de mortalidade materna em mais da metade (51,6%), e uma redução anual de 2,9 (2,5 - 3,3). (3)

A redução da mortalidade materna também teve um padrão variável ao nível das nações. Por exemplo, o Brasil teve uma estagnação na melhoria desse indicador chave de saúde materna no período 2000 a 2015 comparado aos anos 1990 a 2000. Para esse período, a redução anual da razão foi de 4,6 (3,2 – 6,0) e 2,7 (1,3 – 4,0), respetivamente. Por outro lado, Moçambique manteve o padrão de redução anual da razão de mortalidade materna nos mesmos períodos 4,2 (1,8 – 6,7) e 4,2 (2,5 – 5,5). (3)

Em 2015, a estimativa do risco de morte materna ao longo da vida reprodutiva em Moçambique era cerca de trinta vezes superior à do Brasil, 1:40 (54 - 28) e 1:1200 (1500 - 1000), respectivamente. (3) Brasil e Moçambique, tiveram uma redução da razão de morte materna em torno de 50%, no entanto enormes desafios são

necessários superar para atingir os Objetivos de Desenvolvimento Sustentável (ODS), 3 (assegurar uma vida saudável e promover o bem-estar para todos, em todas as idades) e 5.6 (assegurar o acesso universal à saúde sexual e reprodutiva e os direitos reprodutivos). (3) A mortalidade materna continua sendo uma tragédia global, e cerca de 94% das mortes maternas ocorrem em países de baixa e média renda, países que ainda se encontram em estágios iniciais da transição obstétrica, estágios I e II. Os estágios I e II são caracterizados por alta razão de mortalidade materna, alta taxa de fecundidade e acesso limitado a cuidados obstétricos básicos e essenciais. (4, 5)

A transição obstétrica é definida como o processo de mudança do padrão de mortalidade materna, da alta para a baixa mortalidade materna, com predominância de causas indiretas devido à redução das causas obstétricas. Um maior número de mortes maternas está associado a doenças crônicas e não transmissíveis, gravidezes em idade avançada, assistência obstétrica institucionalizada e aumento de intervenções médicas sem uma melhoria correspondente nos resultados maternos e neonatais. (4)

De acordo com Souza e seus colegas, o estágio I é caracterizado por alta mortalidade materna, razão de mortalidade materna (MMR) igual ou superior a 500 mortes por 100.000 nascimentos vivos, alta taxa de mortalidade neonatal, alta fertilidade e baixa esperança de vida. Nesse estágio, a cobertura do sistema de saúde é baixa, há baixo Índice de Desenvolvimento Humano (IDH) e alta desigualdade de gênero. Por outro lado, os estágios 2 e 3 representam uma fase de transição caracterizada por mortalidade materna em nível intermediário a alto (MMR igual ou superior a 300-499 mortes e 100-299 mortes por 100.000 nascimentos vivos, para os estágios 2 e 3, respectivamente), mortalidade neonatal, esperança de vida, indicadores sociais e cobertura do sistema de saúde em nível intermediário. O estágio IV é caracterizado por baixa mortalidade materna (MMR inferior a 100, subdividindo-se em estágios 4A e 4B, MM entre 20-99 e menor que 20 por 100.000 nascidos vivos, estágios 4A e 4B, respectivamente), baixa mortalidade neonatal, baixa taxa de fecundidade e aumento da cobertura e qualidade dos serviços de saúde, comparativamente aos estágios anteriores. Por fim, o estágio 4, sendo um estágio teórico, caracterizar-se-á por indicadores melhores do que o estágio 4B. (4, 6)

Com base na razão da mortalidade materna, em 2020, O Brasil encontrava-se no estágio 4A e Moçambique no estágio 3 da transição obstétrica, respectivamente. (4, 5)

Ao nível global, em 2023 cerca de três quartos (75%) de mortes maternas eram secundárias a causas obstétricas diretas. (7) As principais causas de mortalidade materna direta incluem, a hemorragia (27.1%), distúrbios hipertensivos (14,0%), sepses (10,7%), e complicações do aborto (7,9%). (8) No Brasil, a principal causa direta de morte materna é a hipertensão, seguido de causas hemorrágicas. (9-11) Em Moçambique, 73% das mortes maternas são secundárias a causas obstétricas diretas, sendo a hemorragia responsável por 60.6% dos casos de morte materna, seguida de sepses e distúrbios hipertensivos, representando 20.8% e 12% dos casos de morte materna, respectivamente.(12, 13) A demora no acesso aos cuidados médicos está associada ao dobro de risco de morte materna secundária a causas obstétricas diretas e quase a metade (45%) dos casos de *near miss* materno.(12, 13)

Essas condições maternas, quando combinadas com o trabalho de parto obstruído, as causas indiretas e tardias de morte materna, bem como as complicações agravadas pelo HIV, desempenharam um papel significativo na redução da expectativa de vida ajustada das mulheres em todo o mundo. (14, 15) O aumento do risco de incapacidade, tanto em curto quanto em longo prazo, está correlacionado com a qualidade inadequada dos cuidados fornecidos às mulheres durante o ciclo gravídico-puerperal, o que pode resultar em maior incidência de infecções pélvicas, fístulas obstétricas e transtornos mentais. (16)

A saúde da mulher durante o ciclo gravídico-puerperal é influenciada por diversos fatores e determinantes. Os determinantes relacionados ao sistema de saúde incluem pré-natal inadequado, cuidados assistenciais de baixa qualidade, deficiência de recursos humanos treinados ou com capacidade técnico-científica limitada, escassez de medicamento e material médico-cirúrgicos essenciais, inequidade em saúde, e ausência de responsabilização dos gestores dos sistemas de saúde. (17-21). No entanto, o papel do sistema de saúde não deve ser analisado de forma isolada. Dados do estudo *Better Birth* demostraram que o treinamento dos profissionais de saúde melhorou a adesão aos protocolos baseados em evidências científicas, mas não reduziu a morbidade, mortalidade materna e mortalidade perinatal. (22-24) Estes resultados sugerem que a existência de infraestruturas adequadas e treinamento de

profissionais de saúde é essencial, mas insuficiente para o alcance das metas dos ODS, evidenciando enormes desafios na melhoria dos desfechos maternos, perinatais e neonatais. A adequação dos indicadores de avaliação da qualidade assistencial e a sustentabilidade em longo prazo da adesão às boas práticas, em contextos específicos na assistência obstétrica em diferentes níveis do sistema de saúde, são aspectos chaves na melhoria dos desfechos maternos e perinatais. (23-25)

Igualmente, os determinantes sociais e econômicos, por exemplo, gestação nos extremos da idade reprodutiva (idade materna entre 10 e 19 anos e igual ou superior a 35 anos), baixo grau de escolaridade, pertencer a grupos étnicos-raciais minoritários, residir em áreas rurais, desigualdade de gênero e violação dos direitos sexuais e reprodutivos das mulheres, estão associados a um maior risco de desfechos maternos adversos. (2, 17, 23, 26-30)

Os dados da literatura ilustram que a maioria das mortes maternas em países de baixa e média renda são causadas por fatores preveníveis e ou tratáveis, incluindo as causas indireta de morte materna. (8, 31) Deste modo, é necessária a provisão de cuidados obstétricos adequados e qualificados, durante a gestação, parto e pós-parto, para a redução e ou eliminação das causas preveníveis, diretas e indiretas, de morte materna. (32)

No entanto, a disponibilidade dos cuidados não necessariamente se reflete na melhoria dos desfechos maternos e perinatais. (33) Estudo realizado na Nigéria indica que as mortes maternas estão relacionadas a lacunas na implementação de protocolos ou ferramentas de monitoramento do trabalho de parto ou manejo de complicações obstétricas, como a pré-eclâmpsia, eclâmpsia, hemorragia pós-parto e sepse. (34)

As estratégias para reduzir a morbidade grave (*near miss materno*) e mortalidade materna devem incluir a cobertura universal das intervenções preservadoras da vida (*life-saving interventions*), em conjunto com a disponibilidade universal de cuidados obstétricos de emergência e aprimoramento global da qualidade dos cuidados obstétricos fornecidos. (33) Essas estratégias devem se estender além das intervenções para a redução de causas diretas de morte materna, devendo incluir resposta às demandas da transição obstétrica (bem como das transições epidemiológica e climática), garantindo o acesso aos cuidados de saúde sexual e

reprodutiva, além de oferecer adequado planejamento reprodutivo/familiar, especialmente para as populações vulneráveis, para que as escolhas relacionadas à saúde sexual e reprodutiva sejam livres e baseadas em informações adequadas. (32)

A garantia dos cuidados de saúde de qualidade ao binômio gestante/puérpera-feto/recém-nascido durante a gravidez e após o parto, bem como a prevenção de gestações indesejadas, têm um impacto significativo nos sistemas de saúde. A qualidade da assistência pode ser aprimorada por meio da medição e monitoramento dos cuidados fornecidos às mulheres com condições de saúde potencialmente ameaçadoras da vida (CPAV) e de casos de *near miss* materno durante a gestação, parto e puerpério. (35, 36)

Dados sugerem que para cada morte materna, ocorrem cerca de cinco casos de *near miss* materno, evidenciando a necessidade monitoria, diagnóstico e manejo adequado destas condições. (35, 36) A auditoria dos cuidados obstétricos e dos casos de *near miss* materno permite a identificação e correção de fragilidades no sistema de saúde e na rede assistencial à mulheres gestantes, puérperas e recém-nascidos. (36, 37)

A avaliação sistemática, a magnitude da morbidade materna e seu impacto na saúde da mulher durante a gestação, parto e puerpério, podem ser realizados através da ferramenta e indicadores desenvolvidos pelo Grupo de Trabalho em Morbidade Materna (*A Maternal Morbidity Working Group - MMWG*), da Organização Mundial da Saúde, a ferramenta WOICE (*WHO Maternal Morbidity tool*). A ferramenta reforça a influência dos determinantes relacionados ao sistema de saúde no risco e na gravidade da morbidade materna. Por outro lado, realça o papel crucial do sistema de saúde na redução da mortalidade materna, através da prevenção de complicações e da diminuição da terceira demora na assistência obstétrica. (38)

As demoras na assistência obstétrica podem ser categorizadas em três: a primeira relacionada a fatores socioculturais e econômicos, como a demora na procura de atendimento; a segunda associada à acessibilidade das unidades de saúde e hospitais, envolvendo a demora em chegar a essas unidades; e a terceira demora, influenciada pela qualidade dos serviços oferecidos às gestantes ao chegarem às unidades de saúde, que podem resultar em atrasos no recebimento do tratamento adequado. (39)

A ferramenta WOICE pode ser utilizada para rastrear e diagnosticar complicações, bem como avaliar a saúde funcional da mulher durante a gestação e o puerpério. A implementação adequada deste instrumento pode contribuir de forma significativa para uma experiência positiva das mulheres durante esses períodos. Além disso, pode auxiliar no alcance das metas dos Objetivos de Desenvolvimento Sustentável (ODS), particularmente o Objetivo 3, que visa não apenas a sobrevivência, mas também a promoção de uma vida saudável e bem-estar para todas as pessoas, em todas as idades. (40)

No entanto, os sistemas de saúde, elementos-chave para a redução da mortalidade, foram severamente afetados pela pandemia da COVID-19, especialmente em países com sistemas de saúde mais frágeis. A pandemia da COVID-19 evidenciou as fragilidades no sistema de saúde, especialmente a capacidade de manutenção dos serviços de saúde sexual e reprodutiva, bem como o tratamento de doenças crônicas como tuberculose e assistência a pessoas vivendo com HIV/AIDS. (41, 42) A avaliação da resiliência desses serviços no início da pandemia da COVID-19, em 2020, sugeriu uma redução de cerca de 68% nos serviços de contracepção e 56% nas consultas pré-natais, representando uma ameaça aos avanços obtidos na melhoria dos indicadores de saúde materna globalmente e, particularmente, em países de baixa e média renda, como Moçambique e Brasil. (43)

Esses dados sugerem que os progressos alcançado na redução da mortalidade materna podem ser negativamente afetados por eventos extremos, como crises humanitárias ou emergências em saúde pública. (44) As epidemias do vírus da *Zika* e do vírus influenza H1N1 em 2009 sugerem que os progressos alcançados na saúde materna e perinatal são frágeis e não lineares, sendo que a vigilância constante essencial. (45)

Em 2009, a infecção por H1N1 foi associada a um maior risco complicações graves, incluindo admissão na unidade de terapia intensiva (UTI), CPAV e mortalidade materna. (46) O risco estimado de morte associada a infeção pelo H1N1 no grupo de gestantes e puérperas foi quatro vezes superior à da população geral, com um risco relativo (RR) 3,88 (2,77-5,43). (47, 48) Os desfechos adversos não se limitaram às gestantes, afetando também a morbidade perinatal, evidenciado um aumento de parto prematuro em quatro vezes, razão de chances (OR) de 4,0 (2,7 – 5,9), e um aumento no risco de óbito fetal em até quatro vezes nos casos de infecção grave. (49, 50)

De forma similar, a epidemia de v*írus Zika*, nos anos 2015 e 2016, foi associado a um aumento de desfechos neonatais adversos. (51-53) No Brasil, estudos evidenciaram desafios no acesso de métodos contraceptivos de longa duração, durante a epidemia do *vírus Zika,* apesar da mudança na intenção de gestação entre as mulheres brasileiras em idade reprodutiva. (54, 55)

O acesso aos serviços de SSR também é negativamente impactado pelos eventos meteorológicos e climáticos extremos, como ciclones, tornados, tsunamis e terremotos. Esses eventos foram associados à redução da disponibilidade dos serviços de planejamento familiar, amentando a ocorrência de gestações não planejadas. (56) A dificuldade de acesso aos métodos contraceptivos modernos foi mais acentuada em populações mais vulneráveis, especialmente em grupos étnico-raciais minoritários. Um estudo realizado nos Estados Unidos revelou que as mulheres negras não-hispânicas tinham uma chance maior (OR 2,2) de não ter acesso aos métodos contraceptivos em comparação com as mulheres brancas não-hispânicas. Além disso, o acesso limitado a esses métodos pode persistir por períodos iguais ou superiores a 6 meses. (57, 58) Como resultado, aumenta-se a vulnerabilidade das populações de baixo estrato social aos efeitos deletérios dos “super” determinantes da SSR. (6)

A COVID-19 é uma condição respiratória grave com repercussão sistêmica, causada pelo vírus SARS-CoV-2 que devido a rápida disseminação, alcançou alta relevância no panorama global, sendo declarada uma Emergência em Saúde Pública de Interesse Global em 30 de janeiro de 2020. (59-61)

No contexto de Moçambique, o surgimento do primeiro caso de COVID-19 ocorreu em 22 de março de 2020, resultando em 433 casos registrados até 8 de junho de 2020, com sintomas variados e dois óbitos confirmados. (62) A situação epidemiológica na África revelou uma heterogeneidade marcante, com aproximadamente 80% dos casos concentrados em apenas nove dos 55 países da União Africana, o que pode ser atribuído à baixa capacidade de testagem, desempenho limitado dos sistemas de vigilância epidemiológica e ineficiência na coleta de dados estatísticos vitais. (63)

Um ano após o primeiro caso, a capacidade de testagem em Moçambique permanecia abaixo do ideal, com apenas seis testes realizados para cada caso confirmado de COVID-19, sendo o ideal uma razão igual ou superior a 10 testes por cada caso

confirmado de COVID-19. (64-66) No entanto, o número de óbitos associados a COVID-19 estava abaixo das projeções iniciais, a taxa de letalidade geral foi de 1.3%. (66) Em março de 2023, a incidência da COVID-19 era de 746 casos por 100 000 habitantes, uma taxa de letalidade de 0.96%. (67)

No Brasil, o primeiro caso foi relatado em 26 de fevereiro de 2020, desencadeando uma reorganização significativa dos serviços de saúde para atender à demanda relacionada à COVID-19. (68) A realocação de infraestruturas e pessoal de saúde para atender as demandas relacionadas a COVID-19, resultou no fechamento ou redução das atividades de diversos serviços, incluindo os serviços de SSR, colocando as mulheres em idade reprodutiva em situação de vulnerabilidade. (69, 70)

O país foi severamente impactado pela pandemia, evidenciado por um aumento de 20% na taxa de mortalidade materna associada à Síndrome Respiratória Aguda Grave (SRAG) em 2020. (71-73) Após um ano, a razão de testes por caso confirmado de COVID-19 era de apenas três, com uma taxa de letalidade de 2.4%, quase o dobro da taxa em Moçambique. (74) A incidência e letalidade da COVID-19 no Brasil permaneceram elevadas, com uma taxa de incidência 23 vezes superior à de Moçambique em março de 2023. (67)

No contexto brasileiro, a magnitude da pandemia foi atribuída à emergência de variantes do SARS-CoV-2 altamente patogênicas e com alta capacidade de transmissão, além da implementação de políticas de mitigação baseadas em evidências insuficientes e inércia do Governo Federal na adoção de restrições de mobilidade e outras intervenções não farmacológicas. (75, 76) A distribuição desigual de recursos humanos, infraestrutura e financiamento para o combate à pandemia, juntamente com disparidades socioeconômicas regionais preexistentes, também contribuíram para o impacto significativo da COVID-19 no Brasil. (77)

Os dados relativos à preparação do Sistema Único de Saúde (SUS) no Brasil para lidar com a pandemia de COVID-19 no primeiro trimestre de 2020 indicaram uma distribuição desigual dos serviços de saúde, incluindo hospitais, equipamentos e recursos humanos para terapia de suporte à COVID-19. As regiões Sul e Sudeste apresentavam um maior número de infraestruturas e profissionais de saúde para atender às demandas da pandemia em comparação com as regiões Norte e Nordeste do país. Por exemplo, na região Norte, havia 127 médicos e 19 ventiladores

mecânicos por 100 000 habitantes, enquanto na região Sudeste esses números eram de 347 médicos e 38 ventiladores mecânicos por 100 000 habitantes. (78, 79)

Adicionalmente, em Moçambique, os Serviços de Saúde também enfrentavam desafios significativos para mitigar os impactos da pandemia, incluindo a prevenção de mortes relacionadas à COVID-19. Uma análise da prontidão do Sistema Nacional de Saúde (SNS) de Moçambique em 2020 revelou uma capacidade limitada de resposta às demandas da pandemia e uma acessibilidade geográfica limitada das Unidades de Saúde. Apenas 3.4% dos hospitais tinham capacidade para fornecer terapia suplementar para COVID-19, como oxigênio, e apenas 3 em cada 10 moçambicanos teriam acesso a essas Unidades de Saúde com capacidade de oxigênio em até 60 minutos de carro, enquanto apenas 1 em cada 10 poderia acessá-las a pé. (80)

Estudos anteriores à pandemia de COVID-19 indicavam que as populações de baixa renda e escolaridade tinham menos acesso aos cuidados ou intervenções obstétricas de emergência ou essenciais, como a administração de sulfato de magnésio para o manejo de eclâmpsia e parto por cesárea, quando comparadas às gestantes com escolaridade superior. (28, 81) A pandemia da COVID-19 poderia acentuar essa desigualdade social. (82, 83)

De maneira semelhante aos eventos climáticos e meteorológicos extremos, dados sugeriam uma redução ou interrupção por longos períodos da oferta dos serviços de SSR durante a pandemia da COVID-19. A oferta desses serviços permaneceu reduzida em 35% dos países analisados por período superior a um ano após o início da pandemia da COVID-19. Houve também uma redução significativa na oferta de serviços de planejamento familiar, consulta pré-natal, assistência às vítimas de violência por parceiro íntimo, serviços de aborto seguro e partos institucionais, em cerca de 44%, 39%, 39%, 28% e 25%, respectivamente. (43)

Os fatores associados à interrupção desses serviços estão relacionados ao sistema de saúde, como a redução estratégica dos serviços de SSR por serem considerados "não prioritários". Além disso, existem fatores associados aos usuários do sistema de saúde, como medo, desconfiança das ações do governo, déficit econômico e medo de infecção pelo SARS-CoV-2. (43, 84)

Os dados anteriores à pandemia da COVID-19 indicavam uma frequência de necessidades não atendidas de planejamento familiar entre mulheres casadas em idade reprodutiva substancialmente mais elevada na África subsaariana, registrando 22.9% (20.9-25.0). (85) Em contraste, no Brasil, antes da pandemia da COVID-19, a taxa de utilização de métodos contraceptivos modernos de longa duração era significativamente mais baixa, estimada em cerca de 2,0%, com 2,2% na área urbana e 1,0% na área rural. (86) Dados de modelagem matemática previam efeitos devastadores na saúde materna e perinatal com a redução ou interrupção na ofertados dos serviços de SSR, principalmente em países de baixa e média renda. (87)

A redução da disponibilidade dos serviços de SSR - incluindo a diminuição da oferta de serviços de contracepção, assistência à mulher durante a gestação, parto e pós-parto, e cuidados pós-aborto - sugere um ambiente propício para a estagnação ou retrocesso nos ganhos alcançados na saúde materna.

A oferta limitada dos serviços de planejamento familiar é um dos preditores das altas taxas de gestações não planejadas, aborto inseguro e mortalidade associada às complicações do aborto. Portanto, constitui uma significativa barreira para o alcance das metas dos ODS (2030), especialmente os objetivos 3.1 (reduzir a taxa de mortalidade materna global para menos de 70 mortes por 100.000 nascidos vivos), 3.7 (garantir o acesso universal aos serviços de saúde sexual e reprodutiva, incluindo o planejamento familiar, informação e educação, além da integração da saúde reprodutiva em estratégias e programas nacionais), e 3.8 (alcançar a cobertura universal de saúde, incluindo proteção contra riscos financeiros, acesso a serviços de saúde essenciais de qualidade, e acesso a medicamentos e vacinas essenciais seguros, eficazes, de qualidade e a preços acessíveis para todos). (88, 89)

No Brasil, apesar dos avanços significativos na redução da mortalidade materna entre os anos de 2010 e 2015, observou-se uma estagnação desse indicador, com uma tendência ao aumento da mortalidade materna. (89) Este cenário foi agravado com o advento da pandemia da COVID-19, com aumento significativo da razão de mortalidade materna nos últimos anos. Em 2019, a MMR era de 57 mortes maternas por 100 000 nascidos vivos, enquanto com o advento da pandemia, a razão aumentou para 67 e 107 mortes maternas por 100.000 nascidos vivos nos anos de 2020 e 2021, respectivamente. (21, 89) Por outro lado, em Moçambique, os dados do Banco

Mundial sugerem uma redução de 15.3% na MMR entre os anos de 2019 (150 mortes maternas por 100.000 nascidos vivos) e 2020 (127 mortes maternas por 100.000 nascidos vivos). (89)

A pandemia da COVID-19 pode ter afetado o número de casos de mortalidade materna através do aumento das causas indiretas e diretas de morte materna, consequência da deficiente implementação de medidas de prevenção e do inadequado manejo de complicações obstétricas, condicionada pelo limitado acesso ou baixa qualidade de cuidados obstétricos e sobrecarga do sistema de saúde. (89, 90)

No Brasil, a sobrecarga do sistema de saúde, a perda de recursos humanos e a incapacidade de infraestrutura para responder às demandas da pandemia, juntamente com os fatores relacionados aos usuários dos serviços de saúde mencionados anteriormente, podem ter comprometido a qualidade dos cuidados maternos e perinatais, agravando a problemática dos cuidados obstétricos limitados e prestados tardiamente (*too little, too late*). (91, 92) Além disso, também foram observadas a implementação de medidas farmacológicas e não farmacológicas não efetivas, ou com fraco embasamento científico para o manejo da COVID-19, bem como intervenções efetivas que foram usadas de forma inadequada ou em momento inadequado, o que agravou ou não alterou os desfechos maternos ou neonatais. (93, 94)

No que diz respeito aos fatores de risco relacionados ao indivíduo, as mulheres grávidas apresentaram maior gravidade da doença quando comparadas às mulheres não grávidas e à população geral. (95) Igualmente, a infecção pelo SARS-CoV-2 foi associada a um maior risco de desfechos maternos e perinatais adversos quando comparada às gestantes sem infecção pelo SARS-CoV-2, incluindo um aumento significativo do risco de desfechos perinatais adversos, prematuridade, óbito fetal e aborto. (29, 95, 96) Nas gestantes e puérperas com COVID-19, o risco de evento adverso foi superior em mulheres com idade avançada, pertencentes a grupos étnico-raciais minoritários, com índice de massa corporal elevado e que apresentavam condições médicas de base. (95)

Por outro lado, as mutações do SARS-CoV-2 que originam alterações significativas, ampliando a capacidade viral de transmissibilidade e evasão do sistema imunológico,

reforçaram a necessidade de maior vigilância do impacto das diferentes variantes de preocupação (*Alpha, Beta, Gamma, Delta e Omicron*) nos serviços de saúde e na morbidade materna e perinatal, incluindo a efetividade das medidas não farmacêuticas e farmacológicas de controle da pandemia e redução da morbidade e mortalidade associadas à infecção pelo SARS-CoV-2. (97)

Diante de um evento extremo em saúde pública e com base na experiência de situações prévias de emergência em saúde pública, a implementação de redes colaborativas de estudo do impacto da pandemia em diferentes contextos é de vital importância para fornecer dados concretos e permitir que as decisões em saúde pública sejam baseadas em evidências científicas. (98) Igualmente, permite que informações sejam geradas em tempo hábil para permitir intervenções necessárias para o controle da pandemia, redução da morbidade e mortalidade materna e perinatal. Por outro lado, permite entender melhor o impacto da emergência em saúde pública na saúde materna e reduzir demoras na assistência à mulher no ciclo gravídico-puerperal. (99, 100) Por exemplo, a colaboração em saúde possibilitou o rápido desenvolvimento e disponibilização da vacina, como ação complementar à implementação e adoção de medidas não farmacológicas para o combate à pandemia da COVID-19, constituindo um avanço para a saúde pública de forma geral.

O impacto da pandemia foi contexto-dependente; no entanto, a maior parte das evidências sobre a repercussão da COVID-19 na saúde sexual e reprodutiva era de países de alta renda. Deste modo, em situações de crises em saúde pública, a implementação de estudos em países de baixa e média renda que gerem evidências científicas para elucidar o padrão da evolução da doença no período gestacional e perinatal para melhorar o manejo e os resultados maternos e perinatais nesta população é crucial. Igualmente, fornecer dados sobre a oferta de serviços de SSR essenciais (incluindo a contracepção) e informar sobre os fatores associados à adoção de medidas farmacológicas (por exemplo a vacinação) de prevenção da infecção pelo SARS-CoV-2 em grupos de mulheres em idade reprodutiva, incluindo as gestantes e puérperas, é de vital importância.

2. OBJETIVOS

2.1. Objetivo Geral:

Avaliar os aspectos epidemiológicos do impacto da pandemia da COVID-19 na Saúde Sexual e Reprodutiva em Moçambique e no Brasil.

2.2. Objetivos específicos:

2.2.1. Apelar esforços coordenados para produção de conhecimento científico e partilha de informação para responder de forma pragmática aos desafios da Saúde Sexual e Reprodutiva das mulheres no contexto da pandemia da COVID-19, em países de baixa e média renda;

2.2.2. Avaliar o impacto da COVID-19 nas vendas de métodos contraceptivos modernos no Brasil;

2.2.3. Avaliar a percepção e aceitabilidade da vacina contra a COVID-19 e fatores associados em um grupo de mulheres Brasileiras em idade reprodutiva (gestantes e não gestantes) e seus parceiros.

2.2.4. Estimar a prevalência e o impacto da infecção por SARS-CoV-2 nos desfechos maternos em Moçambique;

2.2.5. Analisar o impacto indireto da pandemia de COVID-19 na proporção de partos prematuros no Brasil;

2.2.6. Comparar o impacto das variantes de preocupação (*Gamma, Delta e Omicron*) na gravidade da COVID-19 e risco de morte materna no Brasil.

3. METODOLOGIA

Para uma avaliação abrangente do impacto da COVID-19 na saúde sexual e reprodutiva, vários projetos de pesquisa foram concebidos, cada um adotando uma metodologia de desenho de estudo específica. Abaixo, descreveremos as metodologias empregadas nesses projetos de acordo com seus objetivos específicos. Globalmente, foram realizadas análises primárias, tanto quantitativas quanto qualitativas, de dados provenientes de estudos originais conduzidos em Moçambique e Brasil. Também foram realizadas análises ecológicas de dados de base populacional brasileira.

3.1. ***Apelar esforços coordenados para produção de conhecimento científico e partilha de informação para responder de forma pragmática aos desafios da Saúde Sexual e Reprodutiva das mulheres no contexto da pandemia da COVID-19, em países de baixa e média renda:***

Devido aos possíveis impactos da pandemia da COVID-19 nos serviços de saúde sexual e reprodutiva, bem como em seus efeitos nos resultados maternos e neonatais na região da África Subsaariana, redigimos uma carta ao editor e um comentário. Nesse sentido, apelamos por esforços coordenados visando o desenvolvimento de pesquisas e a troca de informações. Nosso objetivo era apelar sobre a necessidade de implementação de estratégias práticas de resposta à pandemia e garantir a continuidade dos serviços pré-natais, pós-natais, de rastreio e tratamento de infecções sexualmente transmissíveis e aborto.

Propondo a criação de uma Rede Africana e cooperação sul-sul, abrangendo países de baixa e média renda, para enfrentar a pandemia da COVID-19 no ciclo gravídico-puerperal. Essa rede possibilitaria uma melhor compreensão do papel dos fatores específicos do contexto na evolução, manejo e tratamento da infecção por SARS-CoV-2. Além disso, permitiria a vigilância de variantes emergentes do vírus SARS-CoV-2 e implementação de intervenções baseadas em evidências científicas, com foco no apoio às mulheres durante o ciclo gravídico-puerperal durante a pandemia da COVID-19.

3.2. ***Avaliação do impacto da COVID-19 nas vendas de métodos contraceptivos modernos no Brasil:***

Realizamos uma auditoria e análise descritiva dos dados de venda de contraceptivos modernos para o sector público e privado no Brasil. Foram coletados dados relacionados às vendas mensais de contraceptivos modernos para os sectores públicos e privados do Brasil no período entre janeiro de 2019 a dezembro de 2020, período prévio e durante a pandemia da COVID-19, de todas as farmacêuticas brasileiras. Extraímos os dados mensais e desagregados de diferentes métodos contraceptivos modernos disponíveis no Brasil. Os dados de venda dos métodos contraceptivos modernos de curta duração foram fornecidos pela companhia de auditoria de tecnologia de saúde do Brasil, *IQVIA PMB.* Os dados dos métodos contraceptivos modernos reversíveis e de longa duração foram fornecidos pelas indústrias farmacêuticas ou seus representantes no Brasil. Obtemos os dados de Dispositivo Intrauterino (DIU) de Cobre - *Optima; Injeflex*, São Paulo, Brasil. Os sistemas intrauterinos de levonorgestrel (LNG), Mirena e Kyleena - *Bayer Oy, Turku, Finland*. E o implante de levonorgestrel, *Implanon NXT, MSD, Oss, The Netherlands.*

Os dados relativos aos métodos contraceptivos foram categorizados em cinco grupos: i) pílulas anticoncepcionais de emergência (CE) de 1,5 mg LNG, ii) contraceptivos orais combinados (AOC), pílulas só de progestágeno (POP), anéis vaginais e adesivos transdérmicos; iii) contraceptivos injetáveis, mensais e trimestrais); iv) métodos contraceptivos reversíveis de longa duração (LARCs), DIUs de Cu; e v) LARCs sem a inclusão de DIU de cobre. Usamos essa categorização de LARCs porque o DIU-LNG e o implante de levonorgestrel não estavam disponíveis no setor público, com poucas exceções, como alguns hospitais universitários e acesso restrito.

Estimamos e comparamos as médias mensais de vendas de cada grupo de anticoncepcionais no ano de 2019 com igual período de 2020. Adicionalmente, estimamos o percentual mensal de variação das vendas de cada grupo de anticoncepcionais. Para a análise da variação mensal das vendas, consideramos significativa a variação de 5 pontos percentuais ou mais nas vendas anticoncepcionais entre igual período nos anos 2019 e 2020. Usamos fator de conversão para cada grupo de método contraceptivo considerando a duração de proteção de cada método.

Os resultados das análises foram apresentados em gráficos e tabelas de frequência para cada grupo de método contraceptivo moderno.

3.3. ***Avaliar a percepção e aceitabilidade de doses adicionais da vacina contra a COVID-19 e fatores associados em um grupo de mulheres brasileiras em idade reprodutiva (gestantes e não gestantes) e seus parceiros:***

Realizamos um estudo descritivo, de coorte transversal; foram incluídas no estudo mulheres em idade reprodutiva (gestantes e não gestantes) e parceiros homens. Os participantes foram convidados através das plataformas de redes sociais e de panfletos (contendo *qr-code* com link de acesso ao questionário de pesquisa) afixados nas salas de espera dos ambulatórios de obstetrícia, ginecologia e oncologia do Hospital da Mulher Prof. Dr. José Aristodemo Pinotti – CAISM, UNICAMP, apêndice I.

Após a obtenção do consentimento informado no próprio formulário eletrônico, os participantes responderam a um questionário específico do estudo.

A amostragem foi por conveniência, e os sujeitos foram convidados a participar do estudo através da técnica de “bola de neve”. Os formulários preenchidos estavam vinculados a plataforma REDCap, e foram armazenados para criação do banco de dados, apêndice II.

Critérios de exclusão: adolescentes (idade <=18 anos) e formulários com preenchimento incompleto (< 50%).

Desfecho primários (aceitabilidade da vacina contra a COVID-19).

Desfechos secundários: fatores associados a hesitação no uso da vacina contra a COVID-19, desejo de vacinação no caso de doses adicionais, grau de conhecimento e acesso a informação sobre a vacina contra a COVID-19 nos diferentes grupos (gestantes, não gestantes e seus parceiros).

Análise estatística: Estimamos a frequência e o percentual para os três grupos. Para variáveis numéricas, reportamos a média e o desvio padrão. Utilizamos o teste Qui-quadrado (χ^2), ou teste exato de Fisher (quando necessário), para comparar variáveis categóricas. Recategorizamos as variáveis sobre o conhecimento e percepção COVID-19 e da vacina como resposta dicotômica (Concordo totalmente e concordo = 1; discordo totalmente, discordo e neutro = 0). Utilizamos análise bivariada para avaliar os potenciais fatores de risco para a aceitação do reforço da vacina COVID-19 entre os três grupos.

Além disso, utilizamos a análise bivariada para comparar o risco de hesitação a primeiras doses da vacina entre mulheres grávidas ou recentemente grávidas versus mulheres não grávidas e parceiros. Para a análise multivariada, utilizamos os critérios de seleção de preditores por eliminação- *backward stepwise*.

As prováveis variáveis explicativas (potenciais preditores) do modelo de regressão foram selecionados a partir de análise bivariada e basearam-se no valor de corte de p-valor inferior a 10%.

Realizamos análise de subgrupo para explorar os preditores de aceitação do reforço da COVID-19 para mulheres grávidas ou recentemente grávidas, mulheres não grávidas e parceiros. Relatamos o tamanho do efeito como razão de chances (OR) e os respectivos intervalos de confiança (IC 95%). Consideramos significativo valor de $p < 0,05$. Todas as análises foram realizadas no R Studio (versão 4.3.1).

3.4. ***Estimativa da prevalência e do impacto da infecção por SARS-CoV-2 nos desfechos maternos e perinatais em Moçambique:***

Realizamos um estudo de coorte prospectiva na maternidade de referência e de ensino, Hospital Central de Maputo (HCM), de 20 de outubro de 2020 a 22 de julho de 2021. Foram convidadas a participar do estudo as gestantes e puérperas (até ao 14 dia pós-parto) que foram admitidas no Serviço de Urgência do Departamento de Ginecologia e Obstetrícia do HCM. Após o convite, leitura e assinatura do termo de consentimento livre e esclarecido, as participantes elegíveis responderam a um

questionário sobre a presença de sinais e sintomas de infecção das vias aéreas, seguido de rastreamento laboratorial da infecção pelo SARS-CoV-2, através do exame molecular.

Critérios de inclusão e procedimentos de seleção dos casos

Foram incluídas gestantes e puérperas (até ao 14º dia pós-parto), com contato telefônico válido, após a leitura, compreensão e assinatura do TCLE e ou TALE para as adolescentes.

Critérios de exclusão

Foram excluídas do estudo as participantes que retirarem o seu termo de consentimento no decurso do estudo. E participantes que não realizaram a testagem para a COVID-19.

Tamanho da Amostra

A amostragem foi por conveniência, e composta por todas as mulheres que apresentem os critérios de inclusão durante o período do estudo, face à ausência de estudos sólidos de prevalência e incidência na população gestante no momento do desenho do estudo.

Local de implementação do estudo

O presente estudo foi implementado no departamento de Ginecologia e Obstetrícia do Hospital Central de Maputo, Moçambique.

Seguimento das participantes

Após a inclusão no estudo as participantes foram divididas em dois grupos, quanto a positividade para a infeção por SARS-CoV-2:

- Grupo 1 (expostas): constituído por gestantes ou puérperas (até ao 14º dia) com sintomas respiratórios e gestantes ou puérperas (até ao 14º dia) assintomáticas, ambas com teste positivo para infecção por SARS-CoV-2.

- Grupo 2 (não expostas): constituído por gestantes ou puérperas (até ao 14º dia), assintomáticas e gestantes ou puérperas (até ao 14º dia) com sintomas respiratórios, ambas com teste negativo para a infeção por SARS-CoV-2.

Após a alta hospitalar, o seguimento das participantes foi realizado de forma remota através de internet ou telefone, durante a gestação e até a 6ª semana do puerpério, onde coletamos dados dos desfechos maternos e perinatais. Durante o seguimento realizamos a avaliação e monitoria das repercussões maternas e do recém-nascidos (clínicos, laboratoriais, manejos, disfunções orgânicas e óbitos). A coleta de dados foi realizada através de um formulário eletrônico (*REDCap*) instalado em smartphones e *tablets*.

Os desfechos primários foram morte materna, síndrome respiratória aguda grave (SRAG) e admissão na unidade de terapia intensiva (UTI).

Rastreamento para COVID-19

Todas as gestantes incluídas no estudo foram testadas para SARS-Cov-2. Para tanto, realizamos detecção molecular (RT-qPCR) de SARS-CoV-2 através do uso do aparelho *GeneXpert Cephaid*. A detecção molecular foi realizada a partir de amostras respiratórias da cavidade oral e nasal, obtidas através de *swabs* combinados. A coleta da amostra foi realizada por profissionais de saúde previamente treinados para o efeito e segundo as normas preconizadas pelo MISAU e OMS. As participantes sintomáticas foram testadas de forma individual e as assintomáticas foram testadas usando a estratégia ‘‘pool testing”, figura. (101)

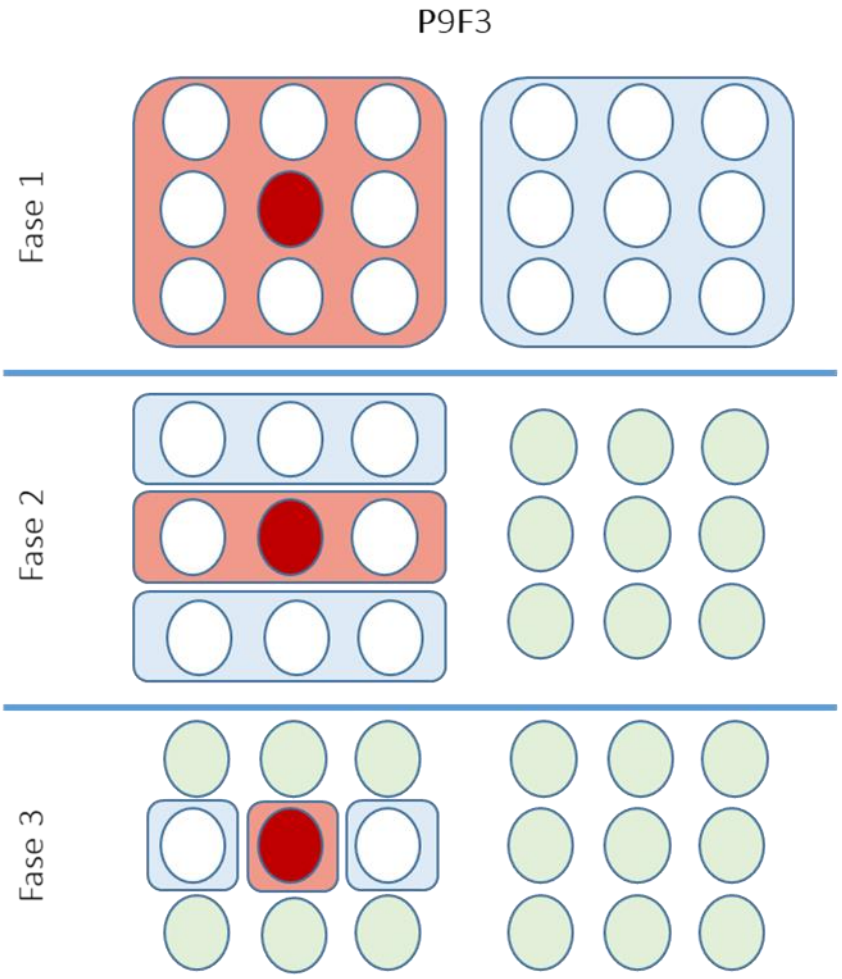

Figura 1: fases de testagem na abordagem pool testing para amostra de pacientes assintomáticas, adaptado de *J.N. Eberhardt et al 2020.*

Analise estatística

Estimamos a prevalência da COVID-19 e o risco relativo não ajustado (95% de IC) para os desfechos maternos e perinatais. Usamos o teste χ^2 ou o teste exato de Fisher para comparar variáveis categóricas (consideramos valor de *p* bicaudal < 0,05 para a significância estatística).

Consideração éticas:

O presente estudo obedeceu aos princípios enunciados na Declaração de Helsinque e nas normas de bioética em pesquisa envolvendo seres humanos vigente em

Moçambique. O estudo teve a aprovação do Comité Nacional de Bioética para Saúde, Ministério da Saúde, Moçambique, Número de aprovação ética: 373/CNBS/20.

3.5. ***Avaliação do impacto indireto da pandemia de COVID-19 na proporção de partos prematuros no Brasil:***

Desenho do estudo

Realizamos um estudo de delineamento quase-experimental usando uma base populacional considerando o período de janeiro de 2017 a dezembro de 2021.

Fonte de dados

Nossa análise foi realizada utilizando os microdados públicos de nascidos vivos do Ministério da Saúde do Brasil e disponibilizados através do Sistema Brasileiro de Informações de Nascidos Vivos (SINASC). (102) O SINASC, um sistema eletrônico de registro de nascimentos desenvolvido pelo Departamento de Informática do Sistema Único de Saúde (DATASUS), o sistema foi inicialmente implementado em 1990 e os dados são rotineiramente coletados através da declaração de nascidos vivos, um documento padronizado que inclui uma ampla gama de variáveis sociodemográficas e obstétricas. O SINASC é uma fonte confiável e abrangente de dados para estudos epidemiológicos.

Os dados para esta pesquisa foram extraídos do SINASC em 12 de agosto de 2023 e atualizados em 15 de abril de 2023, disponíveis em http://svs.aids.gov.br/dantps/cgiae/sinasc/. A extração dos dados e atualização dos dados foi realizada com auxílio da inteligência artificial (Programa R Studio), abrangendo nascidos vivos ocorridos entre janeiro de 2017 e dezembro de 2021, com idade gestacional igual ou superior a 22 semanas.
Um instrumento de coleta de dados especifico foi usado para extração de informação relacionadas as variáveis de interesse, como idade materna, estado civil, etnia, escolaridade, paridade, tipo de parto, região de residência e número de consultas pré-natais.

Analise estatística

Embora tenha havido melhorias recentes na qualidade dos dados do SINASC, os dados disponíveis no SINASC carecem de ajustes e correções, especialmente em níveis geográficos mais desagregados como é caso dos municípios. Para minimizar esses efeitos, a nossa análise se concentrou na avaliação dos dados nacionais e regionais. Após a extração e organização da base de dados com as variáveis de interesse para o nosso estudo, realizamos uma análise exploratória dos dados, com avaliação da qualidade dos dados. No geral, os dados usados no presente estudo eram de boa qualidade e a taxa de subnotificação de dados no Brasil foi aproximadamente de 1%, com exceção das regiões Norte e Nordeste, onde pode chegar a cerca de 1,7%.

A nossa análise foi restringida a comparações entre pares de anos, de 2017 a 2021, para garantir que as tendências anteriores na prevalência de nascimentos prematuros não influenciem de forma significativa nos resultados da presente pesquisa. Excluímos dados anteriores a 2017 para evitar qualquer influência do epidemia do *Zika* vírus que ocorreu entre 2015 e 2016 na contagem de nascimentos e na fertilidade geral.(103)

Realizamos a analise descritiva das características de base para os anos 2017 a 2021. A análise considerou a criação de comparação dos dados considerando os seguintes pares de anos (2017-2018; 2018-2019; 2019-2020 e 2019-2021) cada um com duas variáveis dicotômicas chave de interesse. A primeira variável indicando o desfecho primário – se o nascimento foi prematuro (y = 1), enquanto o valor (y = 0) indicou um nascimento a termo. A segunda variável indicando a variável exposição o período em anos, com o valor (z = 0) representando o ano atual no conjunto de dados e o valor (z = 1) representando o ano seguinte. Esta segunda variável foi particularmente útil para identificar tanto o grupo de controle (partos prematuros que ocorreram antes da pandemia de COVID-19) quanto o grupo de exposição (partos prematuros que ocorreram durante a pandemia).

Realizamos a análise de regressão logística múltipla para ajustar as variáveis de interesse e controlar potenciais fatores de confusão, utilizando uma abordagem quase experimental baseado no método *Propensity Score Weighting* (PSW). O objetivo do

PSW é abordar o viés de seleção em estudos não experimentais, onde é necessário avaliar o efeito médio de uma variável que emula um processo de controle/tratamento. Essa técnica permite abordar o viés de seleção em estudos não experimentais, ajustando a probabilidade de exposição a um determinado estímulo ou intervenção. (104-106)

Incialmente, foi realizada uma análise de regressão logística múltipla para ajustar a variável de controle binária (z) em função das características maternas e obstétricas, como idade, raça/cor da pele, escolaridade, paridade, tipo de parto, número de filhos anteriores, estado civil, número de consultas pré-natais e peso do recém-nascido. Com as estimativas de regressão, foi derivado um vetor (e) que forneceu a probabilidade de atribuição de tratamento a um indivíduo aleatório condicionado a um determinado conjunto de covariáveis (x), ou seja, $e(x) = P(z=1|x)$. Este vetor (e) foi utilizado para controlar o viés de seleção e derivar os pesos de um segundo modelo de regressão. O controle foi obtido através da poda de amostras correspondentes às caudas do vetor *Propensity Score*, retendo apenas amostras que possam ser consideradas comparáveis entre si.

Estimamos a razão de chances (OR) de partos prematuros usando o método *Propensity Score Weighting*. As analises foram realizadas utilizando o pacote estatístico R estúdio (versão 4.3.1).(107)

3.6. ***Comparação do impacto das variantes de preocupação (Gamma, Delta e Omicron) na gravidade da COVID-19 e risco de morte materna no Brasil.***

Desenho do Estudo e Procedimentos:

Realizamos um estudo ecológico utilizando uma base populacional nacional para investigar o impacto da COVID-19 em mulheres grávidas e puérperas durante os períodos de predominância das variantes *Gamma, Delta e Omicron*. Os dados analisados foram obtidos do Sistema de Informações da Vigilância Epidemiológica da Gripe (SIVEP-Gripe), gerenciado pelo Ministério da Saúde do Brasil em colaboração com o Departamento de Informática do Sistema Único de Saúde (DATASUS), disponíveis em https://opendatasus.saude.gov.br. A amostra incluiu mulheres grávidas e puérperas com diagnóstico laboratorial confirmado de COVID-19, abrangendo o período de março de 2021 a agosto de 2022.

Para a caracterização dos casos de COVID-19 na população obstétrica no período em análise, foram extraídas diversas variáveis de interesse de uma base de dados pública e virtual. Estas variáveis incluíram características demográficas, sinais e sintomas, datas de vacinação, hospitalizações, tratamentos médicos, entre outros. Também foram obtidas informações sobre a data de óbito das participantes, quando aplicável.

Os dados extraídos do SIVEP-Gripe foram organizados em um banco de dados virtual especificamente projetado para este estudo. A extração inicial dos dados ocorreu entre julho e outubro de 2022, com atualizações realizadas até janeiro de 2024. No entanto, os dados sobre a genotipagem para cada participante (caso incluído) indicando a variante viral não estavam disponíveis. Portanto, o período de predominância de cada variante foi definido com base nos dados disponíveis no banco de dados brasileiro de genotipagem do vírus da COVID-19 mantido pelo GISAID (*The Global Initiative on Sharing Avian Influenza Data*), acessado em 26 de outubro de 2022, em https://gisaid.org/phylodynamics/brazil/. Foi considerado um período de predominância quando uma variante contribuiu com mais de 70% das infecções por COVID-19 em todo o país. O ponto de corte para a definição do período de predominância de cada variante foi estabelecido considerando os dados da literatura que estabelece que um período em que uma determinada variante é identificada em

70% a 95% das amostras analisadas. Os casos sobrepostos de diferentes variantes foram excluídos.

Após a compilação da base de dados para o presente estudo, realizamos uma análise exploratória dos dados para avaliar a completude e consistência dos mesmos. As análises exploratórias e preliminares estão disponíveis em https://github.com/LucasTramonte/Analysis-SARS-CoV-2-variants.git.

Desfechos Primários e Secundários:

O desfecho primário do estudo foi a morte materna, enquanto o desfecho secundário foi a internação materna na unidade de terapia intensiva (UTI) e o desfecho materno composto, definido como a ocorrência de pelo menos um dos seguintes desfechos: morte materna ou internação em UTI.

Análise Estatística:

Realizamos uma análise comparativa das características sociodemográficas e clínicas dos participantes durante os períodos de predominância das variantes Omicron, Delta e Gama no Brasil. Utilizamos análises estatísticas descritivas, com estimativas das frequências relativas e teste X^2. Posteriormente, foram conduzidos modelos bivariados e de regressão logística para estimar as chances de desfechos maternos graves durante esses períodos. Adicionalmente, realizamos uma análise estratificada das regiões federais brasileiras.

Igualmente, avaliamos a associação entre os sintomas na admissão e os desfechos maternos graves para cada período de predominância das Variantes de Preocupação (VOCs). Os resultados foram apresentados em razão de chances (OR) bruto e ajustado, acompanhados de intervalos de confiança (IC) de 95%. As medidas de efeito foram ajustadas para variáveis como idade materna, período gestacional, etnia, status vacinal, nível educacional e região. Todas as análises foram realizadas utilizando o software Python, sendo considerado um valor de p inferior a 0,05 como estatisticamente significativo.

Considerações Éticas:

Devido à utilização de dados anonimizados provenientes de um banco de dados público, não foi necessária a obtenção de aprovação.

4. RESULTADOS

Os resultados serão apresentados em formatos de artigos.

4.1. Artigos publicados nas revistas *International journal of gynaecology and obstetrics* e *The Lancet Global Health*.

4.1.1. *International journal of gynaecology and obstetrics*

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Obstetrics

The SARS-CoV-2 pandemic scenario in Africa: What should be done to address the needs of pregnant women?

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The SARS-Cov-2 pandemic scenario in Africa - What should be done to address pregnant women needs?

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The SARS-Cov-2 (COVID-19) virus causes an infectious and multisystem disease first diagnosed in China in December 2019 (1). Having evolved rapidly with an exponential

increase in the number of cases and deaths worldwide, COVID-19 was declared a pandemic by the WHO in mid-March 2020. Although in most Sub-Saharan African countries the pandemic is in its initial phase, as of 18 August 2020, the cumulative total cases of COVID-19 in the African Region exceeded one million and it is now at 1 136 405 confirmed cases with 26 304 deaths (2).

Over the same period, about 5.1% of cases (1 136 405 cases) and 3.3 % (26 304 deaths) have been reported in Africa, of the 22 486 892 diagnosed cases and 789 222 deaths reported worldwide (3, 4). Among African nations, the most affected country was South Africa, followed by Nigeria and Ghana (2).

The advent of the pandemic has exhibited the weaknesses of health systems in different settings, testing capacity and strategy being more evident in low and middle-income countries (LMICs) (5, 6). The growing number of COVID-19 cases has forced many countries to reorganise existing health services and reassign available healthcare professionals to combat COVID-19. In this regard, a number of service delivery points were closed due to the lack of healthcare providers.

In response to the COVID-19 pandemic, many countries enforced lockdown restrictions that closed down schools, businesses, restaurants, markets, religious gatherings, and limited mass gatherings and border entry. The lockdowns in some contexts, led to the disruption or suspension of many essential health services including sexual and reproductive health (SRH) services, thus placing women of reproductive age under conditions of greater vulnerability and at risk of suffering devastating effects from COVID-19 (7-10). Furthermore, the scarce laboratory capacity in various African countries limits testing access and may contribute to underreporting of COVID-19 cases and interfere with the effective implementation of measures to control and prevent the spread of infection by SARS-CoV-2.

Although the pandemic affects individuals of all age groups without distinction of sex, race and socioeconomic status, studies suggested that racial factors and socioeconomic determinants might play an important role in the clinical evolution and prognosis of the disease (11-13).

In LMIC countries, the disruption in SRH services such as family planning, prevention and treatment of sexual transmitted infection (STI), safe abortion services, antenatal and postnatal consultations pose risks to women of reproductive age. The disruptions

were generally associated with low coverage of the health network, weak diagnostic capacity for SARS-CoV-2 detection, shortage of trained healthcare personnel and reduced demand for services in the available health facilities due to stigma and fear of acquiring SARS-COV-2 infection.

This situation has the potential to contribute negatively to the incidence of high risk pregnancy, near miss, maternal and perinatal deaths in these LMIC countries, with the consequent compromise of objective 3.1 of the WHO Sustainable Development Goals, 2030 agenda (14).

In the general population, almost 80% of the COVID-19 cases are asymptomatic or are cases with mild symptoms. Among the elderly, patients with underlining medical conditions are at a higher risk of developing severe disease (15, 16). Conversely, although information on the clinical course of the disease and the consequences on maternal and perinatal health are still scarce, the available evidence shows that the prevalence of COVID-19 in women at childbirth varies from 0.43 to 15.4% (17, 18). In pregnant women, the prevalence of SARS-CoV-2 infection varies significantly according to background characteristics, being more prevalent in black and minority ethnic groups (19).

Initial reports of COVID-19 cases in pregnant and postpartum women indicated that the clinical evolution of SARVS-CoV-2 infection in this group was similar to the general population, and pregnant women were not at high-risk group with a greater chance of progressing to severe conditions of the disease (20, 21). However, the physiological processes inherent to the pregnancy-puerperal cycle, physiological changes in the respiratory and immunological systems, may predispose pregnant women to a high risk of respiratory infections with evolution to the severity condition (22). Moreover, studies showed that other respiratory syndromes, such as, severe acute respiratory syndrome (SARS-CoV) and the Middle East respiratory syndrome (MERS), are associated with high mortality rate, 25 to 30%, in pregnant women (23, 24) high incidence of adverse obstetric events, spontaneous abortion, premature birth and foetal growth restriction (25, 26).

More recently, there is evidence that SARS-CoV-2 infection during pregnancy is associated with an increased risk of perinatal complications, including foetal distress,

premature birth, perinatal death (27, 28) and increased rate of admission to the intensive care unit and need for mechanical ventilation (29, 30).

Pregnant women and puerperal women are then placed at an increased risk for greater severity of the disease and evolution to death with higher mortality rate (about 12.7%) (31), Moreover, the mortality rate in women from LMIC countries is 10-times higher than the mortality rate of women in high-income countries (32, 33).

The risk of maternal and perinatal complications may be increased in pregnant women with underlying medical conditions, black pregnant women, and pregnant women from a disadvantaged social class and, in contexts with limited access to adequate healthcare services for COVID-19 management (34, 35). The high rate of morbidity and mortality may be associated with the inadequate antenatal care, presence and management of underlying medical conditions, racial differences and shortages of intensive care units for management of severe COVID-19 cases (34, 35).

Although, the impact of COVID-19 on pregnant women was considered a secondary priority (36), studies involving pregnant women with respiratory diseases caused by other respiratory viruses in addition to the current data from studies of pregnant women with SARS-CoV-2 infection in middle and high-income countries, highlight the need to pay special attention to this group of women, especially in settings where healthcare services are strained.

While global maternal deaths gradually declined between 2000 and 2017, disparities in patterns of mortality still exist with sub-Saharan Africa region alone accounting for approximately 66% of deaths in the continent (37). Due to the increasing number of reported maternal deaths case related to the COVID-19, mostly from LMIC, and deficiencies in reporting cases in those countries, the need for prospective monitoring of COVID-19 cases in the context of LMIC is needed now more than ever.

As SARS COV-2 is a novel virus, knowledge of its impact on sexual and reproductive health (SRH) is now emerging (38). Therefore, to understand the dynamics of SARS-CoV-2 infection in its broad spectrum in the obstetric population of LMIC countries and to minimize the effects of the pandemic on maternal and perinatal health, it is essential to join forces among African researchers to generate evidence to better elucidate the magnitude of the problem. For this, the adoption of interinstitutional and multinational

strategies is essential to optimize the allocation of scarce resources to fight the pandemic.

In response to the SARS-COV-2 pandemic in sub Saharan Africa, domestic and regional level efforts have been undertaken by various partners in multiple sectors (39, 40). A critical component to complement these strategies is the setting up of multi-centre collaborative networks of African researchers to undertake surveillance studies of conditions related to maternal and neonatal morbidity associated with COVID-19 and interinstitutional support for the creation and implementation of care protocols. The building of a collaborative network to study the impact of COVID-19 on the obstetric population in Africa (African Network for fighting COVID-19 in pregnancy- ANCOVID-19) would enable a broad understanding of the pattern of disease evolution in different countries and different contexts, enabling a better understanding of the role of context-specific determinants in the evolution of infection by SARS-CoV-2.

Likewise, the implementation of robust surveillance systems and support to weaker systems by the stronger partnerships may favour the collection of standardised information on related maternal and perinatal morbidity. Continuous monitoring of the impact of the disease on maternal and perinatal health including strategies for remote monitoring of pregnant women through telephone calls and/or digital tools where available coupled with the sharing of clinical information will contribute to a better understanding of the dynamics of infection in this population and the moment of greatest vulnerability for the maternal and newborn health.

An advantage of ANCOVID-19 would be to enable timely sharing of good practices in handling COVID-19 cases in pregnant and postpartum women through the elaboration of guidelines for screening and treating COVID-19 cases, which will optimize the provided care and rational use of personal protective materials, equipment and resources in general to reduce the spread of the pandemic and its consequences.

Thus, we call on women's health researchers in Africa to join in a continental effort to combat COVID-19 and reduce its impacts on maternal and perinatal health in Africa.

Author contributions

Charles CM and Pacagnella RC had the first insights, Charles CM and Amoah E M proposed the first draft. All other authors contributed equally to the writing and critical review of the manuscript. They also reviewed and approved the final version.

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Conflicts of interest

The authors have no conflicts of interest.

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COVID-19 in pregnancy: evidence from LMICs.

We read with great interest the study by Leonard Mndala and colleagues published in The Lancet Global Health.[1] They report maternal and neonatal outcomes of COVID-19 in 261 pregnant and recently pregnant women (up to 42 days post-delivery) in Malawi during the omicron wave, compared with the preceding waves of beta and delta SARS-CoV-2 variants. The authors found that a severe maternal outcome and maternal death were less common during the omicron wave than during the beta and delta waves (p≤0·05). Shortness of breath was the only symptom associated with poor maternal outcomes (p<0·0001), and was less commonly reported in the omicron wave than in the beta and delta waves (p<0·001). There is an urgency to acknowledge that data regarding the burden of COVID-19 on maternal and perinatal outcomes in sub-Saharan Africa and other areas in low-income and middle-income countries (LMICs) are under-represented in the medical literature.

Structured surveillance systems on health outcomes allow for a fast response and uptake of data to support policymakers, and these are mostly implemented in high-income settings. For example, during the early period of the pandemic, the US Centers for Disease Control and Prevention reported increased morbidity with hospitalisation, intensive care unit (ICU) admissions, and mechanical ventilation among pregnant or postpartum women, but not increased mortality (adjusted odds ratio 0·9 [95% CI 0·5–1·5]).[2] As the pandemic evolved, data showed that symptomatic pregnant and post-partum women with confirmed SARS-CoV-2 infection were at greater risk of ICU admission (3·0 [2·6–3·4]), extracorporeal membrane oxygenation (2·4 [1·5–4·0]), and death (1·7 [1·2–2·4]), than were their non-pregnant counterparts.[3] Moreover, data from a living systematic review, including 435 studies, also reported greater risk of severe maternal morbidity (invasive ventilation: odds ratio 2·41 [2·13 to 2·71]), mortality (6·09 [1·82 to 20·38]), stillbirth (1·81 [1·38 to 2·37]) and neonatal death (2·35 [1·16 to 4·76]) than did non-pregnant women with SARS- CoV-2 infection.[4] Most of the included studies were from high-income countries.

Health emergencies are known to shed light on underlying weaknesses in the health system, worsening delays in medical care and revealing inequities within a population. Most countries in sub-Saharan Africa and other LMICs have ineffective epidemiological surveillance systems and, therefore, are underrepresented when considering the

impact of a pandemic on maternal and perinatal health. Even when surveillance is adequately implemented, it rarely translates into timely public health interventions. Brazil, for example—with reliable data from the national surveillance system on severe respiratory syndrome—reported clear inequities and delays in medical care during the COVID-19 pandemic, given that 22·6% of women died without having been admitted to an ICU and 14·6% without ventilatory support early in the pandemic.[5]

Mndala and colleagues' analyses were made possible by the previously implemented national maternal surveillance platform in Malawi (MATSurvey). Another multi-institutional effort in Latin America was the use of the Perinatal Information System (SIP) from the Latin American Center for Perinatology, Women and Reproductive Health, which allowed the uptake of regional data on eight countries, presenting 447 maternal deaths.[6] In keeping with the MATSurvery data, dyspnoea was the most frequent symptom at admission, and was present in 73% of women who died.

Other research initiatives in LMICs implemented before the COVID-19 pandemic also enabled the quick organisation of data collection. In Brazil, the Network of Studies on Reproductive and Perinatal Health, which was implemented over 10 years ago initially for the surveillance of maternal morbidity, provided baseline data for the multicentre REBRACO study (named to denote the Brazilian network of COVID-19 during pregnancy). Data from REBRACO showed that the availability of tests for SARS-CoV-2 and outcomes varied throughout the first year of the pandemic (before the dominance of gamma as a variant-of-concern), with worse outcomes in the initial 4 months.[7] This finding is certainly true for other settings in LMICs. REBRACO joined an ongoing initiative of WHO to use a generic protocol for the reporting of findings on COVID-19 during pregnancy, including in several LMICs in Africa, Latin America, and Asia, with an expected sample size of more than 20 000 women.[8]

The findings reported by Mndala and colleagues, regardless of the small sample size of 261 women, include 28 health-care facilities and contribute substantially to elucidating the burden of different SARS-CoV-2 variants and variants-of-concern on maternal and perinatal outcomes. Most notably, by comparing the dominant time periods of different variants-of-concern, they showed that omicron was associated with better maternal and perinatal outcomes. These findings are similar to those of other studies.[10] There is great disparity in vaccine coverage, especially among countries in Africa, with scarce data available during pregnancy. Overall vaccine coverage varies

from the 3·2% reported in Malawi and 4·6% in Nigeria, to 11·6% in Zambia and 30·0% in South Africa, considering data up to March, 2022. Data from Brazil, in the same period, showed that 40·3% of pregnant and postpartum women were fully vaccinated; among these women, those with COVID-19 infection had a 50% reduction in dyspnoea and ICU admission and an 80% reduction in intubation and maternal mortality when compared with their unvaccinated counterparts.[9] Therefore, there is evidence that vaccination reduces severe outcomes.

The global progress in reducing maternal mortality in the past two decades is notable; however, the 2030 Sustainable Development Goal 3.1 target is far from being achieved, especially in LMICs. The COVID-19 pandemic has aggravated such numbers, drawing attention towards the challenge of prioritising health care. To implement measures to avoid preventable mortality in under-resourced settings, we need the data and we need action.

We declare no competing interests.

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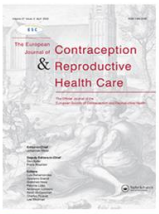

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Comparison of contraceptive sales before and during the COVID-19 pandemic in Brazil

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Comparison of contraceptive sales before and after the SARS-CoV-2 pandemic in Brazil

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Synopsis:

The sales of monthly contraceptive methods had a non-significant variation in 2020 compared to 2019, despite the enormous strain on the Brazilian health system.

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Abstract

Objective: to assess the impact of the COVID-19 pandemic on the sales of modern contraceptive methods in Brazil. **Methods:** We analysed monthly data of short-acting, long-acting reversible contraceptives (LARCs; implants and intrauterine devices [IUD]), and COVID-19 related deaths. We categorised the sales in: i) emergency contraceptive (EC), ii) oral contraceptives, rings and patches, iii) injectable contraceptives, iv) LARC methods, including copper-IUD, and v) LARC methods, except Cu-IUDs. **Results:** Contraceptives sales had a non-significant increase in the year 2020 compared to the year 2019, and the annual average ranged from 12·8 to 13·0 million units/month. We observed an increase in the sales of injectable contraceptives for the February-May/2020 and EC pills for the June-July/2020 and a non-significant variation for pills, patches and rings. The hormonal-IUD/ENG-implant had three patterns: a decrease in sales between February-April, which coincides with the closure of family planning services; an increment of sales since April, which coincide with the first COVID-19 related deaths and an important increment of sales since July/2020. **Conclusions:** The COVID-19 pandemic has disrupted the Brazilian healthcare system and due to the fact that many family planning clinics were closed, the sales of most of the modern contraceptives fall over the year 2020; however, the increment of sales of the LNG-IUD/ENG-implant at private sector indicated the inequity in access of contraception.

Key words: SARS-CoV-2; COVID-19; contraceptive methods; LARCs; SARCs, Brazil; unplanned pregnancy.

1 Background

The SARS-CoV-2 (COVID-19) pandemic has a high transmission rate and poses a health risk to the general population, including women of reproductive age.1 Globally, as of 5 July 2021, more than 184 million cases have been reported. In Brazil, the first case of COVID-19 was detected on 26 February 2020, and it was one of the most severely affected countries, with more than 18·8 million COVID-19 cases and more than 525,112 deaths reported as early July 2021.2 The drama of COVID-19 in Brazil may be due to the emergence of strains with potentially higher transmissibility and inefficient and counterproductive political-administrative decisions.3-5

As might be expected, COVID-19 has placed an enormous strain and burden on health systems between and within countries, with Brazil not being an exception.6 In Brazil, 74% of the population depends on the National Health Service (Sistema Único de Saúde, SUS) as the main source for medical care, including the provision of contraceptive methods at no cost. Brazil has restrictive laws for abortion, being permitted only in a few circumstances (pregnancy as result of rape or violation or severely affected foetus – anencephaly, and pregnancy life-threatening conditions), and there are important barriers to accessing contraceptive methods, especially in the low-income portion of the population. During the COVID-19 pandemic, the health care system was severely disrupted nationwide, and the fragility of the public health system became more evident.7, 8

The pandemic poses a challenge for many women to achieve sexual and reproductive health (SRH) needs, because many services were closed for several reasons. On one hand, many authorities considered these services as non-essential, high number of deaths were reported among health care professionals,9 many of them were reallocated to attend COVID-19 cases and others were exhausted and resigned.10 All these situations impaired the health care system, including SRH services. The deleterious effects are more evident in the low- and middle-income countries (LMICs),11 and among the low-income portion of the population.12

Although equitable and safe access to contraception was declared a human right five decades ago, the provision of contraception (68%) and antenatal care (56%) were the most frequently disrupted services, to some extent, due to the pandemic,13 undermining women rights and SRH services. Moreover, this put women at

reproductive age under the vulnerability of suffering from the direct and indirect effects of COVID-19.14-16

The disruption of many SRH services resulted in lack of access to modern contraceptive methods, mainly long-acting reversible contraceptives (LARCs) with the potential of the increment of unplanned pregnancies.17, 18 It was estimated that, in LMICs, a 10 percentage points reduction in the supply of SRH services (for instance, short-acting reversible contraceptives [SARCs], LARCs and safe abortion services) for a year would result in approximately 48·5 million women with an unmet need for contraceptive methods and therefore 15·4 million unplanned pregnancies and an additional 3·3 million unsafe abortions.19, 20 These certainly lead to increased maternal morbidity and mortality in a fragile region of the world.

Implementing measures to avert the disruption of SRH services, including provision of contraception, is essential for preventing women from suffering other devastating effects of the COVID-19 pandemic, preventing drawbacks on the significant improvement achieved in maternal and perinatal health worldwide over the past two decades.21 We considered the provision of modern contraceptive methods as an essential activity in times of the COVID-19 pandemic. However, there is a paucity of data in this regards, and consequently, our objective was to assess the sales of modern contraceptive methods before (year 2019) and during the COVID-19 pandemic (year 2020) in Brazil.

2 Materials and Methods

We conducted a data-driven audit and descriptive analysis of the sales of modern contraceptive methods in Brazil. Our study was conducted at the Department of Obstetrics and Gynaecology, University of Campinas, School of Medical Sciences, Campinas, SP, Brazil. We collected and analysed the sales data of contraceptive methods to public and private health sectors from an audit company based in Brazil (IQVIA–PMB) regarding SARC methods and from the manufacturers (or representatives) of LARC methods, including the copper-intrauterine device (Cu-IUD, Optima®, Injeflex, São Paulo, Brazil); the two available levonorgestrel-intrauterine devices in the country (LNG-IUDs; Mirena® and Kyleena®, Bayer Oy, Turku, Finland); and etonorgestrel (ENG)-subdermal implant (Implanon NXT, MSD, Oss, The

Netherland), from January 2019 to December 2020. We assessed the sales of contraceptive methods as a proxy of the use of contraceptives.

Data regarding contraceptive methods were categorised into five groups: i) 1·5 mg LNG emergency contraceptive (EC) pills, ii) combined oral contraceptives (COC), progestin-only pills (POP), vaginal rings, and transdermal patches; iii) injectable contraceptives, including once-a-month and depot medroxyprogesterone acetate (DMPA); iv) LARCs, including Cu-IUDs; and v) LARCs without the inclusion of Cu-IUDs. We used this categorization of LARCs because the LNG-IUD and ENG-implant were not available in the public sector, with few exceptions such as some teaching hospitals and restricted access.

The monthly average sales of each group of contraceptives in the year 2019 were compared to the same period in 2020, and we also calculated the monthly percentage of variation for the sales of each group of contraceptives. We considered the variation of 5 percentage points or more on the monthly contraceptive sales for the same period for 2019 and 2020 as significant. The establishment of 5% as the cut-off for significant variation was based on the COVID-19 pandemic context in Brazil. In addition, we obtained the monthly number of deaths caused by COVID-19. This information was extracted from the Brazilian Ministry of Health database.22

3 Results

We estimated that we audited nearly 95% of the sales of contraceptives, including SARCs and LARCs both in the public and private sectors, except for the ENG implant and the two LNG-IUDs available in Brazil, of which the sales were almost totally in the private sector. Overall, the sales of the contraceptive methods had a non-significant increase in the year 2020 when compared to the year 2019, with the annual average ranging from 12·8 to 13·0 million units/month. The high number of sales corresponding to COCs, POPs, transdermal patches, and vaginal rings represented 68·6% of total sales (8·8 to 8·9 million cycles/units/month), followed by EC pills representing 17·4% (26·6 to 27·5 million units/month) of total sales and injectables representing 13·6% (20·4 to 21·8 million injections/month) of total sales. Lastly, the sales of LARC methods (excluding Cu-IUDs) represented 0·4% (32,000 to 77,000 units/month) of total sales.

When analysing individual groups of contraceptives, we found different patterns. When comparing the sales of injectable contraceptives, we observed a significant increase in the sales for the February-May/2020 (~16% median variation) and EC pills for the June-July/2020 (~12% median variation) and a non-significant variation for COCs, POPs, transdermal patches, and vaginal rings. Furthermore, we observed an important increment (9·3 times) in the sales of the Cu-IUDs due to a bulk purchase of 550,000 units by the Ministry of Health for the public sector in the opposite direction for the year 2019 when they did not acquire any units. This pattern for Cu-IUDs, however, does not reflect use, as the sales aimed to replenish the national stock (Figure 1).

Comparing the sales of the ENG implant and the LNG-IUD we observed three patterns of variation. The first pattern was a decrease in sales between February and April 2020, which coincides with the first case of COVID-19 in Brazil; the second pattern was an increment of sales since April 2020, which coincides with the first COVID-19 related deaths; and the third pattern was an important increment in sales since July 2020, which was in accordance with the increasing number of deaths from COVID-19 (Table 1). Figure 2 shows the monthly sales of contraceptive methods and COVID-19 related deaths.

4 Discussion

During the COVID-19 pandemic, the audited data showed that the overall sales of contraceptives had no significant variation; however, EC and ENG-implant/LNG-IUD sales showed important variation during the period. Our findings suggested a fragility of the supply chain for contraceptives. Although there is a wide diversity of reversible contraceptive methods in Brazil, their large use is restricted to COCs, 23 and the absence of significant variation in sales in total contraceptives could be due to the lack in the variation of COC sales.

In Brazil, many contraceptives are available over the counter despite the label approved by the Health Authority, which establish that a prescription is needed. Due to the fact that many SRH public services were closed, including contraceptive provision, we speculate that many women who are habitually served by the National Health System and have the right to receive the contraceptives at no cost; instead, they need for the acquisition of contraceptives directly from the pharmacies.

Another observation was the increment of sales of the LNG 1·5 mg EC pill, which is the only one available in Brazil. This increment could be indicative of the difficulties of women obtaining contraceptives from the health care network or the lack of resources to acquire other contraceptives from the network of private pharmacies. This was also observed at the time of the Zika virus epidemic in Brazil, when the sales of contraceptives were not substantially modified, despite the recommendation from the Health Authority for women to avoid pregnancy. 24

The sales of LARC methods remained low (0·4%), suggesting that the vast majority of women use less effective contraceptive methods, 24 albeit the Cu-IUD is available in the public sector at no cost; but with low prevalence as 1·9% in women aged 15-49 years old. 23 However, the findings of a fall of the sales of the ENG-implant and the two available LNG-IUDs at the beginning of the COVID-19 pandemic could indicate that many women were afraid to visit private offices to insert these methods. However, after this initial fall, the sales presented an increment, which could also indicate that, after the initial impact suffered by many women that refrained from visiting doctors, they came and required implant and LNG-IUD placement. It is important to recall that, in the first months after the COVID-19 pandemic, there are doubts about the possibility of vertical transmission of SARS-CoV-2. 25, 26 Recently, the Brazilian Ministry of Health recommended women avoid becoming pregnancy during the COVID-19 pandemic. 27

We cannot ignore that, if the ENG implant and LNG-IUD are only available in the private sector, the increment of use represented an inequity for most of the population, including those from the low-income portion of society who are unable to fulfil their SRH needs. Our findings are in accordance with previous publications, reporting that LARC methods are almost exclusively available in the private sector and limited in the public sector (except for the Cu-IUD), where the most vulnerable women received attention. 28 Our data was also similar to a previous study showing that the high prevalence of use of modern contraceptives is associated mainly with SARC methods,29 despite the well documented information that LARC methods have low contraceptive failure, are safe, are independent of user compliance after device insertion, are cost-effective, have high continuation rates and are oestrogen-free. 28, 30

The bulk purchase of Cu-IUDs by the Ministry of Health only for the public sector is an action that needs some clarification, despite the fact that it is a commendable action. However, it may not reflect the government initiative to mitigate the effects of COVID-19 on women´s SRH services as the purchase did not occur in 2019 and was aimed to replenish national stock. The COVID-19 pandemic and the lack of strategies to mitigate its consequences from the Brazilian government has increased barriers to accessing family planning clinics and contraceptive methods, especially in the public sector. 12

Usually in Brazil, there are many barriers to IUD use, including lack of training of health care providers, misinformation and myths from health care providers and potential users and contraceptive services centred on doctors rather than on other cadres.31 Fear of women being contaminated with the virus is another barrier to access.32 Moreover, Brazil has more than 5,000 municipalities with thousands of basic health posts distributed in the country. Consequently, the acquisition of IUDs is not equal to their distribution and insertion, and we cannot be sure if they were delivered to those who needed them.

The main limitation of our study was that we did not take into account the sales of condoms; however, the main strength is that, to the best of our knowledge, this is the first study that audited contraceptive sales in one of the countries most devastated by the COVID-19 pandemic, and we are able to audit almost 95% of the contraceptive sales both for the public and private sectors. This information could be important to address women´s contraception needs in a country with severe disruption of SRH services.

Even in situations of enormous pressure on the health care system, the COVID-19 pandemic response must include plans to guarantee women access to appropriate SRH services with quality, including equitable and timely access to contraceptives to avoid unplanned pregnancy, in a situation in which there are still now doubts about vertical transmission of SARS-CoV-2. Brazil’s SRH services were not prepared for the pandemic impact. The sales of contraceptives, although did not present significant variation compared to pre-pandemic data, showed insights of inequity in access with the increasing sales of EC and LNG-IUD and ENG-implant.

In conclusion, the COVID-19 pandemic has disrupted the Brazilian healthcare system and due to the fact that many family planning clinics were closed, the sales of most of the modern contraceptives fall over the year 2020; however, the increment of sales of the LNG-IUD/ENG-implant at private sector indicated the inequity in access of contraception.

Author contributions

CMC, LB and RCP designed the study. CMC and AM collected data. All authors participated equally in data analysis and interpretation. RCP wrote the first version of the manuscript. All the authors read and approved the final version of the manuscript.

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Conflicts of interest

LB received honoraria as lecturer from Bayer Healthcare and MSD. The other authors declared no conflict of interest.

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Table 1. Monthly sales variation of modern contraceptive methods in Brazil. Comparison every month of year 2020 with year 2019.

Figure 1. Monthly sales variation (in percentage) of modern contraceptive methods in Brazil. Monthly comparison (2020/2019)

EC: Emergency contraceptive pills; COC: Combined oral contraceptives; P-only: progestin-only contraceptives; LNG IUS: levonorgestrel-intrauterine system

Figure 2. Monthly sales of modern contraceptive methods in Brazil [January 2019/December 2020] and Brazil's COVID-19 related deaths [April 2020/December 2020]

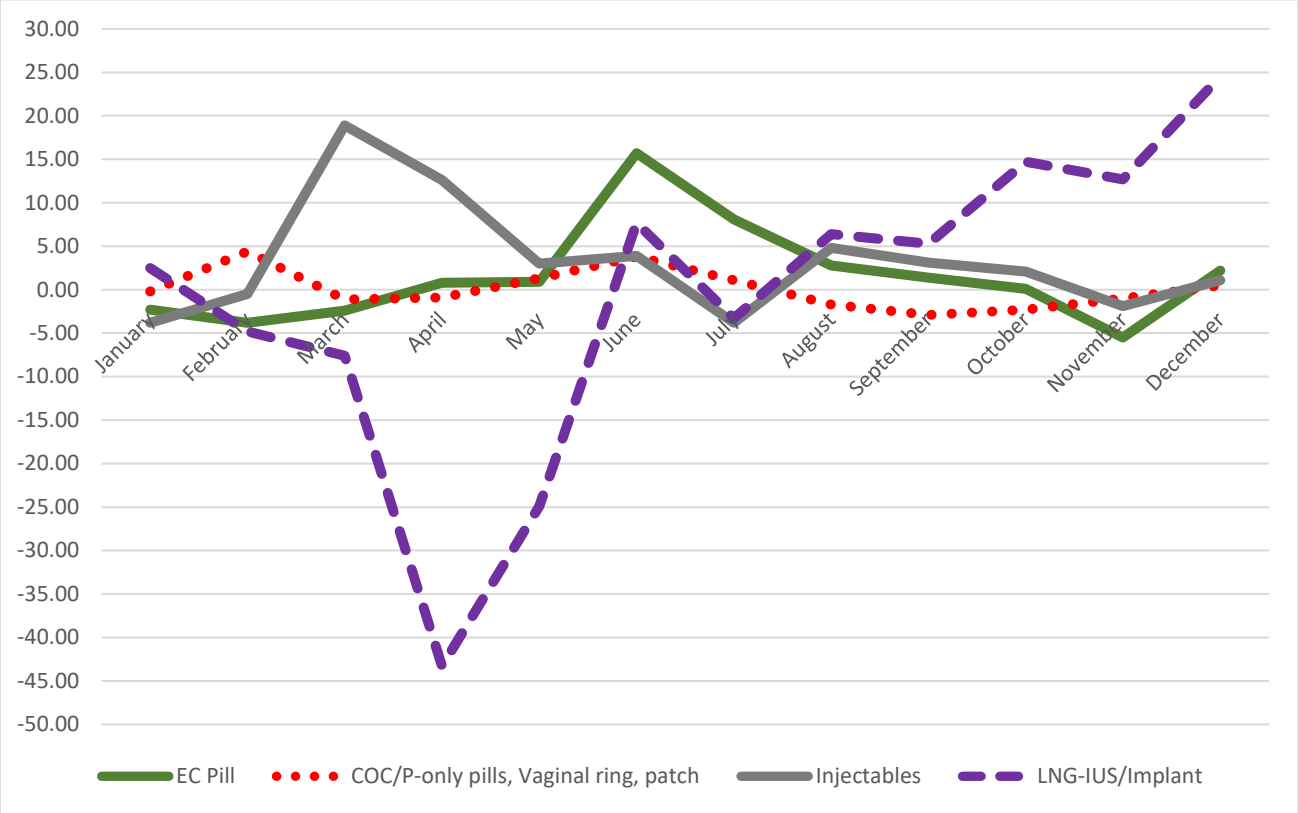
Legend: *(x10); PPR: pills, patch vaginal ring; Black vertical bar: first reported case of COVID-19 in Brazil (February 26 2020); Blue vertical bar: first reported related-death of COVID-19 in Brazil (March 17 2020)

Table 1. Monthly sales variation of modern contraceptive methods in Brazil. Comparison every month of year 2020 with year 2019.

Months	Variation in % from year 2020 in comparison to year 2019			
	EC Pill	**COC/P-only pills, Vaginal ring, patch**	**Injectables**	**LNG IUS/Implant**
January	-2.3	-0.2	-3.8	2.5
February	-3.8	4.4	-0.5	-4.8
March	-2.4	-1.1	18.9	-7.6
April	0.8	-0.9	12.6	-43.3
May	0.9	1.3	3.0	-24.9
June	15.7	3.8	3.9	7.7
July	8.1	1.1	-3.8	-3.3
August	2.8	-1.7	4.8	6.4
September	1.4	-2.9	3.1	5.3
October	0.1	-2.3	2.1	14.7
November	-5.5	-1.0	-1.9	12.7
December	2.2	0.5	1.1	24.5

EC pill: emergency contraceptive pills; COC: combined oral contraceptives; POP: progestin-only pills; LNG-IUS: Levonorgestrel- intrauterine system.

Figure 1. Monthly sales variation (in percentage) of modern contraceptive methods in Brazil. Monthly comparison (2020/2019)



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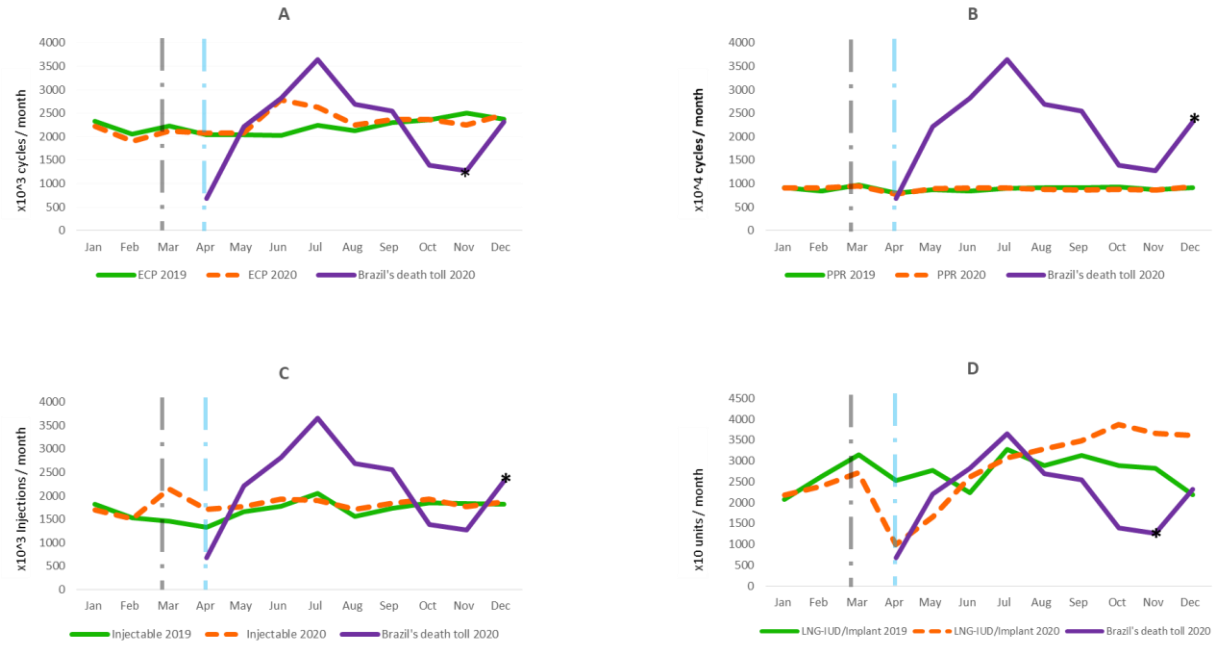

Legend: *(x10); PPR: pills, patch vaginal ring; Black vertical bar: first reported case of COVID-19 in Brazil (26th February 2020); Blue vertical bar: first reported related-death of COVID-19 in Brazil (17 March 2020).

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CLINICAL ARTICLE
Obstetrics

Risk factors related to the SARS-CoV-2 vaccine additional doses hesitancy among pregnant and non-pregnant people of reproductive age and partners: A Brazilian cross-sectional study

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Risk factors related to the SARS-CoV-2 vaccine additional doses hesitancy among pregnant and non-pregnant people of reproductive age and partners: A Brazilian cross-sectional study.

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Synopsis: Pregnant people are more hesitant about COVID-19 vaccine uptake compared to their counterparts, with social determinants and vaccine safety concerns being the key barriers.

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Abstract

Objective: To assess the predictors of acceptance and hesitancy of additional doses of any SARS-CoV-2 (COVID-19) vaccine among pregnant or recently pregnant and non-pregnant people of reproductive age and partners in Brazil. **Methods:** We conducted an online cross-sectional study from June 2022 to April 2023 and invited women and partners between 18 and 49 years old to participate. We employed a snowball strategy to reach all potential eligible participants. Our primary outcome was the acceptance rate of the COVID-19 booster vaccine. We estimated the frequency and percentage for the three groups and compared categorical variables using the Chi-square test. Moreover, bivariate, backward stepwise regression, and subgroup analyses were performed to evaluate risk factors and predictors of COVID-19 vaccine booster hesitancy. We reported the effect size as OR with a 95% CI. **Results:** We included 1,487 participants, and among them, 334 (22.5%) were pregnant or recently pregnant people, 905 (60.8%) were non-pregnant people, and 247 (16.6%) were male partners. Pregnant and recently pregnant people showed greater hesitancy for the COVID-19 vaccine booster than non-pregnant people (28% vs 15%, p<0.001) and male partners (28% vs 16%, p<0.001). Non-pregnant women accepted the COVID-19 vaccine more often than pregnant or recently pregnant people (OR 1.75; 95% CI 1.13 – 2.70). The associated factors to the reduced COVID-19 vaccine booster acceptance were family income between US$ 566 – 945.00 (54%), evangelic religion (65%), concern about vaccine safety (80%) and perceived common vaccine importance (93%). **Conclusion:** Pregnant people were more hesitant than non-pregnant people to accept the COVID-19 boost vaccine. Family income, religious beliefs, vaccine safety concerns, and perceived common vaccine importance were significant barriers to accepting COVID-19 booster vaccines. The impact of these factors was more evident among pregnant or recently pregnant people, emphasizing the harmful effect of misinformation among this vulnerable population.

Keywords: COVID-19; non-pregnant people; predictors; pregnant people; vaccine acceptance; vaccine hesitancy.

Introduction

The SARS-CoV-2 (COVID-19) pandemic has severely affected the health system and individual routines. Brazil was one of the most severely affected countries, with a higher COVID-19-related maternal mortality compared to Mexico and South Africa. [1-3] To control the COVID-19 pandemic, prevent the health system from overburdening, and reduce morbidity and mortality, various effective non-pharmaceutical interventions (NPIs) have been implemented worldwide, tailored to specific context and based on evidence. [4, 5] However, implementing these strategies was inequitable between and within countries; in some contexts, the high hesitancy hampered the NPIs' compliance. [6] In addition, the effect of NPIs on non-communicable and high-burden diseases becomes evident. [6, 7]

The introduction of the COVID-19 vaccine was a window of opportunity in tackling the pandemic. After a period of pregnant people's underrepresentation in both the COVID-19 treatments and vaccine clinical trials and the lack of scientific evidence, the World Health Organization (WHO) and other health authorities recommended the vaccine to pregnant people. [8, 9] In Brazil, vaccination against COVID-19 began on 17th January 2021. Nevertheless, the conspiracy theories, misinformation, and uncoordinated actions, in many cases supported by the federal government, hindered the vaccine rollout and the reduction of preventable COVID-19-related mortality and morbidity. [10] Moreover, the pseudo-scientific vaccine rumours cast doubts on vaccine safety and efficacy and enabled vaccine hesitancy. [11, 12] Data suggested that it is challenging to debunk science-relevant misinformation. [13]

We refer to vaccine hesitancy as the delay in accepting or refusing vaccination despite the availability of vaccines. [14] According to the WHO, vaccine hesitancy is a multifaceted and context-sensitive phenomenon that poses a considerable threat to global health. [15] Brazil has a history of well-implemented nationwide vaccination; however, the COVID-19 vaccination was influenced by misinformation and political misleading. Despite the initial slow COVID-19 vaccine rollout, the country had a high rate of COVID-19 vaccination coverage; as of 5th June 2023, the vaccination coverage was 80.6% (complete primary series), and 51.9% of the population had additional doses. [16] This data suggested that a well-implemented vaccination strategy in a context with a robust national immunization program may overcome crucial vaccine barriers. [17, 18]

Vaccine coverage and acceptancy vary globally, and the pivotal reasons differ from one vaccine's low access to vaccine hesitancy-related factors. [19] Initial data on vaccine acceptance suggested a lower vaccination willingness among pregnant people (52%) compared to non-pregnant people (73%). [20] For pregnant people, the vaccine uptake ranged from 27.5% to 49%; predictors of vaccine uptake were age, ethnicity, trust in COVID-19 vaccines, low level of education, and the fear of severe COVID-19 during pregnancy. [21, 22] Moreover, the conflicting message provided to pregnant people and the initial paradox exclusion of pregnant people from COVID-19 trials halt the COVID-19 vaccine uptake among these vulnerable populations. [23] Nevertheless, healthcare providers and community leaders may leverage vaccine acceptance. [24, 25]

There is growing evidence of the completion of the COVID-19 vaccine primary series; however, the evolution of SARS-CoV-2 remains uncertain and vaccine-induced immunity is crucial for controlling its transmissibility. Brazil is one of the countries most severely affected by the COVID-19 pandemic and the pregnant people vulnerability reinforces the importance of understanding the factors influencing vaccine hesitancy among these group. Therefore, our study aimed to assess the predictors of COVID-19 vaccine acceptance and hesitancy of additional doses among people of reproductive age (pregnant or recently pregnant people and non-pregnant people) and partners in Brazil.

Methods

Study design and procedures

We conducted an online survey from June 2022 to April 2023, including 18-49-year-old pregnant, recently pregnant, and non-pregnant people and partners. We excluded potential participants who disagreed with the online informed consent, lived outside the Brazilian territory, and did not complete the questionnaire (less than 50% of responses). Following the ethical approval and data protection policy, the online survey was implemented using the REDCap system. [26]

All potential eligible participants were reached using a snowball, non-probabilistic sampling process. [27, 28] The initial recruitment process was via QR code on Flayer, made available at outpatient clinics (antenatal care, gynaecology, and oncology) from the Women's Hospital “Professor Doutor José Aristodemo Pinotti”, CAISM, University

of Campinas, Campinas, SP, Brazil. At the end of the questionnaire response, the participants were encouraged to share the link with their social network. Moreover, we advertised the study via an institutional social media platform to reach potential participants.

The structured specific questionnaire encompassed sociodemographic, obstetric history, previous influenza vaccination, vaccine and COVID-19 knowledge, COVID-19 infection and disease severity, vaccine access and acceptance, reason for vaccination and non-vaccination, beliefs toward COVID-19 vaccination, COVID-19 and vaccine source of information, and the Government's Vaccine Action Plan. In addition, the questionnaire included variables that explored underlying medical conditions, religion, and non-vaccination regret. We used the 5-point Likert scale to collect data regarding knowledge and perception of the COVID-19 vaccine. The questionnaire comprised 60 questions, and the estimated response time was at least 15 minutes.

All data forms were redirected to the REDCap database hosted at the University of Campinas, and twice a week, the research team accessed the data quality, checking the data inconsistency and duplicity.

The primary outcome was the acceptance of the COVID-19 booster vaccine. The secondary outcomes were the COVID-19 vaccine primary series uptake frequency, and non-vaccination regret prevalence among pregnant or recently pregnant, non-pregnant people and partners. [14]

At the time of the study implementation, scarce data addressed the theme; therefore, we intentionally estimated a sample size of 1,500 participants. However, a post hoc power analysis suggested a 92.2% and 99.8% study power for the sample size, considering alpha 5%, the COVID-19 vaccine booster hesitance of 28%, 15%, and 16%, for pregnant or recently pregnant, non-pregnant people, and partners, respectively. [29]

Statistical analysis

We estimated the frequency and percentage for the three groups. For numerical variables, we have reported the mean and standard deviation. We used the Chi-square test, or Fisher exact test (if necessary), to compare categorical variables. We summed the variables COVID-19 and vaccine knowledge and perception as a dichotomy

response (Completely agree and agree = 1; completely disagree, disagree and neutral = 0). We used bivariate analysis to assess the potential risk factors for COVID-19 vaccine boost acceptance among the three groups.

Moreover, we used the bivariate analysis to compare the risk of vaccine primary series hesitancy and non-vaccination regret between pregnant or recently pregnant people versus non-pregnant people and partners. For the multivariate analysis, we used the backward stepwise predictor selection criteria. The initial predictors for the regression model were selected from bivariate analysis and were based on the p-value cut-off of 10%.

We conducted a subgroup analysis to explore the predictors of COVID-19 booster acceptancy for pregnant or recently pregnant people, non-pregnant people, and partners. We reported the effect size as odds ratio (OR) and confidence interval (95% CI). We considered significant a p-value <0.05. All analyses were conducted using the R studio (version 4.3.1).

Ethics declarations

The Ethical Committee of the University of Campinas approved the study protocol, and all the participants signed an online informed consent (Letters of Approval numbers: 5.435.831).

Results

We included 1,487 participants; 334 (22.5%) were pregnant or recently pregnant people, 905 (60.8%) were non-pregnant people, and 247 (16.6%) were partners **(Figure 1)**. The (mean ± SD) age was 31± 6.1, 34± 8.3, and 41± 12.5 for pregnant or recently pregnant people, non-pregnant people and partners, respectively. Almost one-third, 527 (35.5%) of participants were non-white, 1011 (68.4%) attained at least 12 years of schooling, and 624 (43.5%) were aged 35 years or older. The prevalence of COVID-19 infection was higher among non-pregnant people compared to pregnant or recently pregnant people and their partners, 511 (57%), 152 (46%), and 107 (44%), respectively, **Table 1** and **Table 2**.

Underlying medical conditions were more frequent among pregnant or recently pregnant people 148 (44%). Pregnant and recently pregnant people had a higher

hesitancy for the COVID-19 vaccine booster (p<0.001) than non-pregnant people and partners, with hesitancy rates of 90 (28%), 132 (15%), 38 (16%), respectively. The same pattern was observed in the COVID-19 vaccine primary series hesitancy among pregnant or recently pregnant people compared to non-pregnant *(*p<0.001), with hesitancy rates of 14 (4.2%) and 11 (1.2%), respectively. However, the difference between the pregnant or recently pregnant person and partner was a non-significant (p=0.164), the hesitancy rate was 14 (4.2%) and 5 (2.1%), respectively, **Table 2, Figures S1 and S2**.

The primary reported reasons for not being vaccinated and for the COVID-19 vaccine booster hesitancy were concern about the vaccine side effects 46 (18%) and vaccine efficacy 39 (15%). Regarding the perception of the COVID-19 vaccine rollout, most participants 728 (52%) were unsatisfied with the Government's Vaccine Action Plan. Almost one-third 510 (36%) were concerned about the vaccine's adverse effects and 558 (40%) about the short period of the vaccine development. However, eight out of ten participants said the vaccine was safe 1233 (80%) and would protect pregnant and recently pregnant people 1181(84%), **Figure 2**.

Factors associated with COVID-19 booster acceptancy

Being non-pregnant people was an independent predictor of higher acceptance of the COVID-19 vaccine than pregnant or recently pregnant people (OR: 1.75; 95% CI 1.13-2.70). A similar pattern was observed among parous people (OR: 2.57; 95%CI 1.26 – 5.48), for participants who believed the vaccine was important for their health (OR: 4.25; 95%CI 2.78 – 6.51), and for their relatives' protection (OR: 2.55; 95%CI 1.73 – 3.78). Family monthly income between US$ 566 – 945.00, evangelic religion, vaccine safety concern, and perceived common vaccine importance were associated with lower COVID-19 vaccine booster acceptance, 54%, 65%, 80%, and 93% reduction, respectively, **Figure 3**.

Pregnant or recently pregnant people

The social predictors of lower acceptance (reduction of 48% to 67%) of COVID-19 vaccine booster were being evangelic (OR: 0.52; 95%CI 0.29 – 0.90), religious beliefs not aligned with the COVID-19 uptake (OR: 0.33; 95%CI 0.17 – 0.63), and COVID-19 mandatory vaccination police (OR: 0.47; 95%CI 0.25 – 0.90), **Table 3**. Moreover, have concerns regarding the COVID-19 vaccine efficacy (OR: 0.47; 95%CI 0.26 – 0.87),

safety (OR: 0.19; 95%CI 0.11 – 0.32), perceived common vaccine importance (OR: 0.02; 95%CI 0.01 – 0.09), and limited COVID-19 vaccine knowledge (OR: 0.36; 95%CI 0.19 – 0.67) were related with a higher significant COVID-19 vaccine booster hesitancy, **Table 3**.

The factors related to higher COVID-19 vaccine booster uptake were vaccine importance (OR: 4.58, 95%CI 2.60 - 8.16), getting COVID-19 vaccine from health care providers (1.92, 95%CI 1.12-3.39), the availability of COVID-19 and vaccine information (OR: 1.92, 95%CI 1.10 – 3.33), **Table 3**.

We explored the anticipated regret about non-COVID-19 uptake, and pregnant or recently pregnant people felt less regret of getting severe COVID-19 disease (or had severe outcome) if unvaccinated 18 (5.5%) compared to non-pregnant people 20 (2.4%), $p < 0.008$. There was a non-significant difference between pregnant people or recently pregnant people 18 (5.5%) and partners 10 (4.1%), $p < 0.467$, **Table 2**.

In the multivariate analysis, the evangelical participants have a 64% lower acceptance of COVID-19 vaccine booster (OR: 0.36, 95%CI 0.17 – 0.70). Moreover, the other predictors for higher COVID-19 vaccine booster hesitance were vaccine safety concern (OR: 0.33, 95%CI 0.17 – 0.63) and perceived low vaccine importance (OR: 0.03, 95%CI 0.01 - 0.20). Conversely, the main predictor of higher COVID-19 vaccine booster acceptance was the perceived vaccine importance for themselves (OR: 4.03, 95%CI 1.93 - 8.51), **Table 4**.

Non-pregnant people

The factors related to the lower acceptance of COVID-19 vaccine booster were similar to those observed in pregnant and recently pregnant people. Evangelic participants, religious beliefs not aligned with the COVID-19 vaccine uptake and vaccination mandatory policy were associated with lower vaccine acceptance, 58%, 41% and 55% reduction of vaccine acceptance, respectively, **Table 3**. However, the perceived high importance of vaccination and protection for relatives were the predictors' factors of higher COVID-19 vaccine booster acceptance, four and two-fold, respectively, **Table 4**.

Partners

In the bivariate and multivariate analysis for partners, most of the factors related to the COVID-19 vaccine booster hesitancy were similar to pregnant or recently pregnant people and non-pregnant people, **Table 3 and Table 4.** Being evangelic, religious beliefs against vaccination, and concern about vaccine safety were significantly associated with lower COVID-19 vaccine boost acceptancy, 86%, 79% and 97% reduction, respectively. Conversely, the perceived importance of vaccinating to protect family and friends was strongly associated with the COVID-19 vaccine boost acceptancy, **Table 4**.

Discussion

We found that pregnant or recently pregnant people had low COVID-19 vaccine knowledge and higher hesitancy to get the COVID-19 vaccine (primary series and vaccine booster) compared to non-pregnant people. However, this group was at higher risk of severe disease and worse outcomes.

Implementing public health social measures was crucial to responding to the COVID-19 pandemic and controlling the infection. However, the effect of NPI on mental health and health-care-seeking behaviour for high-burden disease is evident. [6, 30] Therefore, massive immunization and vaccine-derived immunity are essential and long-lasting tools to avert the COVID-19 burden. We found that the three groups of participants had a similar influenza vaccine uptake in the previous years of 2020 and 2021. This finding suggests higher Influenza vaccine coverage compared to the earlier studies. [30, 31] However, the region differences where the studies were implemented may explain these findings. The overall COVID-19 vaccine acceptance (primary series) was 97.5%. Among pregnant or recently pregnant people, the vaccine acceptancy was higher (96%) compared to the findings from other individual studies and systematic reviews. [22, 32]

The heightened concern regarding vaccine safety, perceived common vaccine importance, and perceived low vaccine effectiveness might explain the higher COVID-19 vaccine hesitancy. [33] These findings align with previous studies in which the authors reported associations between gender, knowledge and vaccine acceptance. [34] Moreover, data has highlighted the high COVID-19 vaccine booster hesitance among this high-risk population compared to non-pregnant people. [35] Although the

overall rate of COVID-19 vaccines increased in the general population, among pregnant and recently pregnant people, there are many drivers of low vaccine uptake.

Multiparity was associated with a high vaccine hesitancy; these findings are like the studies investigating the acceptance of a seasonal vaccine and previous systematic reviews. [22, 33, 36] Therefore, additional effort is warranted to address COVID-19 vaccine booster hesitancy among this group.

Our finding suggested that social factors, such as religious beliefs and the mandatory vaccine policy, are independent predictors of higher vaccine hesitance. Vaccination is vital to protect the population's health and well-being; however, vaccination should balance individual liberty and the population's benefits. [37] Therefore, the authorities should engage all stakeholders in the vaccination process and encourage women to be vaccinated voluntarily, foregrounding the vaccine benefits, efficacy, effectiveness, and safety. [38, 39] Using strategies, for instance, persuasion and the use of trusted endorsers - community leaders, the community health workers and traditional healers. [40, 41]

We found that the role of religious beliefs in vaccine uptake was evident. A similar effect was observed in a study conducted in the United States. [42] Data from the Brazilian Institute of Geography and Statistics (IBGE) suggested that one out of five Brazilians considered themselves evangelical. [43] This finding might significantly impact vaccine uptake and disease control. It is important to note that evangelist leaders supported the previous Brazilian federal administration, which denied the COVID-19 pandemic and refused the massive vaccination of the population.

Therefore, the communication strategies for leveraging vaccine acceptance must include the anticipated non-vaccination regret. In addition, involve the religious leaders to address vaccine religion-related barriers and create a favourable and optimum environment for vaccination. [41]

Other factors independently associated with a low acceptance of COVID-19 vaccine booster were participants' concerns about safety and efficacy. In addition, the perceived minor vaccine importance. This finding was consistent within the three groups assessed. The systematic review by Wilson and colleagues highlights barriers to routine antenatal immunization. This study highlighted barriers related to pregnant people (vaccine safety, belief that vaccines are not needed or ineffective, not

recommended by healthcare workers, low knowledge about vaccines) and healthcare providers-related (increased workload, inadequate training and reimbursement). [44]

The COVID-19 vaccine confidence and acceptance were undermined by the dissemination of misinformation and anecdotal evidence, phenomena observed in Brazil and worldwide. [45, 46] For instance, there are concerns among women of reproductive age that vaccines may lead to infertility or menstrual cycle disruption despite considerable evidence of vaccine safety, even during pregnancy. [47-49] Lessons learned from previous health emergencies suggested that the government, police makers, and healthcare providers should promote context-tailored actions and community engagement to increase vaccine confidence and public health measures compliance by listening to and addressing the vaccine misinformation and population concerns and meeting expectations via different platforms. [25, 50]

Conversely, the high COVID-19 vaccine booster acceptancy predictors were the perceived vaccine importance, safety, and access to COVID-19 and vaccine information. These findings support that the COVID-19 acceptance is multifactorial. [20] Moreover, it reinforces the importance of addressing critical factors, for instance, social determinants, perceived vaccine importance, safety or effectiveness. In addition, the vital role of healthcare providers is as a pivotal source of trusted information, community engagement, and trust building on vaccine safety and effectiveness to avert the deleterious effect of COVID-19 intervention hesitancy. [20]

Our study addressed one of the top 10 global health threats, comparing pregnant people and their counterparts in a country severely affected by the COVID-19 pandemic. In addition, our findings provide important information on the critical barriers to vaccine uptake and factors behind the COVID-19 booster vaccine acceptance in Brazil and suggest some interventions to address it. Additionally, the high hesitancy of the COVID-19 vaccine among pregnant people indicates that health literacy strategies should prioritize this vulnerable group, focusing on COVID-19 risk and vaccine safety and effectiveness to achieve high and equitable vaccine booster uptake.

The limitations of our study were that the design and data collection approach may be susceptible to selection bias. We included only participants with internet access, mostly from urban areas. Furthermore, online surveys are prone to high non-response rates, misperceptions, and data misreporting. [51]

Conclusion: Our findings suggest that the social determinants (religious beliefs), vaccine safety concerns, and perceived vaccine importance are critical barriers to COVID-19 vaccine uptake and hesitancy of additional doses. Moreover, the impact of these factors was more evident among pregnant or recently pregnant people, highlighting the harmful effect of misinformation and the further challenge to leverage vaccine acceptance among this vulnerable population.

Author contributions

CMC, RCP, LB, JGC, SFB, KSP and RTS conceptualized the study. CMC, AM, MN, SM, SFB, KSP and MN were responsible for designing the questionnaire and overseeing data management and quality control. CMC, NG, RTS, and RCP conducted the statistical analysis. CHM, NG, and RCP wrote the first draft of the manuscript. All the authors read and approved the final version of the manuscript.

Data availability

Additional data will be made available upon a reasonable request. All the requests should be addressed to the corresponding author.

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Conflicts of Interest

The authors have no conflicts.

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The titles of figures

Figure 1: Study flowchart.

Figure 2: Perception about the COVID-19 vaccine among pregnant or recently pregnant people, non-pregnant people and partners (Degree of agreement/Likert scale) (n=1325).

Figure 3: Multivariate logistic regressions to identify predictors independently associated with COVID-19 vaccine acceptance (all groups n=1093).

Figure S1: Frequency of use of the COVID-19 vaccine by population groups, pregnant or recently pregnant (n= 331), non-pregnant people (n=886) and partners (n=241).

Figure S2: Acceptability of booster doses/additional doses of (3+) COVID-19 vaccine, reported by participants, pregnant or recently pregnant (n= 317), non-pregnant people (n=872) and partners (n=236).

Figure 1: Study flowchart.

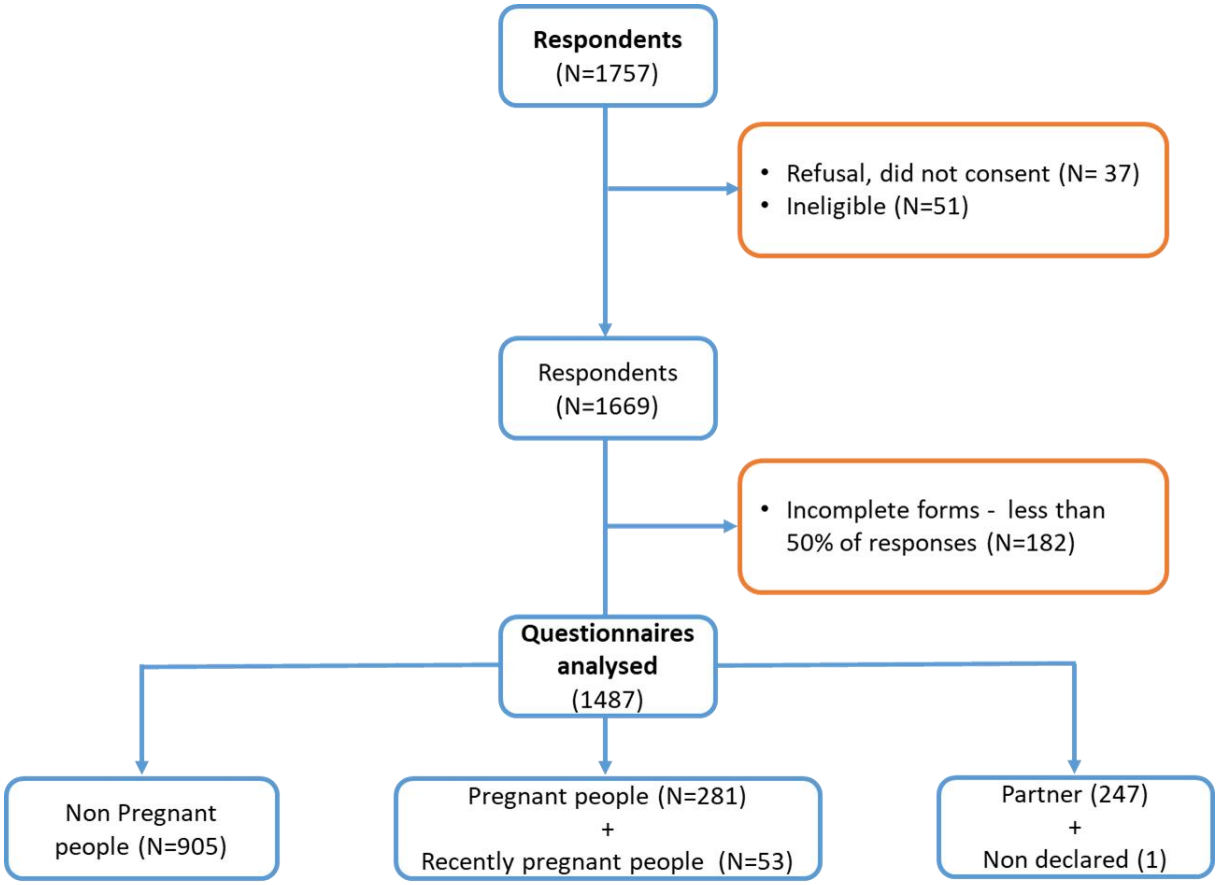


Figure 2: Perception about the COVID-19 vaccine among pregnant or recently pregnant people, non-pregnant people and partners (Degree of agreement/Likert scale) (n=1325).

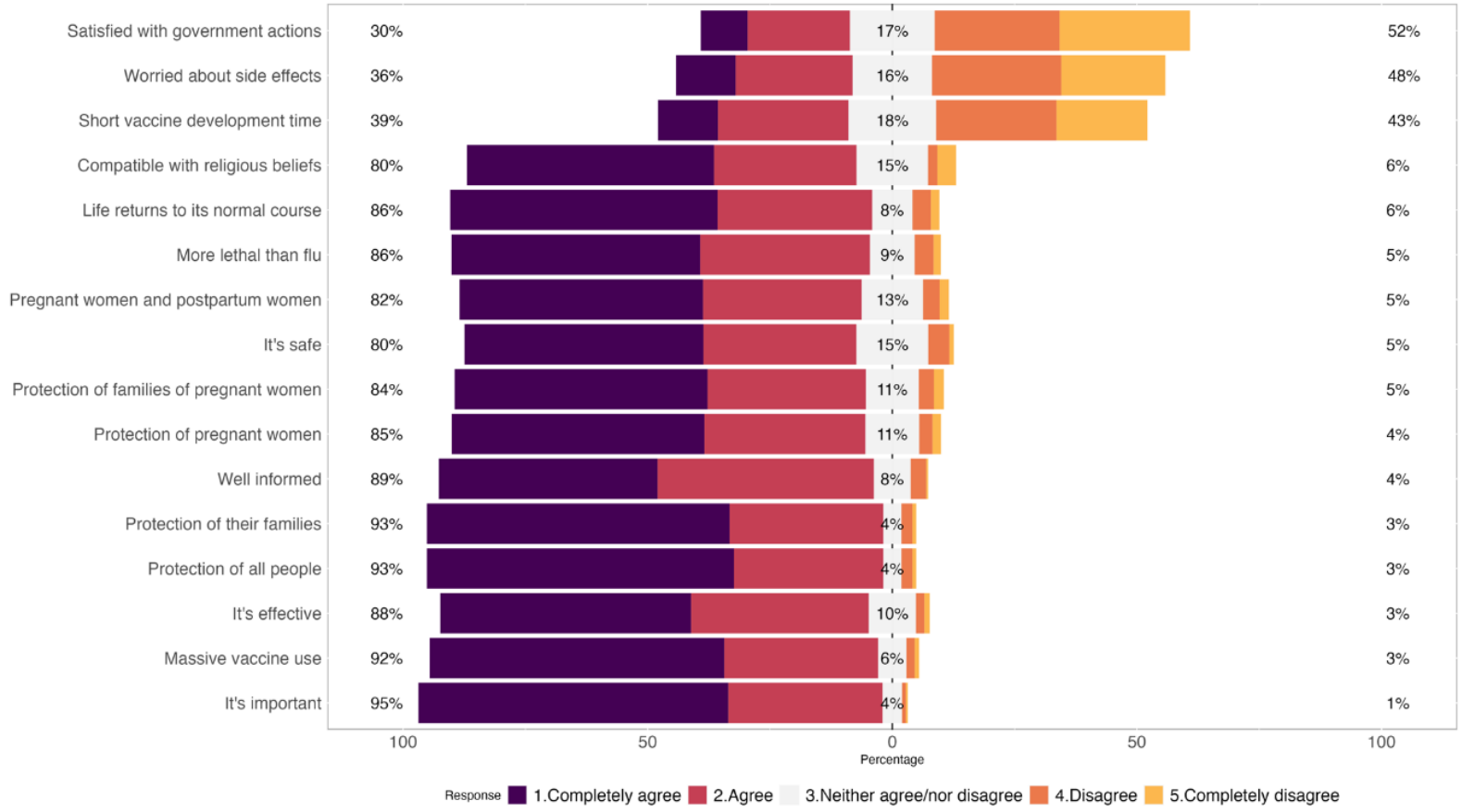


Figure 3: Multivariate logistic regressions to identify predictors independently associated with COVID-19 vaccine acceptance (all groups n=1093).

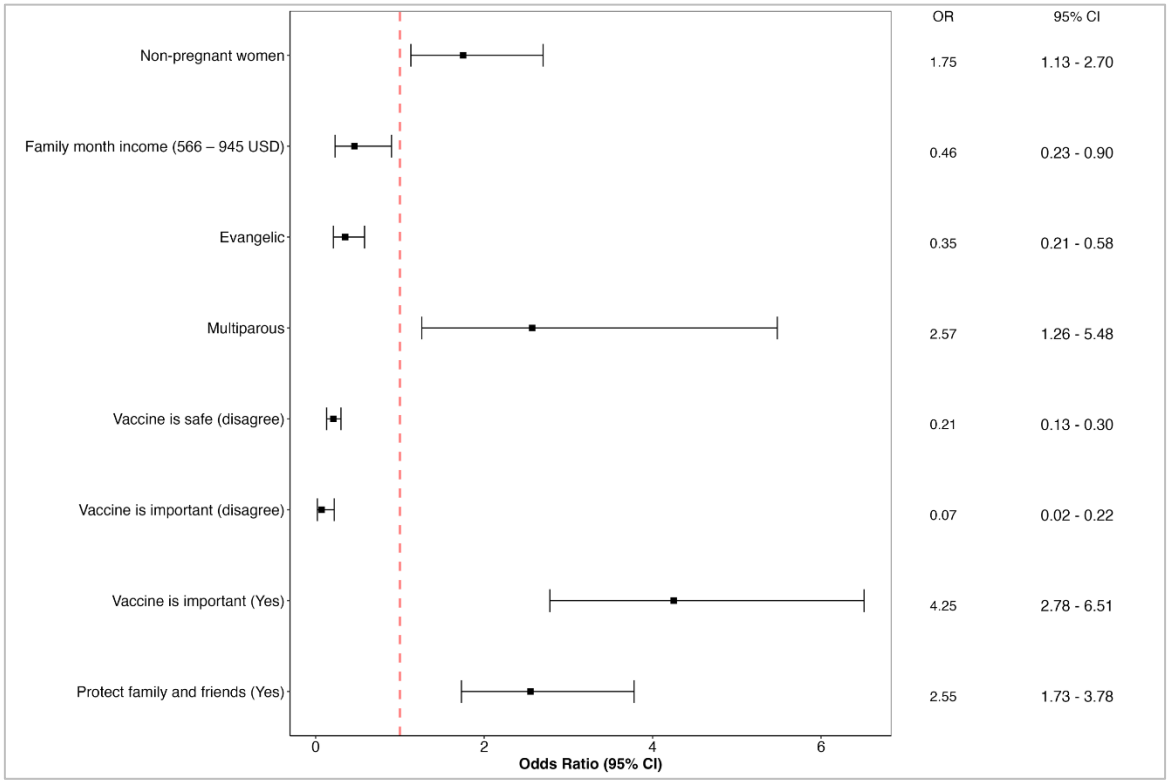


Table 1: Auto-declared Participants' Sociodemographic characteristics, (n=1487), Pregnant or recently pregnant people (n = 334), Non-pregnant people (n= 905), Partner (n=247).

Characteristics	**N**	**Pregnant or recently pregnant people** N (%)	**Non-pregnant people** **N (%)**	**Partners** N (%)
Age (years)	1,433			
18-24		66 (20%)	148 (17%)	19 (8.2%)
25-35		189 (57%)	321 (37%)	66 (28%)
≥ 36		75 (23%)	401 (46%)	148 (64%)
Missing		4	35	14
Skin colour	1,481			
White		150 (45%)	637 (71%)	167 (68%)
Black		46 (14%)	59 (6.5%)	27 (11%)
Brown		131 (39%)	178 (20%)	44 (18%)
Others		6 (1.8%)	28 (3.1%)	8 (3.3%)
Missing		1	3	1
Schooling (years)	1,478			
≤ 9		52 (16%)	28 (3.1%)	6 (2.4%)
10 - 12		173 (52%)	173 (19%)	35 (14%)
> 12		109 (33%)	698 (78%)	204 (83%)
Missing		0	6	2
Marital status	1,481			
With partner		301 (90%)	662 (73%)	194 (79%)
Without partner		32 (9.6%)	240 (27%)	52 (21%)
Missing		1	3	1
Occupation	1,478			
Employed		110 (33%)	74 (8.2%)	16 (6.5%)
Unemployed		199 (60%)	655 (73%)	195 (79%)
Student		8 (2.4%)	120 (13%)	17 (6.9%)
Others		17 (5.1%)	48 (5.4%)	19 (7.7%)
Missing		0	8	0
Family monthly income (USD**)**	1,473			
≤200		81 (24%)	68 (7.6%)	3 (1.2%)
201 - 565		109 (33%)	179 (20%)	28 (11%)
566 – 945		77 (23%)	199 (22%)	38 (16%)
946 – 1320		17 (5.1%)	132 (15%)	41 (17%)
> 1320		48 (14%)	318 (35%)	135 (55%)
Missing		2	9	2
Region	1,486			
North, Northeast and Midwest		6 (1.8%)	26 (2.9%)	4 (1.6%)
South and Southeast		328 (98%)	879 (97%)	243 (98%)
Religion	1,477			
Catholic		118 (35%)	305 (34%)	97 (39%)
Evangelic		142 (43%)	135 (15%)	28 (11%)

Protestant		13 (3.9%)	39 (4.4%)	13 (5.3%)
Without		29 (8.7%)	245 (27%)	77 (31%)
Others		32 (9.6%)	172 (19%)	32 (13%)
Missing		0	9	0
Residence	1,459			
Rural		28 (8.7%)	27 (3.0%)	5 (2.1%)
Urban		295 (91%)	866 (97%)	238 (98%)
Missing		11	12	4
Parity	1,201			
0		106 (32%)	476 (55%)	0 (NA%)
1 - 2		174 (52%)	340 (39%)	0 (NA%)
≥ 3		53 (16%)	52 (6.0%)	0 (NA%)
Missing		1	37	NA
Underlying medical conditions*	1,486			
No		186 (56%)	683 (75%)	176 (71%)
Yes		148 (44%)	222 (25%)	71 (29%)

* Hypertension, Asthma, Cancer, Diabetes, Chronic pulmonary disease, Immunosuppressive disorders, using any Immunosuppressive drugs.

Table 2: Influenza and COVID-19 vaccine uptake, source of information on COVID-19, COVID-19 vaccine and reported reasons/feelings for vaccine uptake by groups of Brazilian participants (pregnant recently pregnant people, non-pregnant people and partners).

Characteristics	**N**	**Pregnant or recently pregnant people** N (%)	**Non-pregnant people N (%)**	**p-value[a]**	**Partners** N (%)	**p-value[b]**
COVID-19 vaccine uptake (primary series)	1,464			**0.001**		0.164
No		14 (4.2%)	11 (1.2%)		5 (2.1%)	
Yes		317 (96%)	875 (99%)		236 (98%)	
Missing		3	19		6	
COVID-19 vaccine additional dose acceptance	1,425			**<0.001**		**<0.001**
No		90 (28%)	132 (15%)		38 (16%)	
Ye		227 (72%)	740 (85%)		198 (84%)	
Missing		17	33		11	
Influenza Vaccine Uptake (2020)	1,460			0.061		0.952
No		129 (39%)	296 (33%)		94 (39%)	
Yes		201 (61%)	592 (67%)		148 (61%)	
Missing		4	17		5	
Influenza Vaccine Uptake (2021)	1,458			0.572		0.732
No		121 (37%)	314 (35%)		94 (39%)	
Yes		205 (63%)	574 (65%)		150 (61%)	
Missing		8	17		3	
Influenza Vaccine Uptake (2020 or 2021)	1,458			0.969		0.596
No		87 (27%)	236 (27%)		70 (29%)	
Yes		239 (73%)	652 (73%)		174 (71%)	
Missing		8	17		3	
COVID-19 infection	1,464			**<0.001**		0.622
No		179 (54%)	378 (43%)		137 (56%)	
Yes		152 (46%)	511 (57%)		107 (44%)	
Missing		3	16		3	
Reasons for COVID-19 vaccine uptake						
Important for health	1,428			0.405		0.635
No		67 (21%)	166 (19%)		46 (19%)	
Yes		250 (79%)	709 (81%)		190 (81%)	

Missing		17	30		11	
Was mandatory	1,428			**0.015**		**0.011**
No		270 (85%)	690 (79%)		181 (77%)	
Yes		47 (15%)	185 (21%)		55 (23%)	
Missing		17	30		11	
To protect family and friends	1,428			**0.046**		0.186
No		155 (49%)	371 (42%)		102 (43%)	
Yes		162 (51%)	504 (58%)		134 (57%)	
Missing		17	30		11	
Previous Family or friends with COVID infection	1,428			**0.028**		0.533
No		291 (92%)	763 (87%)		220 (93%)	
Yes		26 (8.2%)	112 (13%)		16 (6.8%)	
Missing		17	30		11	
High-risk group for COVID-19	1,428			0.237		0.782
No		288 (91%)	813 (93%)		216 (92%)	
Yes		29 (9.1%)	62 (7.1%)		20 (8.5%)	
Missing		17	30		11	
Work in public	1,428			**<0.001**		**<0.001**
No		270 (85%)	630 (72%)		172 (73%)	
Yes		47 (15%)	245 (28%)		64 (27%)	
Missing		17	30		11	
Source of COVID-19 information						
Radio and TV	1,486			**0.008**		**<0.001**
No		169 (51%)	381 (42%)		89 (36%)	
Yes		165 (49%)	524 (58%)		158 (64%)	
Social media	1,486			**<0.001**		**<0.001**
No		162 (49%)	572 (63%)		170 (69%)	
Yes		172 (51%)	333 (37%)		77 (31%)	
Healthcare providers	1,486			**<0.001**		**<0.001**
No		224 (67%)	386 (43%)		110 (45%)	
Yes		110 (33%)	519 (57%)		137 (55%)	
Source of COVID-19 vaccine information						
Radio or TV	1,486			**<0.001**		**<0.001**
No		190 (57%)	411 (45%)		102 (41%)	
Yes		144 (43%)	494 (55%)		145 (59%)	
Social media	1,486			**<0.001**		**0.005**
No		187 (56%)	599 (66%)		167 (68%)	
Yes		147 (44%)	306 (34%)		80 (32%)	
Healthcare providers	1,486			**<0.001**		**<0.001**
No		233 (70%)	396 (44%)		111 (45%)	
Yes		101 (30%)	509 (56%)		136 (55%)	

Feel regret if not get COVID-19 Vaccine	1413					
No		18 (5.5%)	20 (2.4%)	**0.008**	10 (4.1%)	0.467
Yes		310 (94.5%)	824 (97.6%)		231 (95.9%)	
Missing		6	61		6	

a) Pregnant recently pregnant people vs Non-pregnant people,
b) Pregnant recently pregnant people vs Partners

Table 3: Bivariate logistic regressions to identify potential predictors of pregnant or recently pregnant people, non-pregnant people, and partners' COVID-19 vaccine acceptance/reluctance.

COVID-19 vaccine booster uptake											
Predictors	**Pregnant or recently pregnant people**				**Non-pregnant people**				**Partners**			
	N	**OR**	**95% CI**	**p-value**	**N**	**OR**	**95% CI**	**p-value**	**N**	**OR**	**95% CI**	**p-value**
Age (years)	313				838				223			
18-24		1.37	0.71 – 2.79	0.358		**2.60**	**1.33 – 5.58**	**<0.008**		0.93	0.25 – 4.51	0.915
25-35		Ref.				Ref.				Ref.		
≥ 36		1.20	0.66 – 2.25	0.564		0.99	0.66 – 1.49	0.975		1.00	0.43 – 2.21	0.907
Skin colour	316				869				235			
White		Ref.				Ref.				Ref.		
Black		0.69	0.34 – 1.43	0.313		0.93	0.46 – 2.08	0.847		0.67	0.24 – 2.17	0.464
Brown		1.18	0.68 – 2.04	0.562		0.81	0.52 – 1.30	0.371		0.49	0.22 – 1.19	0.101
Others		0.59	0.10 – 4.63	0.576		4.70	0.98 – 84.44	0.130		1.12	0.19 – 21.38	0.920
Schooling (years)	317				867				234			
≤ 9		Ref.				Ref.				Ref.		
10 - 12		0.80	0.39 – 1.59	0.532		1.27	0.39 – 3.48	0.663				0.987
> 12		1.53	0.69 – 3.31	0.296		1.82	0.59 – 4.72	0.251				0.988
Marital status	316				869				235			
With partner		Ref.				Ref.				Ref.		
Without partner		1.20	0.54 – 2.95	0.675		1.15	0.75 – 1.79	0.529		1.58	0.66 – 4.40	0.337
Occupation	317				865				234			
Unemployed		0.80	0.47 – 1.36	0.398		0.96	0.51 – 1.93	0.901		0.71	0.21 – 3.25	0.608
Employed		Ref.				Ref.				Ref.		
Student		0.88	0.18 – 6.28	0.881		**2.75**	**1.38 – 6.29**	**<0.008**		0.46	0.16 – 1.54	0.174
Others		0.50	0.18 – 1.45	0.186		1.41	0.63 – 3.78	0.441				0.986
Family income (USD)	315				865				234			

≤200		Ref.	Ref.	Ref.		Ref.				Ref.		
201 - 565		0.90	0.45 – 1.78	0.767		0.66	0.28 – 1.42	0.312				0.989
566 – 945		0.52	0.25 – 1.04	0.068		0.64	0.28 – 1.36	0.273				0.989
946 – 1320		1.58	0.45 – 7.44	0.506		1.27	0.50 – 3.09	0.596				0.989
> 1320		1.29	0.54 – 3.20	0.569		1.11	0.48 – 2.33	0.794				0.989
Region	317				872				236			
North, Northeast and Midwest		Ref.				Ref.				Ref.		
South and Southeast		0.63	0.03 – 4.31	0.678		0.72	0.17 – 2.12	0.605				0.990
Religion	317				867				236			
Catholic		Ref.				Ref.				Ref.		
Evangelic		**0.52**	**0.29 – 0.90**	**0.022**		**0.42**	**0.26 – 0.70**	**<0.001**		**0.15**	**0.06 – 0.39**	**<0.001**
Protestant		0.30	0.09 – 1.03	0.051		0.63	0.28 – 1.55	0.280		0.81	0.19 – 5.67	0.803
Without		1.87	0.65 – 6.77	0.284		1.64	0.96 – 2.88	0.075		2.76	0.93 – 10.16	0.088
Others		1.30	0.51 – 3.78	0.601		1.02	0.60 – 1.78	0.929		0.88	0.30 – 2.94	0.819
Residence	308				861				232			
Rural		Ref.				Ref.				Ref.		
Urban		1.46	0.63 – 3.26	0.360		1.70	0.61 – 4.09	0.262		1.28	0.06 – 8.99	0.825
Parity	316				839					-	-	-
0		Ref.				Ref.				-	-	-
1 a 2		1.51	0.88 – 2.59	0.137		**0.48**	**0.32 – 0.71**	**<0.001**		-	-	-
≥ 3		1.36	0.66 – 2.92	0.415		0.78	0.35 – 1.99	0.574		-	-	-
Influenza Vaccine Uptake	314				872				236			
No		Ref.				Ref.				Ref.		
Yes		0.71	0.39 – 1.26	0.256		**1.57**	**1.05 – 2.33**	**0.025**		1.60	0.75 – 3.28	0.210
COVID-19 infection	317				872				236			
No		Ref.				Ref.				Ref.		
Sim		1.07	0.65 – 1.74	0.799		0.92	0.63 – 1.34	0.680		0.74	0.37 – 1.48	0.390

Underlying medical condition	317				872				236			
No		Ref.				Ref.				Ref.		
Yes		0.77	0.47 – 1.25	0.287		0.90	0.59 – 1.37	0.604		1.33	0.62 – 3.15	0.484
COVID-19 and COVID-19 Vaccine's Perception												
Vaccine is effective	312				833				233			
Agree		Ref.				Ref.				Ref.		
Disagree		**0.47**	**0.26 – 0.87**	**0.015**		**0.06**	**0.04 – 0.10**	**<0.001**		**0.02**	**0.00 – 0.05**	**<0.001**
Vaccine is safe	309				831				233			
Agree		Ref.				Ref.				Ref.		
Disagree		**0.19**	**0.11 – 0.32**	**<0.001**		**0.07**	**0.04 – 0.11**	**<0.001**		**0.02**	**0.01 – 0.05**	**<0.001**
Vaccine is important	311				827				233			
Agree		Ref.				Ref.				Ref.		
Disagree		**0.02**	**0.00 – 0.09**	**<0.001**		**0.01**	**0.00 – 0.03**	**<0.001**		**0.03**	**0.00 – 0.10**	**<0.001**
COVID-19 is more lethal than flu	313				831				233			
Agree		Ref.				Ref.				Ref.		
Disagree		0.61	0.30 – 1.28	0.180		**0.33**	**0.21 – 0.52**	**<0.001**		**0.23**	**0.10 – 0.49**	**<0.001**
COVID-19 vaccination aligned with religious beliefs	301				829				230			
Agree		Ref.				Ref.				Ref.		
Disagree		**0.33**	**0.17 – 0.63**	**0.001**		**0.59**	**0.39 – 0.90**	**0.013**		**0.31**	**0.15 – 0.65**	**<0.001**
Well-informed about COVID-19 vaccine	312				830				232			
Agree		Ref.				Ref.				Ref.		

Disagree		**0.36**	**0.19 – 0.67**	**0.001**		**0.24**	**0.15 – 0.40**	**<0.001**		**0.09**	**0.03 – 0.25**	**<0.002**
Reason for vaccine uptake (primary series)												
Important	317				872				236			
No		Ref.				Ref.				Ref.		
Yes		**4.58**	**2.60 – 8.16**	**0.001**		**9.80**	**6.53 – 14.83**	**<0.001**		**9.97**	**4.65 – 21.98**	**<0.001**
Mandatory	317				872				236			
No		Ref.				Ref.				Ref.		
Yes		**0.47**	**0.25 – 0.90**	**0.021**		**0.45**	**0.30 – 0.68**	**<0.001**		**0.29**	**0.14 – 0.61**	**0.001**
Protect family and friends	317				872				236			
No		Ref.				Ref.				Ref.		
Yes		**2.98**	**1.79 – 5.03**	**<0.001**		**4.01**	**2.70 – 6.05**	**<0.001**		**16.25**	**6.16 – 56.12**	**<0.001**
Family or friend had COVID-19 infection	317				872				236			
No		Ref.				Ref.				Ref.		
Yes		3.27	1.10 – 14.0	0.059		**3.51**	**1.64 – 9.14**	**0.004**		3.03	0.59 – 55.68	0.290
I have an underlying medical condition	317				872				236			
No		Ref.				Ref.				Ref.		
Yes		0.73	0.33 – 1.70	0.447		1.22	0.60 – 2.83	0.611		1.33	0.62 – 3.15	0.484
Work in public	317				872				236			
No		Ref.				Ref.				Ref.		
Yes		**1.56**	**0.76 – 3.45**	**0.244**		**2.14**	**1.35 – 3.56**	**0.002**		3.70	1.40 – 12.78	**0.018**
Family or friend had COVID-19 infection	315				869				236			
No		Ref.				Ref.				Ref.		
Yes		**1.46**	**0.75 – 2.76**	**0.253**		0.67	0.23 – 1.58	0.405		**4.25**	**1.45 – 11.91**	**0.006**
Well-disseminated COVID-19 and	313				861				234			

Vaccine Information											
No		Ref.				Ref.				Ref.	
Yes		**1.92**	**1.10 – 3.33**	**0.020**		**1.52**	**1.04 – 2.21**	**0.030**		**2.46**	**1.21 – 5.22**	**0.015**
COVID-19 Source of Information											
TV or Radio	317				872				236		
No		Ref.				Ref.				Ref.	
Yes		1.08	0.66 – 1.77	0.748		**1.65**	**1.14 – 2.39**	**0.008**		**2.09**	**1.03 – 4.25**	**0.039**
Social media	317				872				236		
No		Ref.				Ref.				Ref.	
Yes		1.46	0.90 – 2.40	0.127		1.14	0.78 – 1.69	0.513		0.84	0.41 – 1.79	0.633
Healthcare providers	317				872				236		
No		Ref.				Ref.				Ref.	
Yes		**1.92**	**1.12 – 3.39**	**0.020**		**1.91**	**1.32 – 2.78**	**0.001**		1.99	0.99 – 4.07	0.056
COVID-19 Vaccine Source of Information											
TV or Radio	317				872				236		
No		Ref.				Ref.				Ref.	
Yes		1.53	0.93 – 2.56	0.097		**1.62**	**1.12 – 2.35**	**0.011**		**2.03**	**1.01 – 4.13**	**0.048**
Social media	317				872				236		
No		Ref.				Ref.				Ref.	
Yes		1.25	0.76 – 2.06	0.385		1.25	0.85 – 1.89	0.269		0.92	0.45 – 1.96	0.820
Healthcare providers	317				872				236		
No		Ref.				Ref.				Ref.	
Yes		1.13	0.67 – 1.94	0.654		**1.53**	**1.06 – 2.22**	**0.024**		**2.26**	**1.12 – 4.68**	**0.024**

Table 4: Multivariate logistic regressions to identify potential COVID-19 vaccine booster acceptance predictors among pregnant or recently pregnant people, non-pregnant people, and partners.

	COVID-19 vaccine booster acceptance		
Predictors	*Odds Ratios*	95%*CI*	*p-value*
Pregnant or recently pregnant people (N=307)			
(Intercept)	2.47	1.12 – 5.70	**0.028**
Evangelic	0.36	0.17 – 0.70	**0.003**
Vaccine is safe (disagree)	0.33	0.17 – 0.63	**0.001**
Vaccine is important (disagree)	0.03	0.00 – 0.20	**0.004**
Vaccine is important (yes)	4.03	1.93 – 8.51	**<0.001**
Non-pregnant people (N=749)			
(Intercept)	3.23	1.78 – 6.03	**<0.001**
Evangelic	0.38	0.18 – 0.79	**0.011**
Vaccine is effective l (disagree)	0.35	0.16– 0.80	**0.007**
Vaccine is safe (disagree)	0.29	0.14 – 0.61	**<0.001**
Vaccine is important (disagree)	0.14	0.02 – 0.61	**0.020**
Vaccine is important (yes)	4.07	2.23 – 7.41	**<0.001**
Protect family and friends (yes)	2.41	1.34– 4.43	**<0.001**
Partners (229)			
(Intercept)	10.44	3.99 – 33.82	**<0.001**
Evangelic	0.14	0.03 – 0.58	**0.007**

Vaccine is safe (disagree)	0.03	0.01 – 0.11	**<0.001**
COVID-19 vaccination aligned with religious beliefs (disagree)	0.21	0.05 – 0.85	**0.029**
Protect family and friends	7.50	2.25 – 31.42	**0.002**

Values in bold mean they are statistically significant.

Figure S1: Frequency of use of the COVID-19 vaccine by population groups, pregnant or recently pregnant (n= 331), non-pregnant people (n=886) and partners (n=241).

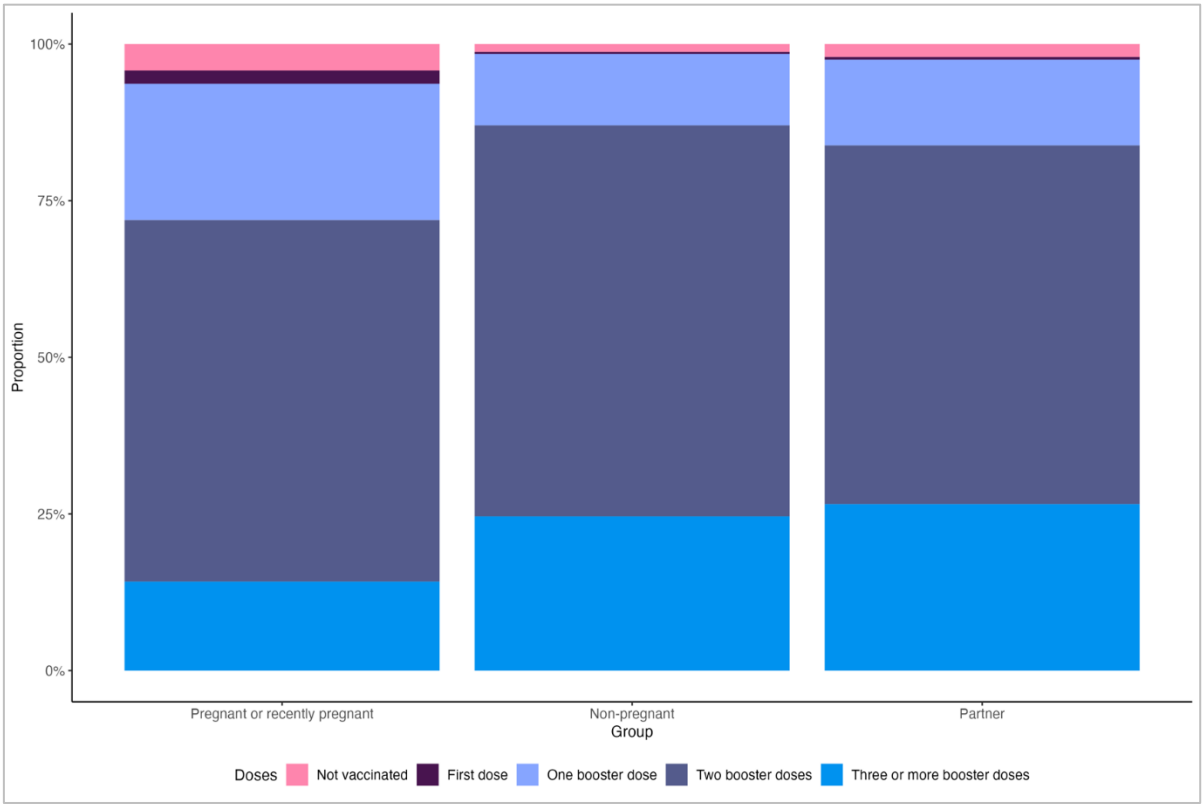
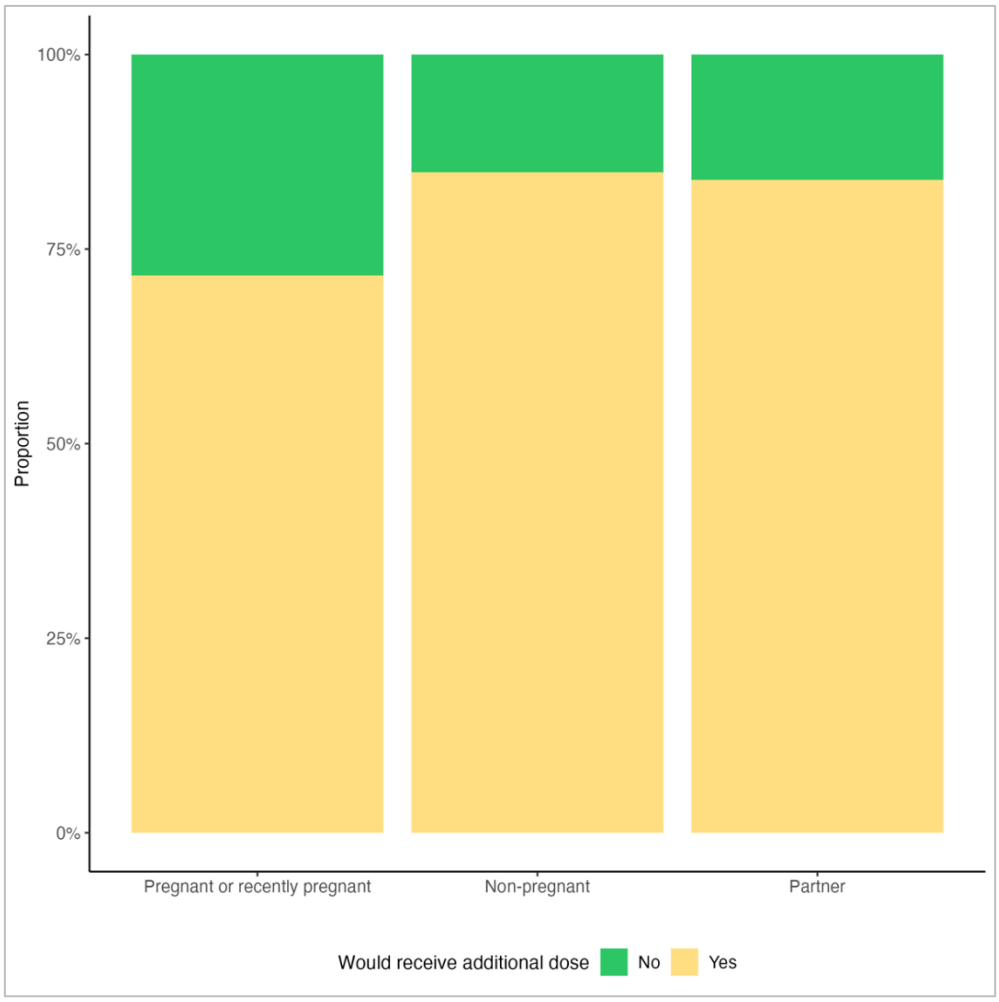


Figure S2: Acceptability of booster doses/additional doses of (3+) COVID-19 vaccine, reported by participants, pregnant or recently pregnant (n= 317), non-pregnant people (n=872) and partners (n=236).



4.4. Artigo publicado na revista *Reproductive Health*.

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Aspectos clínicos y epidemiológicos de la infección por SARS-CoV-2 en mujeres embarazadas y puérperas en Mozambique: un estudio de cohorte prospectivo

Charles M'poca Charles, Nafissa Bique Osman, Domingos Arijama, Benjamim Matingane, Tomás Sitoé, Darlene Kenga, Cesaltina Lorenzoni, Elvira Luís, Rodolfo de Carvalho Pacagnella & Jahit Sacarlal for the Mozambique Study group of SARS-COV-2

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Clinical and Epidemiological aspects of SARS-CoV-2 infection among pregnant and postpartum women in Mozambique: a prospective cohort study.

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Abstract:

Background: Although there is a significant increase of evidence regarding the prevalence and impact of COVID-19 on maternal and perinatal outcomes, data on the effects of the pandemic on the obstetric population in sub-Saharan African countries are still scarce. Therefore, the study aims were to assess the prevalence and impact of COVID-19 on maternal and perinatal outcomes in the obstetric population at Central Hospital of Maputo (HCM), Mozambique. **Methods:** Prospective cohort study conducted at teaching and referral maternity, HCM, from 20 October 2020 to 22 July 2021. We collected maternal and perinatal outcomes up to six weeks postpartum of eligible women (pregnant and postpartum women - up to the 14th day postpartum) screened for COVID-19 (individual test for symptomatic participants and pool testing for asymptomatic). The primary outcome was maternal death, Severe Acute Respiratory Syndrome (SARS), and Intensive Care Unit (ICU) admission. We estimated the COVID-19 prevalence and the unadjusted RR (95% CI) for maternal and perinatal outcomes. We used the chi-square or Fisher's exact test to compare categorical variables (two-sided p-value < 0.05 for statistical significance). **Results:** We included 239 participants. The overall prevalence of COVID-19 was 9.2% (22/239) and in the symptomatic group was 32.4 % (11/34). About 50 % of the participants with COVID-19 were symptomatic. Moreover, the most frequent symptoms were dyspnoea (33.3%), cough (28.6%), anosmia (23.8%), and fever (19%). Not having a partner, being pregnant, and alcohol consumption were vulnerability factors for SARS-CoV-2 infection. The risk of adverse maternal and neonatal outcomes (abortion, fetal death, preterm birth, Apgar, and NICU admission) was not significantly increased with COVID-19. Moreover, we did not observe a significant difference in the primary outcomes (SARS, ICU admission, and maternal death) between COVID-19 positive and COVID-19 negative groups. **Conclusion:** The prevalence of COVID-19 in the obstetric population is higher than in the general population, and fifty percent of pregnant and postpartum women with COVID-19 infection are asymptomatic. Not having a partner and alcohol consumption were factors of greatest vulnerability to SARS-COV-2 infection. Moreover, being pregnant versus postpartum was associated with increased vulnerability to COVID-19. Data suggest that pregnant women have a higher frequency of COVID-19 infection, reinforcing the need for universal testing,

adequate follow-up for this population, and increasing COVID-19 therapy facilities in Mozambique. Moreover, provide counseling during Antenatal care for COVID-19 preventive measures. However, more prospective and robust studies are needed to assess these findings.

Keywords: COVID-19, risk factors, maternal and perinatal morbidity, low-income country, Mozambique.

Plain English summary

The epidemiological pattern of the COVID-19 pandemic in Africa is heterogeneous, and many African countries are still struggling to establish efficient testing policy, guarantee sufficient laboratory supply and achieve or maintain adequate testing capacity. In addition, evidence suggests that sexual and reproductive health services were the most affected by the pandemic; this scenario might have devastating effects on maternal and perinatal health. Moreover, data from non-sub-Saharan countries the SARS-CoV-2 infection among pregnant and postpartum women is associated with an increased risk of adverse maternal and neonatal health (preterm birth, preeclampsia and maternal death).

Although there is a significant increase of evidence regarding the prevalence and impact of COVID-19 on maternal and perinatal health, data on the effects of this condition on the obstetric population in low-income countries are scarce. Therefore, the study objective were to assess the prevalence and impact of COVID-19 on maternal and neonatal health at referral maternity in Maputo, Mozambique.

Our findings suggest that the prevalence of COVID-19 in the obstetric population is higher than the general population, and most pregnant and postpartum women are asymptomatic. Being pregnant, not having a partner and alcohol consumption were factors of greatest vulnerability to SARS-COV-2 infection. Moreover, the risk of COVID-19 among pregnant was seven-fold higher than in postpartum women.pregnant women with COVID-19 may have a higher frequency of adverse gestational outcomes (foetal death and abortion). Although the risk of adverse maternal outcomes (death, Severe Acute Respiratory Syndrome and Intensive Care Unit admission) did not differ significantly between the COVID-19 and COVID-19 negative groups, universal screening for COVID-19 should be implemented to ensure adequate management of pregnant women and newborns.

Background

On the African continent, contrarily to previously developed prediction models, epidemiological data suggest that the progression of the first and second wave of the pandemic was slower, with fewer reported cases and lower disease-related mortality rate (1-3). However, the epidemiological pattern of the COVID-19 pandemic in Africa is quite heterogeneous: about four-fifths (82.6%) of cases were reported in 9 of the 55 countries of the African Union (South Africa [38·3%], Morocco [15·9%], Tunisia [5·1%], Egypt [5·0%], Ethiopia [4·5%], Libya [3·6%], Algeria [3·6%], Kenya [3·5%], and Nigeria [3·2%]) (4). This heterogeneous pattern is due to several factors as the low testing capacity, weak and inefficient epidemiological surveillance systems, and variation in the COVID-19 pandemic progression and response (4).

Many African countries are still struggling to establish efficient testing policy, guarantee sufficient laboratory supply and achieve or maintain the adequate testing capacity, testing at the level of ten negative tests to one positive (test per case ratio ≥ 10) (5, 6). Nevertheless, during the pandemic, in most African countries, the COVID-19 diagnostic capacity was expanded through the GeneXpert platforms previously deployed to diagnose tuberculosis (7, 8), and Mozambique was not an exception.

In Mozambique, the first case of COVID-19 was reported on 22 March 2020. As of 19 September 2021, the Mozambique Ministry of Health (MoH) had reported 150 018 cases (tests per case ratio: 5.9) and 1 903 COVID-19 deaths (case fatality ratio: 1.27%) (9). Data suggest that sexual and reproductive health (SSR) services were the most affected by the pandemic, reducing or interrupting these services in more than 50% of cases (10). Furthermore, this reduction in the provision of services might have devastating effects on maternal and perinatal health due to the increase in maternal and child mortality (11).

The prevalence of COVID-19 in pregnancy was estimated at 41% in symptom-based screening (12) or 7% in universal screening (13), finding from studies conducted in France and the United States of America, respectively. However, the COVID-19 prevalence can vary according to several factors, for example, epidemiological patterns of COVID-19 in the region and country, type of test used

for SARS-CoV-2 detection and testing policy (universal or symptoms based screening), among others.

Data from two systematic reviews (SR) and meta-analysis suggested that the SARS-CoV-2 infection among pregnant and postpartum women is associated with an increased risk of adverse maternal and perinatal outcomes (14, 15). In addition, data from Brazil and a living SR and meta-analysis suggested that pregnant women with advanced age, black race, obesity, and associated comorbidities such as hypertension, and diabetes mellitus have a higher risk of severity (15, 16). These maternal and perinatal health effects are disproportionately higher in the low-income population, where health systems are fragile and less responsive to extreme adverse public health events (17). For example, in Mozambique, hospitals are not adequately equipped (0.4% of hospitals with oxygen therapy available) and have low geographic accessibility (18).

Although there is a significant increase of evidence regarding the prevalence and impact of COVID-19 on maternal and perinatal outcomes (19), data on the effects of the pandemic on the obstetric population in sub-Saharan African countries are still scarce. Therefore, the present study aims to assess the prevalence and impact of COVID-19 on maternal and neonatal outcomes in the obstetric population admitted to the maternity hospital of the Central Hospital of Maputo (HCM), Mozambique.

Methods

Study population and study location

A prospective cohort study included pregnant and postpartum women (up to the 14th day of postpartum), asymptomatic or diagnosed with flu syndrome and / or suspected COVID-19, regardless of age, admitted to the Gynaecology and Obstetrics service of the Central Hospital of Maputo (HCM), Mozambique, from 20 October 2020 to 22 July 2021.

The HCM is a teaching and referral maternity hospital for the region and the country, with comprehensive obstetric care. The screening for SARS-CoV-19

infection in pregnant and postpartum women is similar to the general population, focused on symptomatic individuals or those with a history of contact with a positive case. We intentionally estimated a sample size of 300 participants (pairs of pregnant women and newborn) as the evidence on the effects of COVID-19 on pregnancy was paucity when we were implementing our study.

Procedure

The study protocol included pregnant (regardless of the gestational age) and postpartum women (up to 14th day of puerperium) who attended the HCM obstetrical and gynaecological services and provided or signed the consent form. At hospital admission or soon after, the research team (nurses, resident doctors and consultant obstetrician) identified, invited and assessed for eligibility criteria all potentials participants (in the emergency room and/or patient wards) after giving complete study information, including procedures.

After reading and signing the informed consent form, the participants were asked to provide upper respiratory specimens for laboratory screening of SARS-CoV-2 infection. We excluded all women with invalid telephone numbers who did not accept providing upper respiratory specimens or withdrew their consent form during the study.

We collected nasopharyngeal and oropharyngeal specimens through swabs. For asymptomatic patients, we collected specimens in duplicate. After collecting the specimens, they were placed in a viral transport medium (VTM) containing antifungal and antibiotic supplements. We storage and shipped the specimens in cooler boxes on ice (at 2-8 °C) to the local laboratory for viral detection. All sample viral detection was done via GeneXpert platforms for COVID-19, and the results were available within 24 hours (2hour for symptomatic participants and 24 hours for asymptomatic participants).

The laboratory detention virus followed two approaches: the symptomatic participants and/or severe acute respiratory illness and high-risk contacts were individually tested. Conversely, samples from asymptomatic participants with no history of positive contact for COVID-19 were tested using a *pool testing* strategy. Pool testing is a technique in which specimens collected from different participants

are organised into groups ('pools') and tested together (20). At the time of study implementation, the data from the Mozambican obstetric population suggested that the prevalence of COVID-19 was around 6% (21). Therefore, we estimated a pool of nine samples (P9S3) analysed in three stages (20, 22). The pool tests positive was further divided into sub-pools of three specimens before retesting each specimen in the pool individually to determine which individual(s) are positive.

The specimens' collection, processing, and testing were carried out by health professionals previously trained for this purpose and according to the standards recommended by the Ministry of Health Mozambique and the World Health Organization for collecting and handling clinical specimens for COVID-19 testing.

Subsequently, the included participants were allocated into two groups according to the test result. The COVID-19 positive group consisted of pregnant and postpartum women (up to the 14th day) with a positive test for SARS-CoV-2 infection. The second group (COVID-19 negative) consisted of pregnant and postpartum women with a negative test. During the follow-up, participants with a negative test could move to the COVID-19 positive group if they were positive for SARS-CoV-2 infection COVID-19 when retested.

During inclusion and follow-up (until the 6th week postpartum), data on sociodemographic and obstetric characteristics (including usual means of transportation, alcohol consumption, source of antenatal care, and underlying medical condition), clinical characteristics of SARS-CoV-2 infection, adverse maternal events, maternal and perinatal outcomes were collected by the research team. Data were collected through in person or /and telephone interview and medical record review. Moreover, all study data were collected and managed by the research team using REDCap (Research Electronic Data Capture) electronic data capture tools installed in smartphones (tablets) hosted at Eduardo Mondlane University, Maputo, Mozambique (23, 24).

The primary outcome was the severe maternal outcome (maternal death, SARS and UCI admission). Secondary outcomes were: pregnancy outcomes (abortion, foetal death), preterm birth, preeclampsia/ eclampsia, mode of delivery, Apgar,

NICU admission, neonatal death, congenital anomaly and any composite of adverse pregnancy outcome (NICU admission, preterm birth, foetal death, neonatal death, miscarriage/abortion). In addition, we have considered potential confounders variables, other viral respiratory syndromes, history of adverse pregnancy outcomes, and all factors related to the three-delay model in obstetric care.

Statistical analysis

We describe and compare the sociodemographic, obstetric and clinical characteristics of pregnant and postpartum women included in the study according to exposure (COVID-19 positive and COVID-19 negative groups). Likewise, we estimated the prevalence of COVID-19 in the general population, in the symptomatic and asymptomatic groups, and compared the clinical and severity characteristics in the group of symptomatic women according to the exposure group and estimated the level of significance (we considered Two-sided p-value < 0.05 as statistically significant).

We additionally have considered the time of symptom onset before admission, the duration of symptoms, the most prevalent symptoms, the type of management at the time of admission, admission to the intensive care unit and the presence of the severe acute respiratory syndrome. Finally, we estimated the unadjusted relative risk with a 95% interval to evaluate the risk of adverse maternal and perinatal outcomes. For comparisons of categorical variables, we used the chi-square test or Fisher's exact test when indicated. Statistical analyses were performed using the IBM SPSS statistic program (version 27.0).

Ethical Issues

The study protocol was approved by the Mozambique National Review Board (Letter of approval number 61/CNBS/2020). Moreover, all participants were fully informed regarding the study procedure and provided written or oral consent before their inclusion in the study. In addition, all participants had adequate clinical management (for SARS-CoV-2 positive cases) and psychological support when needed.

Results

We included 239 participants; 22 were COVID-19 positive, and 217 were COVID-19 negative. Maternal and neonatal outcomes were available in 93% of the included participants (223/239) (figure 1). The average age was 28 years (SD 6.1), and the majority of the population was Black (92.1% [220/239]).

At the time of study admission, about 37% (83/226) were pregnant, two-thirds of the participants had had at least four antenatal care consultations, and the majority (69.4% [150/216]) of the participants had prenatal consultations in public services (table 1).

The overall prevalence of COVID-19 was 9.2% (22/239) and in the symptomatic group was 32.4% (11/34) (figure 2A and 2B). About 48% of the participants with COVID-19 were asymptomatic (figure 2C). Dyspnoea (33.3%), cough (28.6%), anosmia (23.8%), and fever (19%) were more frequent symptoms. Hyposmia/anosmia (p-value = 0.00) and ageusia (p-value = 0.02) were symptoms statistically associated with COVID-19 diagnoses (table 2). We were unable to assess maternal and perinatal outcome for sixteen participants.

The sociodemographic factors significantly associated with increased risk of SARC-CoV-2 infection were not having a partner, being pregnant, and consuming alcohol during pregnancy (table 1). Moreover, the risk of COVID-19 among pregnant was seven-fold higher than in postpartum women (RR: 7.32 [2.54 to 21.03] 95% CI, p-value = 0.0002).There were non-significant differences between the COVID-19 positive and COVID-19 negative groups for the following outcomes: duration of symptoms, initial management, the presence of severe acute respiratory syndrome and admission to the intensive care unit at any time (table 2). The risk of adverse maternal and neonatal outcomes (abortion, foetal death, preterm birth, apgar, and NICU admission) was not significantly increased with COVID-19. (table 3). Moreover, We found no s significant difference between COVID-19 positive and COVID-19 negative groups for the remain maternal and perinatal outcomes (table 3). Moreover, during the cohort follow-up, we did not record any cases of maternal death.

Discussion

This prospective and exploratory study report the prevalence of COVID-19 in pregnancy and its impact on maternal and perinatal health in the obstetric population of Maputo, Mozambique. The overall prevalence of COVID-19 in pregnant and postpartum women was 9.2%. Almost half of the population was asymptomatic at the time of diagnosis. In addition, the sociodemographic and gestational factors commonly associated with greater vulnerability to SARS-CoV-2 infection were being pregnant, alcohol consumption, and not having a partner.

These data suggest that the overall prevalence of COVID-19 in pregnant and postpartum women is higher than the general Mozambican population, which was 2-4 % (25). Likewise, this prevalence is relatively higher than that of the study in pregnant and postpartum women, also carried out in Maputo city (21). The difference in the COVID-19 prevalence might be due to the testing strategy, as the studies previously conducted in Mozambique (in general and obstetric population) were seroepidemiologic, and the COVID-19 pandemic magnitude in the country at the time of the studies implementation.

Conversely, our findings are similar to the results of the systematic review by Allotey and colleagues and another epidemiological study carried out in Zambia, which estimated an overall prevalence of COVID-19 in pregnant and postpartum women of 10% and 11.7%, respectively (15, 26).

The prevalence of COVID-19 was 32.4 % in the group of symptomatic women at study admission. These findings are similar to other studies in which testing was based on clinical symptoms (15, 27). Therefore, these data reinforce that the best testing approach is universal in places where resources are available to ensure proper management of pregnant women and newborns once even asymptomatic patients have an increased risk of maternal outcomes, maternal morbidity (RR:1.24 [1.00-1.54]95%CI) and preeclampsia (RR: 1.63[1.01-2.63]95%CI,)(28).

Our data show that the risk of adverse maternal and neonatal outcomes (abortion, foetal death, preterm birth, Apgar, and NICU admission) was not significantly increased with COVID-19. However, our finding suggests a higher frequency of foetal death (9.5% vs 2.0%) and abortion (4.8% vs 0%) in the COVID-19 positive group..

These findings are similar to the systematic review, which estimated increased risk of stillbirth (OR: 1.29 [1·06–1·58] 95%CI)(14) and (RR 2.84 [1.25–6.45])(15). The higher frequency of adverse maternal outcomes observed in our cohort may be due to the third delay (receiving adequate and appropriate treatment)(29), which the COVID-19 pandemic has exacerbated.

We did not observe significant differences in the risk of admission to the intensive care unit, development of severe acute respiratory syndrome, preeclampsia, preterm birth, NICU admission and neonatal death between the COVID-19 positive and COVID-19 negative groups. Our data are similar to systematic reviews (14, 30) and individual studies (28). On the other hand, our findings differ from those of other published studies for maternal ICU admission outcomes, preeclampsia, which increased risk in pregnant women with COVID-19 (30, 31).

The major limitation of this study is related to the sample size. The sample size was small as it might not have the power to detect a difference between the exposure and non-exposure groups for some maternal and perinatal outcomes. Furthermore, although we have estimated a sample size of 300 participants (pairs of pregnant women and newborn), a scarcity of laboratory supplies (SARS-CoV-2 GeneXpert cartridges) at the national level hindered the study implementation. Therefore, reinforcing the difficulty of implementing prospective studies in places with few resources. In addition, the scarcity of SARS-CoV-2 GeneXpert cartridges might have influenced the lower test per COVID-19 case ratio de 5.8 observed in Mozambique, which is almost half of the recommended ratio. The second limitation would be related to the testing strategy for the asymptomatic participant. Although the pooling test strategy might raise some concerns regarding the test performance (32), studies suggest that this testing modality could be implemented without compromising the sensitivity and specificity of the test (20, 33, 34). We consider that this technique should be implemented in a low-resource setting (for example, Mozambique) to upscale the test capacity.Moreover, we implemented the study in a referral hospital with comprehensive and specialised obstetric care. In addition, we included a population mainly from the urban region; thus, the sample might not represent the entire population. Therefore, the study finding should be interpreted with caution, limiting their generalizability.

Conversely, our study has some strengths. First, we conducted a prospective study. Prospectively collected data were used to implement an adequate measure and appropriate COVID-19 cases management at the hospital level, with early isolation of positive cases, rational use of protective equipment and reduction of COVID-19 hospital transmission. Second, to the best of our knowledge, this is the first study developed in low-resource countries in sub-Saharan Africa and might be used as a baseline for future studies. Third, our study highlighted the role of modifiable factors (alcohol consumption) and the risk of SARS-CoV-2 infection. Likewise, the evidence of a risk increase of COVID-19 among pregnant women can raise awareness for greater attention to this group of patients and guide the construction and implementation of public policies to deal with COVID-19 in the obstetric population at the local and regional level.

Conclusions

The prevalence of COVID-19 in the obstetric population is higher than in the general population, and fifty percent of pregnant and postpartum women with COVID-19 infection are asymptomatic. Not having a partner and alcohol consumption were factors of greatest vulnerability to SARS-COV-2 infection. Moreover, being pregnant versus postpartum was associated with increased vulnerability to COVID-19. Data suggest that pregnant women have a higher frequency of COVID-19 infection, reinforcing the need for universal testing, adequate follow-up for this population, and increasing COVID-19 therapy facilities in Mozambique. Moreover, provide counseling during Antenatal care for COVID-19 preventive measures. However, more prospective and robust studies are needed to assess these findings.

List of abbreviations

ICF: Informed Consent Form

HCM: Maputo Central Hospital

MoH: Mozambique Ministry of Health

NICU: Neonatal Intensive Care Unit

P9S3: Pool of nine samples analysed in three stages

REDCap: Research Electronic Data Capture

SRH: Sexual and Reproductive health

VTM: viral transport medium

Ethics approval and consent to participate

The study protocol was approved by the Mozambique National Review Board (Letter of approval number 61/CNBS/2020). Moreover, all participants were fully informed regarding the study procedure and provided written or oral consent before their inclusion in the study. In addition, all participants had adequate clinical management (for positive cases) and psychological support when needed.

Availability of data and materials

The datasets used during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

CMC, RCP, NO, and JS conceived and designed the study. CMC, DK, BM, DA, TS, CL collected data. CMC, RCP, and EL were responsible for data analysis and interpretation. RCP and CMC wrote the first version of the manuscript. RCP, JS and

NO critically reviewed the manuscript. All the authors read and approved the final version of the manuscript.

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Figure 1: Study flowchart.

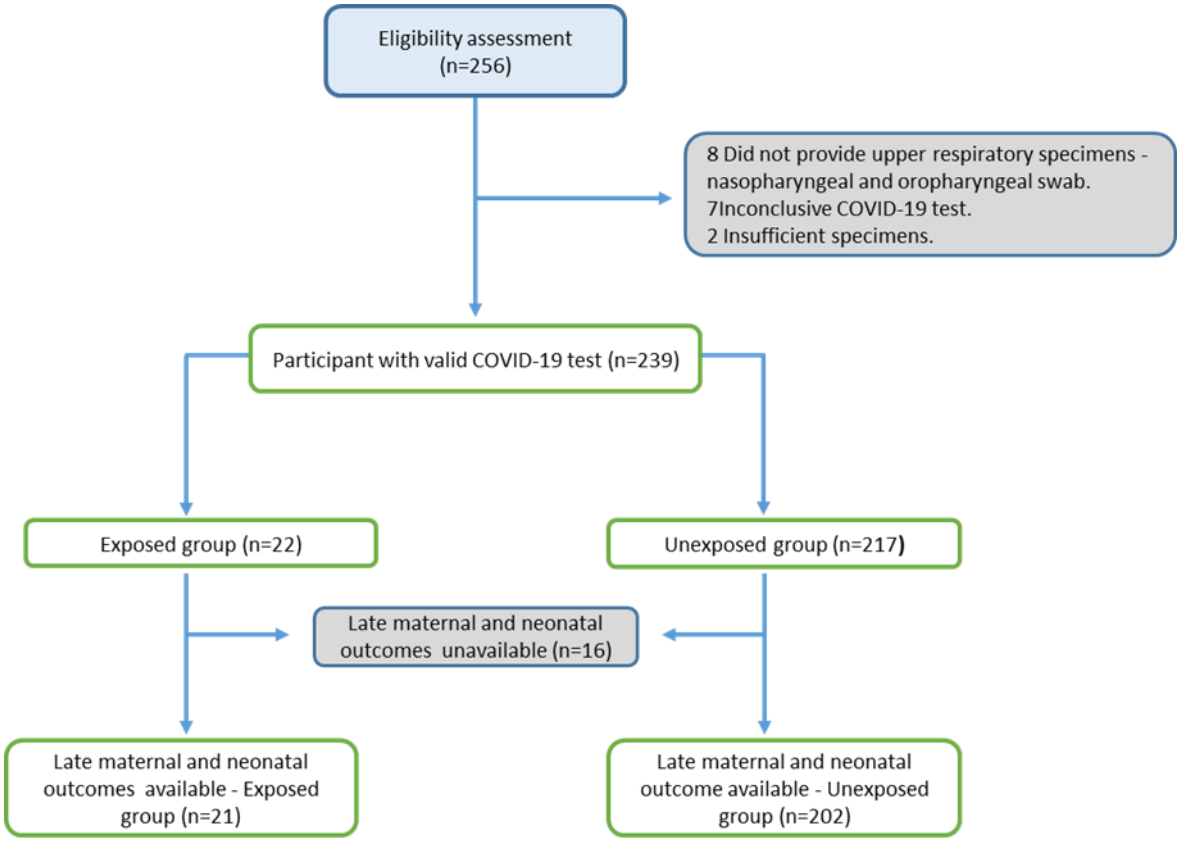

Figure 2: Prevalence of COVID-19 and symptoms among pregnant and postpartum women.

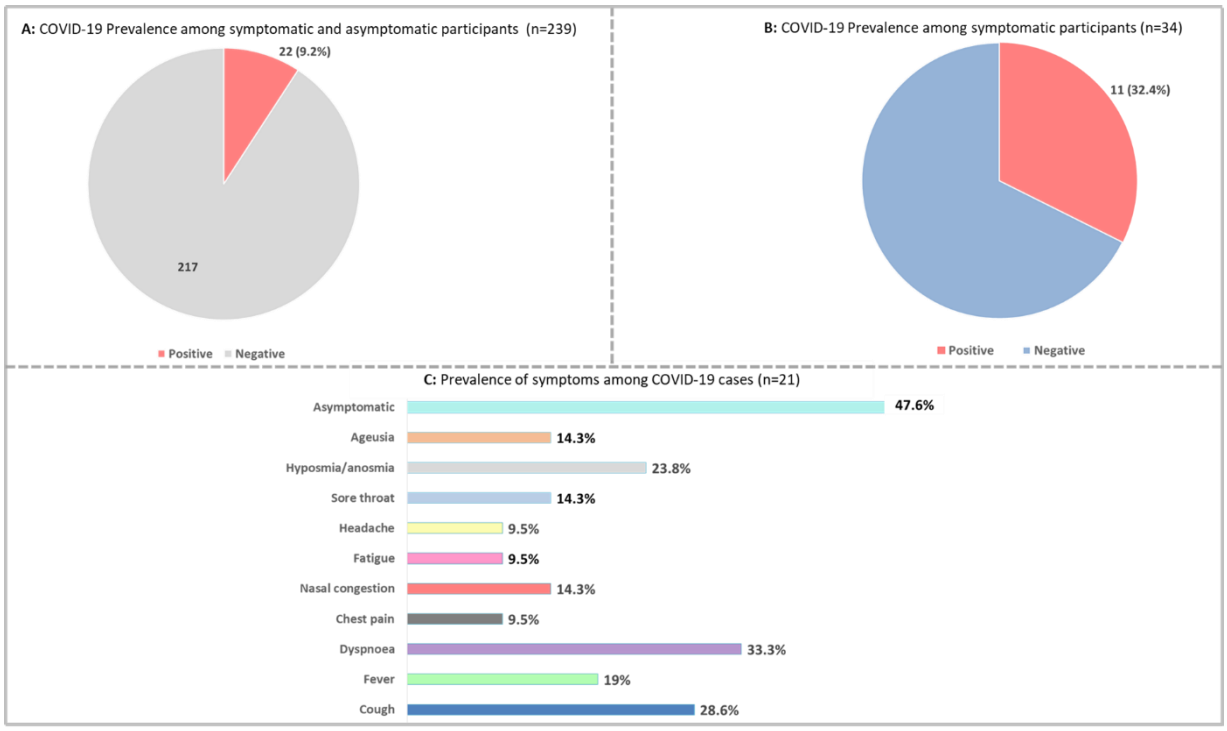

Table 1: Sociodemographic and obstetric characteristics of Maputo Central Hospital included in the study (n=239).

Characteristics	Confirmed COVID-19 n= 22	Negative COVID-19 n= 217	*p*-value
Age [a]			0.326
≤19	2 (9.1%)	15 (7.4%)	
20-35	14 (63.6%)	155 (76.0%)	
>35	6 (27.3%)	34 (16.7%)	
Ethnicity [b]			0.390
Black	20 (95.2%)	200 (98.0%)	
Non-black	1 (4.8%)	4 (2.0%)	
Area of residence [c]			0.461
Peri-urban	19 (86.4%)	183 (90.6%)	
Urban	3 (13.6%)	19(9.4%)	
Marital Status [d]			**0.043**
With partner	13 (61.9%)	164 (80.8%)	
Without partner	8 (38.1%)	39 (19.2%)	
Schooling [e]			0.883
None or Primary or Secondary	12 (63.2%)	131 (64.9%)	
College or more	7 (36.8%)	71 (35.1%)	
Usual means of transport [f]			0.096
Public	10 (52.6%)	140 (71.1%)	
Private	9 (47.4%)	57 (28.9%)	
Source of antenatal care [g]			0.112
Public	17(68.9%)	181 (94.3%)	
Private	3 (15.0%)	11 (5.7%)	
ANC consultation [h]			0.667
None	1 (5.0%)	7 (3.5%)	
1-3	5 (25.0%)	60 (30.0%)	

≥ 4	14 (70.0%)	133 (66.5%)	
Provenience [i]			1.00
Home	18 (81.8%)	168 (82.8%)	
Referral	4(18.2%)	35 (17.2%)	
Parity [j]			0.447
0	12 (57.1%)	87(42.0%)	
1-2	7 (33.3%)	98 (47.3%)	
≥3	2 (9.5%)	22 (10.6%)	
Planned pregnancy [k]	11 (52.4%)	134 (65.4%)	0.237
Multiple pregnancy	1 (4.8%)	7 (3.4%)	0.544
Pregnancy status at enrolment [l]			**0.000**
Pregnancy	17 (81.0%)	66 (32.2%)	
Post-partum	4 (19.0%)	139 (67.8%)	
Chronic hypertension	1 (4.5%)	6 (2.8%)	0.496
Pre-existing diabetes	0(0.0%)	0 (0.0%)	NA
Asthma	1 (4.5%)	2 (0.9%)	0.252
Anemia	0 (0.0%)	10 (4.6%)	0.427
HIV	2 (9.1%)	28 (12.9%)	0.749
Alcohol drinking [n]	13 (65.0%)	62 (31.0%)	**0.002**
Symptoms [m]			**0.000**
Yes	11 (52.4%)	22 (10.9%)	
No	10 (47.6%)	180 (89.1)	

Missing information: a)13, b)14 c)15, d)15, e) 18, f) 23, g)27, h)19, i) 19, j)13, k)13, l)13 m) 1, n) 19

Table 2. Clinical features and severity of COVID-19 infection among symptomatic women (n=32).

Clinical features and severity	Confirmed COVID-19 n=10	Negative COVID-19 n= 22	*p*-value #
Number of days with symptoms before enrolment			1.00
<7	7 (70.0%)	14 (63.6%)	
≥7	3(30.0%)	8 (36.4%)	
Symptoms (Prevalence ≥ 20%)			
Cough	6 (60%)	13 (63.6%)	1.00
Fever	4(40%)	10 (45.5%)	1.00
Dyspnoea	7 (70%)	7 (31.8%)	0.06
Chest pain	2 (20%)	2 (9.1%)	0.57
Nasal congestion	3 (30%)	5 (22.7%)	1.00
Fatigue	2 (20%)	2 (9.1%)	0.57
Headache	2 (20%)	5 (22.7%)	1.00
Sore throat	3 (30%)	2 (9.1%)	0.29
Hyposmia /anosmia	5 (50%)	0 (0%)	**0.00**
Ageusia	3 (30%)	0 (0%)	**0.02**
Initial management			0.087
Discharge from ER	4 (40.0%)	1 (4.5%)	
Ward admission or Labour ward	5 (50.0%)	17 (77.3%)	
ICU admission	1 (10.0%)	4 (18.2%)	
SARS	1 (10.5%)	3 (14.3%)	1.00
ICU admission at any time	1 (10.0%)	7 (31.8%)	0.38

#Fisher's exact test

Table 3: Risk estimates for adverse pregnancy and neonatal outcomes according to COVID-19 exposure (n=223).

Pregnancy outcomes	COVID-19 positive n= 21	COVID-19 negative n= 202	p-value
Pregnancy outcome			
Abortion	1 (4.8 %)	0 (0.0%)	0.08
Foetal Death	2 (9.5%)	4 (2.0%)	0.09
Live birth	18 (85.7%)	198 (98.0%)	
Preterm birth [a]	3 (15.0%)	49 (25.4%)	0.42
Pre-eclampsia	1 (4.8%)	52 (25.7%)	0.03
Mode of delivery			
Vaginal birth	18 (85.7%)	154 (76.2%)	Ref.
Elective C-section	2 (9.5%)	21 (10.4%)	1
Intrapartum C-section	1 (4.8%)	27 (13.4%)	0.48
Apgar <7 at 1rst minute [b]	1(5.9%)	36(19.1%)	0.31
Apgar <7 at 5th minute [b]	0 (0.0%)	14 (7.4%)	-
Neonatal respiratory distress[c]	0(0.0%)	25 (14.7%)	-
Neonatal mechanical ventilation[d]	0 (0.0%)	8 (4.7%)	**-**
NICU admission[e]	2 (12.5%)	36 (20.6%)	0.74
Any neonatal morbidity	2 (9.5%)	43 (21.3%)	0.26
Congenital anomaly	0 (0.0%)	2 (1.12%)	
Neonatal death	0 (0.0%)	5 (2.9%)	
Any APO/WHO*	7 (33.3%)	67(33.2%)	0.98
Any gestational intercurrence **	5 (23.8%)	48 (23.8%)	0.99

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Preterm births prevalence during the COVID-19 pandemic in Brazil: results from the national database

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Preterm births prevalence during the COVID-19 pandemic in Brazil: results from the national database

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Abstract

Background: The SARS-CoV-2 (COVID-19) pandemic impacted the health systems between and within countries, and in the course of the pandemic sexual and reproductive health services were the most disrupted. Findings from high-income settings have reported significant changes in preterm birth prevalence during the pandemic period. **Objective:** To understand the possible effects of the COVID-19 pandemic on preterm birth numbers at the Brazilian national level. **Methods**: we compare the number of preterm deliveries during the COVID-19 pandemic period (2020 and 2021) with previous years. We conducted a population-based cross-sectional study taking the period from January 2017 to December 2021 to account. We use individual-level live births data from the Brazilian Live Birth Information System (SINASC), and we estimate the odds ratio (OR) of preterm deliveries using propensity score weighting analysis in Brazil and its regions. **Results:** During the study period (from 2017 to 2021), about 2.7 million live births were recorded per year, and the missing value for gestational age at delivery was less than 1.5%. The preterm birth prevalence slightly increased during the COVID-19 pandemic compared to the pre-pandemic period (11.32 % in 2021 vs 11.09% in 2019, p-value < 0.0001). After adjusting for sociodemographic variables, the OR of preterm births in Brazil has significantly increased, 4% in 2020 (OR: 1.04 [1.03-1.05] 95% CI, p-value <0.001), and 2% in 2021(OR: 1.02 [1.01-1.03] 95% CI, p-value <0.001), compared to 2019. At the regional level, the preterm birth pattern in the South, Southeast and Northeast regions show a similar pattern. The highest odds ratio was observed in the South region (2020 vs 2019, OR: 1.07 [1.05 – 1.10] 95% CI; 2021 vs 2019, OR: 1.03 [1.01 – 1.06] 95% CI). However, we also observed a significant reduction in the ORs of preterm births in the northern region during the COVID-19 pandemic (2020 vs 2019, OR: 0.96 [0.94 – 0.98] 95% CI) and (2021 vs 2019, OR: 0.97 [0.95 – 0.99] 95% CI). **Conclusion:** Our analysis shows that the pandemic has increased regional variation in the number of preterm births in Brazil in 2020 and 2021 compared to the pre-pandemic years.

Introduction

The COVID-19 pandemic impacted Latin American countries as hard as in more developed locations. Due to the sanitary crises, we saw in many countries disrupting health systems, and as consequence, mortality exceeded its usual numbers and life expectancy reductions in many countries (1). In addition to controversial health policies, conflicting messages and long-time central government resistance to implementing population mobility restrictions (2), Brazil was one of the most affected countries by COVID-19 worldwide. Pregnant women were also a risk group, as maternal mortality skyrocketed during the pandemic (3).

Maternal mortality is also an important proxy for the quality of country's health services. Another obstetric condition that is sensitive to suboptimal clinical care is preterm birth (4). Studying preterm birth is important because it is the primary cause of neonatal deaths, and its prevalence is rising in most low- and middle-income countries, despite many efforts to revert it (5, 6). While several risk factors have been well-established, the key factor responsible for preterm deliveries remains unknown in half of the cases (7). Since the onset of the pandemic, several studies have identified an association between COVID-19 infection and adverse perinatal outcomes, such as stillbirths and premature deliveries (8, 9, 10, 11). These findings are also contradictory because some analyses indicate that the number of preterm deliveries increased during the pandemic, while other studies suggested a reduction in such types of pregnancies (11).

One of the most important underlying mechanisms for preterm birth is the inflammatory condition. The systemic inflammation may trigger cervical effacement and uterine contraction through increasing prostaglandins (12). The SARS-CoV-2 infection is a systemic inflammatory disease; therefore, we may argue that it could lead to preterm birth. For example, among women with SARS-CoV-2 pneumonia, empirical evidence shows an increased preterm birth rate (13). However, the infection itself may not represent the whole mechanism related to preterm delivery.

In addition, we may also argue that changes in individual behavior are associated with lockdown and other population restrictions policies, implemented to mitigate SARS-CoV-2 dissemination, and that may have influenced to some extent the number of preterm births. As an example, an Australian study showed a lower risk of preterm birth in pregnant women during lockdowns in comparison to those born before the pandemic

(14). Other studies also indicate a decrease in preterm birth rates (15, 16), although the same empirical evidence was not corroborated elsewhere that fail to identify differences in the number of preterm pregnancies (17).

Despite inconclusive findings, there is a consensus that the COVID-19 pandemic period brought many challenges to the country's health systems, and there is still scarce information about its real consequences on perinatal health while considering low- and middle-income countries. Therefore, in this study, we aim to assess the changes in preterm birth counts in Brazil and its regions, by comparing the number of preterm deliveries during the pandemic (2020 and 2021) and pre-pandemic periods (2017, 2018 and 2019).

Methods

We performed extensive use of the publicly available microdata of live birth, collected by the Brazilian Ministry of Health, and launched by the Brazilian Live Birth Information System (SINASC in Portuguese)(18). The SINASC is an e-birth registration system developed by the Department of Informatics of the National Unified Health System (DATASUS). This system was implemented in 1990. The data are collected routinely immediately after each birth through a standardized document (declaration of live births), which was updated in 2010 to ensure a better quality of the information recorded (19). The updated version included many important variables for the study of preterm birth, such as sociodemographic and obstetric variables.

The data was downloaded (as of August 12, 2022), and updated (as of April 15, 2023) from http://svs.aids.gov.br/dantps/cgiae/sinasc/, and we consider all live births equal or superior to 22 weeks, from January 2017 to December 2021. We extracted individual-level data regarding gestational age at birth, maternal age, marital status, ethnicity, schooling (as a proxy of women's income), parity, gravidity, mode of delivery, region and federal state of residence, number of living children, number of antenatal care (ANC) visits, and newborn's weight and sex. These variables are available in the SINASC for each birth, and they are highly associated with preterm delivery. We did not exclude multiple pregnancies and neonates with congenital anomalies for the analysis. All categorical variables were converted to binary dummies by using the one-hot encoding procedure. Less than 1.5% of the data had missing or unknown information. Notwithstanding, SINASC data quality has recently shown enormous

improvement. Of course, while considering more disaggregated geographical levels, the data may still need some adjustments and corrections. For this study, we work with Brazil and great regions, and that reduces significantly defective concerns such as under-registration of birth counts; as in Brazil and its regions, the rate of underreported data is generally less than 1%, except in the North and Northeast regions where the rate is about (20,21) 1.7%. In addition, Castanheira and Kohler considered inadequate to apply any correction method to birth registrations, given the recent fertility dynamics in the country (22). Lima et al (23) also show that recent SINASC information does not require data corrections at lesser disaggregated levels, such as Federal States and great regions. However, we acknowledge that the unprecedented burden on the health system during the pandemic may have influenced the data quality. The study protocol was published elsewhere (24).

To reduce the influence of past trends in prematurity prevalence, we restrict our preterm birth analysis to pairwise years comparison, initiating from 2017 until 2021. We did not include data before 2017 to avoid the influence of the Zika virus outbreak (between 2015-2016) on birth counts and overall fertility (25). We created four stacked datasets (2017-2018; 2018-2019; 2019-2020; 2019-2021) and we added, for each dataset, two dichotomous variables of interest: one to indicate whether the birth was preterm (y=1) and (y=0) otherwise, and another measure indicates the period, i.e. the current year in the dataset (z=0) vs. the following year (z=1). This last variable is useful for identifying the control group (preterm births occurring in years before COVID-19) and the treatment group (preterm deliveries occurring during the pandemic).

Statistic model

Our analysis was based on a quasi-experimental approach using a Propensity Score Weighting (PSW) method (26, 27). PSW was designed to control for selection bias in non-experimental studies, for which it is desirable to assess the average effect of some variable that emulates a control/treatment process. Propensity scores are used to match untreated versus treated individuals, understanding that there is a probability of these last being exposed to a certain stimulus or intervention (28).

As the first step, a multiple logistic regression analysis was used to fit the binary control variable (z) as a function of the mother's and obstetrics' characteristics: age, ethnicity/skin colour, schooling, parity, mode of delivery, number of previous children,

marital status, number of antenatal care visits and new-born weight. With the regression estimates, we extracted a vector (e) that gives the probability of treatment assignment to a random individual conditioned to a given set of covariates (x), i.e. e(x)=P (z=1| x).

The vector (e) is called the Propensity Score, and it was used to control for selection bias and to derive the weights of a second regression model. The control was made by pruning samples corresponding to the tails of the Propensity Score vector, to keep only samples that can be considered comparable to each other. Figure 1 shows the kernel density estimate (KDE) plot for the Propensity Score referring to births in Brazil in the years 2019 and 2020, before (a) and after (b) a 10% pruning of each tail. In this example, 80% of the original dataset was selected for the final phase of the analysis.

[Figure 1]

The set of weights was estimated as follows: for the individuals in the treatment group, w=1/e(x), and for the individuals in the control group w=1/(1-e(x)). As a final step, we estimate a new regression, fitting the outcome of interest (preterm birth) controlled by the covariates and using the propensity scores as weights.

Results

About 2.7 million live births were recorded annually from 2017 to 2021 (18). In Table 1, we present the percentage share of clinical and socioeconomic mother's characteristics, comparing the last three years of our analysis, 2019 until 2021.

[Table 1]

Overall, in Brazil, the preterm birth counts were around 11%, and this number did not change much compared to pre-pandemic years, in this case, 2019. Also, in terms of the mother's characteristics, we did not identify considerable changes in the last three years of our analysis.

In Table 2, we show the results of the multiple regression analysis using PSW for Brazil, by pairwise year comparison. We were interested to see if the pandemic (treatment period, 2020, and 2021) somehow affected the chances of preterm birth counts in the country. Our results show that the Odds Ratio (ORs) of preterm births in Brazil has increased by 4% in 2020 (95% CI, 1.03-1.05), and 2% (95% CI, 1.01-1.03) in 2021, compared to 2019 after controlling for other sociodemographic variables.

[Table 2]

In addition, the pairwise comparison for the period 2017 to 2019 shows small or non-significant changes in the ORs of preterm births, and the odds ratios of preterm pregnancies fluctuated between values of below and above 1%. This means that during the pandemic the chances of preterm deliveries have increased somewhat to two and four per cent.

In figure 2, we bring the odds ratios for Brazil and its regions. These estimates are based on complete models, controlled by the same variables described in table 2. Across regions, the odds ratios of preterm births showed a small decline or even stalled values between the pre-pandemic periods of 2017-2019, seen especially in the South and Midwest regions of Brazil. However, while we consider the pandemic period effect (2019 vs. 2020, and 2019 vs. 2021), the chances of preterm pregnancies increased again. In the Southeast and the less developed Brazilian region of the Northeast, for example, there was a small decrease in the odds ratios between 2017-2019, but during the pandemic period, the chances of preterm births increased even more, especially in the Northeastern part of Brazil. The Northern region was the only location that had a reduction in the odds ratios of preterm births during the COVID-19 pandemic period (2020 and 2021). These results may also indicate that the effect of the pandemic on the prevalence of preterm births was uneven across subnational areas of the country.

[Figure 2]

Our finding showed a significant change in caesarean delivery rate during the pandemic period compared to the previous period (OR: 1.09 [1.08- 1.10] in 2020, and OR: 1.10 [1.09-1.11] in 2021), table 2. The analysis of the mode of delivery by gestational age, for the pairwise comparison of 2019 and 2020, showed a trend of increasing caesarean delivery in all gestational age groups. Moreover, preterm babies had a higher risk of being delivered by caesarean in 2020 and 2021 compared to the previous years. This pattern was also observed in the South, Southeast, and Northeast regions, figures 3 and 4.

Discussion

Using Ministry of Health data, we assessed the odds ratios of preterm births in Brazil and its regions, before and during the pandemic. Our results indicated that, during the pandemic years of 2020 and 2021, preterm births have significantly increased as compared to pre-pandemic periods. This increase was not homogeneous across the country, and in certain regions, the pandemic has disrupted previous decline patterns or even accelerated the past trend of preterm deliveries growing; as observed in Northeastern, Southeastern, and Southern regions.

The ethnicity (indigenous women), low level of education, low number of antenatal care visits, and multiparity, extreme maternal ages, were associated with an increased risk of PTB. These data are similar to the findings of other population-based studies (29, 30).

Finding from individual studies and systematic review has suggested a global reduction in ANC clinic visits, maternity healthcare-seeking, and unscheduled care visits (31); the same pattern was also observed in Brazil, where the quality of ANC was low (only 35.8% of the study participants had adequate), In addition, the risk of inadequate ANC was higher among pregnant women with black/brown skin colour and multiparous when compared to their contra part (32). These factors potentially contributed to worsening pregnancy outcomes (including the preterm birth rate), even for married/cohabiting women.

During the COVID-19 access to the Internet and DICT (Digital Information and Communication Technologies) was heterogeneous within the Brazilian regions, and municipality, public and private health systems. And, to the best of our knowledge, data regarding the coverage of virtual or remote antenatal care were not available in the database [SINASC], and the ANC visits are not desegregated by the mode of consultation [remote vs in-person]), therefore, we have not considered this variable in our analysis.

The pandemic brought the attention of health experts and demographers that took the time to understand how COVID-19 could affect birth counts and, for instance, the chances of preterm deliveries in the country. Brazil is a country that suffered excessive mortality due to the COVID-19 pandemic (2, 33), as well as health facilities also were stressed by the high number of COVID-19 cases, and many services could not be properly provided by health units (34). This exogenous sanitary problem might have

also affected women's antenatal care, especially among those that require more attention from public health services, i.e. mothers from low socioeconomic strata. Uncertainty and economic restrictions caused by the pandemic context may also play an important role in reproduction (35), and compromise pregnancy and antenatal care in Brazil.

Among Brazilian regions, the Northeast requires special attention because this is a region marked by historically lower socioeconomic development that could be in turn associated with restricted health services access (36, 37), and the lack of strategy to mitigate the impact of the pandemic at different governmental levels (3, 33). Notwithstanding, the COVID-19 pandemic brought an enormous burden to Brazil's Northern and Northeastern regions and revealed a sudden disruption of health care services (38, 39). These setbacks might in turn affect the preterm birth rate.

Our findings differ from other studies that indicated a reduction in preterm deliveries during the COVID-19 pandemic (10, 14, 40-44). This could be partly explained by the measures applied to face the pandemic, which was uncoordinatedly implemented in Brazil (36). Regional inequality in health services access and the slow degree of responsiveness of the Brazilian National Health System could have played a role in the unequal pandemic effects on preterm births across Brazilian regions. As previous studies indicate, less sub-national inequality is seen in high-income countries, recognized by strict lockdown policies and with developed health services according to the needs posed by the pandemic. Moreover, Brazil had more severe cases; one out of seven maternities had intensive unit beds, therefore resulting in the phase three delay - concerning receiving proper diagnosis and timely treatment (1, 45, 46).

However, our findings suggested a different pattern of preterm birth rate in the Northern region. In the Northern region of Brazil, more than two–thirds of pregnant women did not attend antenatal care, and higher excess mortality (especially in Manaus city), which might have caused severe perinatal outcomes (miscarriage and fetal death) (47, 48).

Our study suggested an increased rate of caesarean delivery among preterm babies in 2020, and 2021 compared to previous periods. Therefore, we may speculate that the increased risk of PTB in 2020, and 2021 may be related to non-spontaneous (provider-initiated) preterm birth (49, 50).

It is important to mention that we concentrate our analysis and interpretations on the year's effect only (comparison between control versus treatment, or pre-pandemic vs. pandemic period), and we do not get into detail about the other control variables, despite the models have shown important differences in preterm pregnancies among distinguished demographic and socioeconomic groups.

This study has some strengths and limitations. Our data covers the entire population of live births in Brazil, with information at the individual level (20). The analysis of the different geographic regions allowed us to picture preterm birth developments in a country recognized for its regional inequality. The main limitation is related to the study design, which does not allow us to infer causality but only refers to the association between the pandemic and preterm births. We also did not assess the direct impact of COVID-19 on the occurrence of preterm births, and we considered the years 2020 and 2021 as risk factors that caused changes (from social, economic, and epidemiological order) brought by the pandemic onset. Likewise, our model did not include all variables associated with preterm birth, for example, human development index, availability and access to health services before and during the COVID-19 pandemic, cigarette smoking, BMI, maternal income, unemployment, maternal underlying medical conditions, and maternal infection (vector-borne diseases, urinary tract, genital, and respiratory infection [including COVID-19]). We did not assess the prevalence of fetal deaths and the abortion rates. But we recognize that these outcomes could have increased in situations of reduced access to adequate health services, impacting Brazil’s birth rates.

Although we did not see an expressive increase of preterm births, we still argue that the disruption of sexual and reproductive health services may have influenced pregnancy outcomes. Therefore, monitoring the preterm birth rate might be an essential strategy for assessing the quality of maternal and perinatal care and might help providers and policymakers to develop strategies to mitigate the problem.

Contributors

RCP, CMC, LB, JGC, CT and RTS conceived the study. CMC, AM, LAN, TA, and CFS extracted the data from the SINASC. RCP, CT, EECL, LAN, and CFS conducted the statistical analysis, and collaborate in writing the manuscript first draft. RCP, LB, MLC, CMC, and CFS collaborated to statistical analysis. RCP, CT, EECL, LAN, EECL, and

CMC wrote the first Draft. All authors critically reviewed the manuscript. All the authors read and approved the final version of the manuscript.

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Competing Interests

None declared.

Data availability

The datasets analysed during the current study are publicly available from the Brazilian Live Birth Information System (SINASC) http://svs.aids.gov.br/dantps/cgiae/sinasc/.

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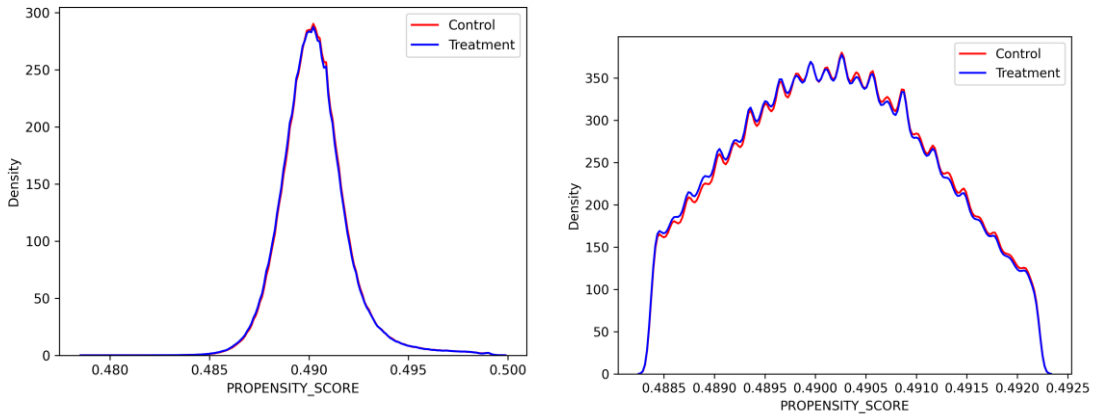
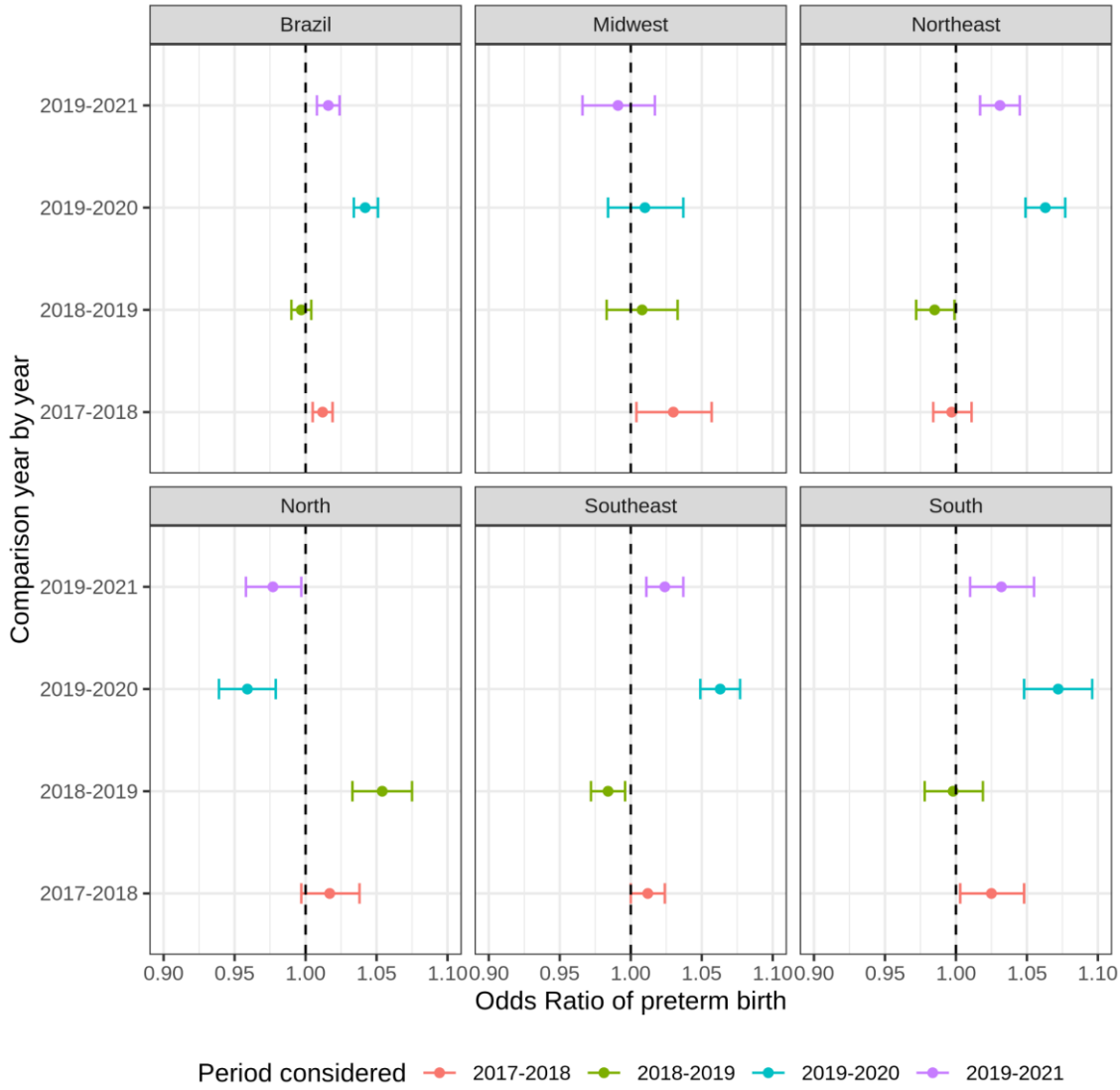
Figure 1: Example of Kernel density estimate (KDE) plot for the Propensity Score referring to births in Brazil in the years 2019 and 2020.



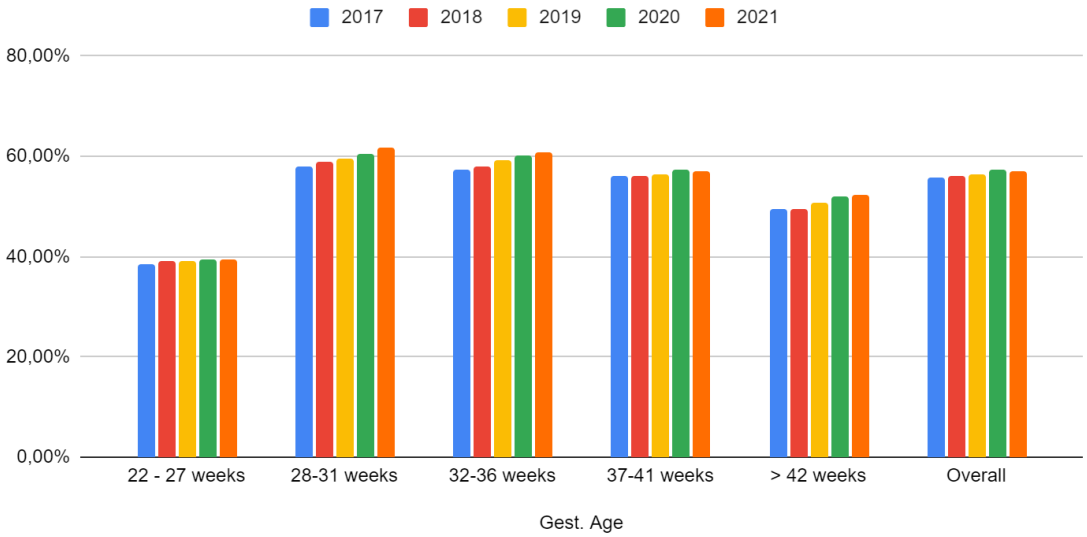
Source: Brazilian Live Birth Information System (SINASC) (2023).

Figure 2: Odds-ratios of preterm birth for Brazil and its regions 2017 to 2021.



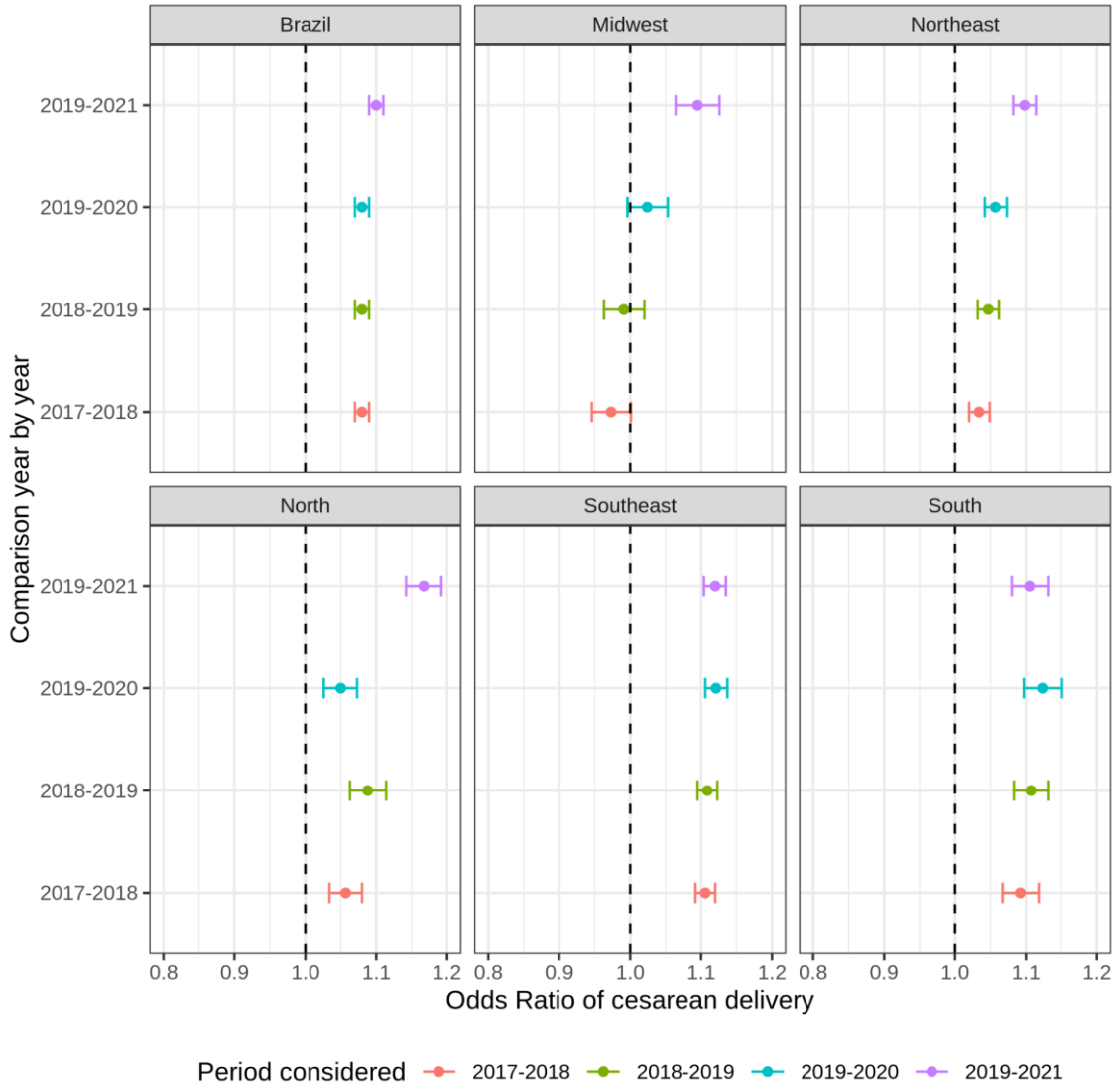
Source: Brazilian Live Birth Information System (SINASC) (2023).

Figure 3: Caesarean delivery rate for categories of gestational ages in Brazil (2017 to 2021).



Source: Brazilian Live Birth Information System (SINASC) (2023).

Figure 4: Odds-ratio of caesarean delivery among preterm babies in Brazil and regions (2017 to 2021).



Source: Brazilian Live Birth Information System (SINASC) (2023).

Table 1 – Descriptive statistics for Brazil live births 2019, 2020 and 2021.

Variables	*2019*		*2020*		*2021*	
	%	**N 2,849,146**	*%*	**N 2,730,145**	*%*	**N 2,672,046**
Gestational Age at delivery						
Term	87.64	2,497,002	87.40	2,386,104	87.28	2,332,351
Preterm	11.09	315,831	11.31	308,702	11.32	302,677
Not stated/Unknown	1.27	36,313	1.30	35,339	1.38	37,018
Mother's age						
<19	10.38	295,832	9.88	269,839	9.62	257,026
19-34	69.84	1,989,893	69.90	1,908,361	69.93	1,868,652
>34	19.78	563,421	20.22	551,945	20.45	546,368
Parity						
Primiparous	37.54	1,069,586	37.04	1,011,438	36.79	983,071
Multiparous	62.46	1,779,560	62.95	1,718,707	63.20	1,688,975
Mode of delivery						
Vaginal	43.63	1,243,104	42.69	1,165,641	42.89	1,145,970
Caesarean	56.3	1,604,189	57.22	1,562,282	57.04	1,524,013
Not stated/Unknown	0.07	1,853	0.08	2,222	0.08	2,063
Newborn Sex						
Male	51.15	1,457,226	51.20	1,398,043	51.16	1,367,051
Female	48.84	1,391,486	48.78	1,331,658	48.82	1304590
Not stated/Unknown	0.02	434	0.02	444	0.02	405
Race/color						
White	33.85	964,557	32.26	908,547	32.47	867,657
Black	6.19	176,224	6.34	179,416	6.81	181,875

Asian	0.45	12,738	0.44	12,309	0.45	12,106
Brown	55.96	1,594,267	57.06	1,533,251	56.75	1,516,269
Indigenous	0.93	26,373	0.91	25,741	1.06	28,216
Not stated/Unknown	2.63	74,987	3.00	70,881	2.47	65,923
Mother's schooling						
0 to 7 years	16.22	462,063	5.36	431,144	14.21	379,799
8 to 11 years	61.36	1,748,186	62.23	1,698,877	62.62	1,673,570
12 and more	21.27	606,145	21.12	589,807	21.48	583,779
Not stated/Unknown	1.15	32,752	1.31	29,178	1.30	34,898
Mother's marital status						
Single	45.14	1,285,998	47.02	1,283,754	48.39	1,292,963
Married/Cohabit	52.39	1,492,765	50.34	1,374,363	48.76	1,302,820
Widow	0.16	4,693	0.17	4,603	0.19	4,978
Divorced	1.36	38,748	1.45	39,619	1.48	39,576
Not stated/Unknown	0.95	26,942	1.02	27,806	1.19	31,709
Type of pregnancy						
Single	97.76	2,785,200	97.74	2,668,636	97.72	2,611,194
Twin	2.13	60,61	2.11	57,846	2.14	57,061
Triplet and more	0.05	1,467	0.05	1,262	0.05	1,319
Not stated/Unknown	0.07	1,869	0.08	2,401	0.09	2,472
Number of antenatal visits						
None	1.52	43,406	1.73	47,276	1.84	49,085
1 to 3	5.35	152,483	6.04	164,943	5.34	142,687
4 to 6	20.26	577,17	20.70	565,211	19.15	511,652
7 and more	72.43	2,063,669	71.01	1,938,920	73.14	1,954,282
Not stated/Unknown	0.44	12,418	0.50	13,795	0.54	14,430

Source: Brazilian Live Birth Information System (SINASC) (2023).

Table 2 – Logistic regression analysis using Propensity Score Weighting for preterm birth in Brazil 2017-2021.

	Odds Ratio (95% CI)			
	2017-2018	**2018-2019**	**2019-2020**	**2019-2021**
Intercept	157.97*** (152.54-163.60)	31.54*** (29.90-33.27)	33.12*** (31.39–34.95)	35.41*** (33.56-37.36)
Year	1.01** (1.00-1.02)	1.00 (0.99-1.1)	1.04*** (1.03-1.05)	1.02*** (1.01-1.03)
Weight	0.99*** (0.99-0.99)	0.99*** (0.99-0.99)	0.99*** (0.99-0.99)	0.99*** (0.99-0.99)
Mother's age				
19-34	ref.	ref.	ref.	ref.
<19	1.10*** (1.11-1.12)	1.20*** (1.19-1.21)	1.19*** (1.18-1.21)	1.20*** (1.19-1.22)
>34	1.24*** (1.23-1.25)	1.23*** (1.22-1.24)	1.26*** (1.25-1.27)	1.26*** (1.25-1.27)
Multiparous	1.11*** (1.10-1.12)	1.17*** (1.16-1.18)	1.19*** (1.18-1.20)	1.20*** (1.19-1.21)
Caesarean delivery	1.08*** (1.07-1.09)	1.08*** (1.07-1.09)	1.09*** (1.08- 1.10)	1.10*** (1.09-1.11)
Sex				
Female	ref.	ref.	ref.	ref.
Unknown	1.74*** (1.40-2.18)	2.66*** (1.93-3.67)	2.79*** (2.03-3.84)	2.55*** (1.83-3.55)
Male	1.38*** (1.37-1.39)	1.38*** (1.37-1.39)	1.39*** (1.38-1.40)	1.40*** (1.39-1.41)
Race/colour				

White	ref.	ref.	ref.	ref.
Black	0.90*** (0.88-0.92)	0.90*** (0.89-0.91)	0.90*** (0.88-0.91)	0.89*** (0.88-0.91)
Asian	0.90 (0.85-0.95)	0.94 (0.89-0.98)	0.99 (0.94-1.05)	0.97 (0.92-1.03)
Brown	0.98*** (0.97-0.99)	0.99 (0.98-1.00)	1.03*** (1.02-1.04)	1.04*** (1.03-1.05)
Indigenous	1.05*** (1.01-1.10)	1.10*** (1.07-1.14)	1.50*** (1.44-1.54)	1.60*** (1.57-1.63)
Mother's schooling				
12 and more	ref.	ref.	ref.	ref.
8 to 11 years	0.96 (0.95-0.97)	1.04*** (1.03-1.05)	1.05*** (1.04-1.06)	1.05*** (1.03-1.06)
0 to 7 years	1.00 (0.99-1.01)	1.14*** (1.13-1.16)	1.15*** (1.13-1.16)	1.14*** (1.12-1.16)
Mother's marital status				
Single	0.95*** (0.94-0.96)	0.97*** (0.96-0.98)	0.93*** (0.92-0.94)	0.95*** (0.94-0.96)
Married/Cohabit	ref.	ref.	ref.	ref.
Widow	1.00 (0.92-1.98)	0.99 (0.89-1.09)	0.96 (0.88-1.06)	1.05 (0.96-1.15)
Type of pregnancy				
Single	ref.	ref.	ref.	ref.
Twin	2.91*** (2.86-2.96)	3.44*** (2.36- 3.52)	3.44*** (3.36-3.52)	3.49*** (3.42-3.58)
Triplet and more	11.70*** (9.55-14.34)	4.36*** (2.68 – 7.09)	4.56*** (2.86–7.28)	5.24*** (3.29- 8.34)
Number of antenatal visits				
None	ref.	ref.	ref.	ref.
1 to 3	1.52*** (1.48-1.57)	1.59*** (1.53-1.64)	1.50*** (1.45-1.55)	1.44*** (1.39-1.49)
4 to 6	1.26*** (1.23-1.30)	1.32*** (1.28-1.37)	1.28*** (1.24-1.33)	1.24*** (1.20-1.29)
7 and more	0.66***	0.70***	0.70***	0.67***

	(0.64-0.67)	(0.68-0.72)	(0.67-0.72)	(0.65-0.69)
N	4.379.012	4.363.507	4.218.951	4.169.362

Source: Brazilian Live Birth Information System (SINASC) (2023).
Significance level p <0·05*, p <0·01** and p <0·001***

4.6. Artigo submetido para publicação na revista *International Journal of Gynecology & Obstetrics*.

The Impact of SARS-CoV-2 variants of concern on severe maternal outcomes in Brazil: An ecological study.

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Synopses: The risk of severe maternal outcomes among symptomatic pregnant people remains significant, although the Omicron variant poses a lower risk compared to the Delta and Gamma periods.

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Abstract:

Background: Study data suggests that the effect of SARS-CoV-2 variants of Concern (VOC) on maternal and perinatal health varies. Our study compared maternal outcomes during Omicron's predominance with Delta and Gamma's periods in Brazil and Regions. **Methods:** We conducted a retrospective ecological study that involved Brazilian pregnant and postpartum women who had Severe Acute Respiratory Syndrome (SARS) caused by COVID-19. The data was analyzed from the Brazilian Influenza Epidemiological Surveillance Information System for the period of March 2021 to August 2022, encompassing the Gamma, Delta, and Omicron predominance. The primary outcome was maternal death, and the secondary outcome was maternal intensive care unit (ICU) admission and composite of maternal outcome. We reported the crude and adjusted odds ratios (OR) with a 95% confidence interval (CI). All analyses were conducted using Python Software, and a $p < 0.05$ was considered significant. **Results:** We analyzed data from 11,474 registries, out of which 6,635 (57.8%), 1,469 (12.8%), and 3,370 (29.4%) were from the periods of Gamma, Delta, and Omicron variant predominance, respectively. Our analysis revealed that during the Omicron predominance period, the risk of ICU admission reduced significantly by 72% and 76% compared to the Gamma and Delta variants predominance eras, respectively. Additionally, the risk of maternal mortality also reduced significantly during the Omicron predominance period compared to the previous VOCs (Gamma and Delta variants) predominance era, with a reduction of 69% and 51%, respectively. We found that the presence of fever, dyspnoea, respiratory discomfort, lower oxygen saturation, and fatigue upon admission is associated with a higher risk of ICU admission and maternal mortality during the Omicron era compared to the previous VOCs ($p < 0.001$). Furthermore, during the Omicron era, the composite of severe maternal outcomes was more prevalent than the Gamma era at the country level (OR: 1.13; 95%CI 1.01-1.26). **Conclusion:** The Omicron variant was associated with a lower risk of severe maternal outcomes than the Delta and Gamma period predominance era. However, symptomatic pregnant and postpartum women still have a significant risk of severe maternal outcomes during the Omicron variant era. Upon admission, the presence of cough, fever, and dyspepsia was found to be associated with worse maternal outcomes.

Keywords: Severe maternal morbidity, pregnancy, postpartum, maternal mortality, variants of concerns, COVID-19, Intensive care admission, Brazil.

Introduction

The global outbreak of COVID-19 has brought about significant disruptions in the realm of sexual and reproductive health, both within and between nations. These disruptions have not only posed a threat to public health but have also resulted in numerous casualties and significant life expectancy reduction. (1)

The pandemic's far-reaching effects have created a challenging situation, necessitating the implementation of effective measures to address the numerous issues arising from these disruptions. (2)The pregnant and postpartum were at great vulnerability and risk of severe infection and poor outcomes - an increased risk on intensive care unit (ICU) admission, mechanical ventilation, maternal mortality, preterm birth, foetal death compared to a non-pregnant women and pregnant women without SARS-CoV-2 infection. (3, 4)

The SARS-Cov-2 changed over time, and some virus changes has affected its capability of spread, disease severity and the performance of COVID-19 interventions, including the vaccine-induced immunity. (5, 6)Currently, there are 5 main SARS-CoV-2 variants of concern (VOCs), the alpha, Beta, Gamma, Delta and Omicron.(7) Data from individual and national data-based studies suggested that the impact on maternal and perinatal health varied across different SARS-CoV-2 variants and variants of concern (VOC).(8)

As of 26 November 2021, the World Health Organization, advised by the Technical Advisory Group on SARS-CoV-2 Virus Evolution, designated the Omicron (B.1.1.529) as a variant of concern. Since then, this variant has become the most dominant worldwide.(9) In the general population, the risk of hospitalization and severe disease was lower during the Omicron predominance compared to the previous Variants of Concern. (10) Among pregnant and recently pregnant women, data suggested a similar pattern, higher transmissibility and less severe maternal and neonatal outcomes during the Omicron predominance era. (11-13)

In low and middle-income countries, the evidence on the impact of different SARS-CoV-2 variants of concern among pregnant and postpartum women is paucity. The study aimed to compare the severity of maternal outcomes during the Omicron variant with Delta and Gamma predominance periods in Brazil.

Methods:

Study design and procedures

We conducted a national population-based ecological study analysing data from the Brazilian Influenza Epidemiological Surveillance Information System, available at https://opendatasus.saude.gov.br. We extracted data of pregnant and postpartum women with Severe Acute Respiratory Syndrome (SARS) and included data of participants with laboratory-confirmed COVID-19 infection from March 2021 to August 2022. We have analysed data on pregnant and postpartum women infected with COVID-19 during the Gamma, Delta, and Omicron predominance periods.

To properly characterize the COVID-19 case, we extracted from the online public available database the following information: the age of the participants, the region in which they reside, signs and symptoms, the onset of symptoms, skin colour, gestational period, educational background, the presence of underlying medical conditions, and the number of COVID-19 vaccines administered, including the date of administration. Hospital admissions, mechanical ventilation, and admission to the intensive care unit (ICU) were also extracted. The date of ICU admission, the type of COVID-19 diagnostic test, the sample used, the results, health status at hospital discharge, and the date of the SARS-CoV-2 diagnostic test were considered.

The participant's date of death, if applicable, was recorded. All the data were cross-checked for accuracy and consistency. We considered the predominance period for the Gamma variant from March to July 2021, for the Delta variant from September to November 2021, and for the Omicron variant from January to August 2022. To determine the period of variant predominance, we used the Brazilian GISAID data platform as of 26 October 2022 since the information about specific viral strains affecting the participant was unavailable. We considered a cut-off period for specific VOC predominance if it contributes to more than 70% of COVID-19 infections nationally. We excluded all COVID-19 cases of the VOC era overlapping. The era of VOC predominance can range from 70% to 95% of the sample being analysed. (13)

The primary outcome was maternal death, and the secondary outcome was maternal intensive care unit (ICU) admission and composite of maternal outcome. The

composite maternal outcome was defined as a patient that have experienced at least one of the following outcomes: maternal death or UCI admission.

Statistical analysis

We compared the participant's baseline characteristics and clinical features using frequency, percentages, and chi-square test for trend analysis. To estimate the odds of severe maternal outcomes, we used bivariate and logistic regression models to compare the Omicron period with the Delta and Gamma predominance, as well as the Delta period with the Gamma period in Brazil. Furthermore, we conducted a stratified analysis considering Brazilian federal regions.

We also explored the association between symptoms at admission and severe maternal outcomes for each VOC era. Our results are reported as crude and adjusted odds ratios (OR) with a 95% confidence interval (CI). The effect size was adjusted for maternal age, gestation period, skin colour, vaccine status, education and region. All analyses were conducted using Python Software, and a p <0.05 was considered significant.

Ethics declarations

The study utilized de-identified data from a public database. Thus, ethical approval was not required.

Results

We included 11 474 registries, of which 6635 (57.8%), 1469 (12.8%), and 3370 (29.4%) were from Gamma, Delta and Omicron predominance eras, respectively, **Figure 1**. Almost 75% (8630) were pregnant women, of which 9% (786) were in the first trimester of gestation. The baseline participants' characteristics were similar across the three groups (p > 0.05). Nearly 42.5% (4872) of participants were from the southeast region, and 38.2% (4387) had attained secondary education, **Table 1**. There were non-significant differences in the frequency of SARS-CoV-2 infection symptoms within the three VOCs' predominance eras (p > 0.05), **Table 2**. During the Omicron predominance period, the risk of ICU admission has significantly decreased by 72% and 76% compared to the Gamma and Delta variants predominance era, respectively.

Moreover, the risk of maternal mortality has also significantly reduced during the Omicron predominance period compared to the previous VOCs (Gamma and Delta variants) predominance era, with a reduction of 69% and 51%, respectively, **Table 3**. Upon admission, the presence of fever, dyspnoea, respiratory discomfort, lower oxygen saturation, and fatigue is associated with a higher risk of ICU admission and maternal mortality during the Omicron era compared to the previous VOCs ($p < 0.01$), **Table 4 and 5**. During the Omicron era, the composite of severe maternal outcomes was more prevalent compared to the Gamma era at the country level (OR: 1.13; 95%CI 1.01-1.26). The stratified analysis shows a two-fold increased risk of the composite of severe maternal outcome in the Midwest Brazilian region (OR: 2.04; 95%CI 1.02 – 4.11) during the Omicron era compared to Delta era and a 62% higher risk of the composite outcome (OR: 1.62; 95%CI 1.23 – 2.13) during the Omicron era compared to Gamma era, **Figure 2**.

Discussion

Similar to the general population, from an ecological perspective, our findings suggest a lower prevalence of maternal severe outcomes during the Omicron variant predominance.(14)

In Brazil, the Omicron variant predominance era was associated with lower-risk of maternal ICU admission and mortality compared to the Gamma and Delta Variant predominance period. The risk of maternal mortality had 69% and 51% reduction during the Omicron variant predominance compared to the Gamma and Delta variant predominance respectively. These findings are similar to the previous individual's studies and systematic review. (13, 15, 16)In addition, are consistent to the studies that reported lower risk of ICU admission during the Omicron predominance compared to the previous COVID-19 variants of concerns. (17) These findings suggest a decreased severity of Omicron variant compared to the previous variants of concern despite the higher transmissibility. Moreover, the vaccination may paid a pivotal role on the reduction of severe COVID-19 case during the Omicron predominance period. (17-19) Although we did not assessed the impact of vaccination for each variant, the multinational study by Villar and colleagues has highlighted the benefit of full vaccination on the reduction of the risk of severe symptoms, outcomes and maternal

death. (20) Moreover, a study conducted in Brazil has suggested a lower severe maternal outcome among vaccinated pregnant and post-partum women. (21, 22)

Upon admission to the health care facility, participants who were experiencing fever, respiratory discomfort and lower oxygen saturation during the omicron predominance had higher risk of ICU admission and maternal death compared to the Gamma and Delta variant. These figures are in line with the multi countries Latin America studies where 69% and 73% of maternal death COVID-19 related experienced fever and dyspnoea at admission. (23)

Nevertheless, our data suggest similar symptoms prevalence across the three periods. This finding are different from the study conducted by Mndala L and colleagues. The difference might be explained by the unequal COVID-19 vaccine coverage between the countries. (18)

In the era of Omicron, the presence of fever and dyspnoea upon admission has been found to be linked with a worse maternal outcome. According to a systematic review conducted by Verde and colleagues, fever and dyspnoea were the most frequent symptoms observed at admission among COVID-19 maternal casualties. (24)This finding highlights the severity of the impact of COVID-19 on mothers and emphasizes the need for identification and management of symptomatic women.

The risk of composite of severe maternal outcome was higher during the omicron era compared to Delta and Gamma predominance period in the Midwest Brazilian region. This figure may suggest different impact of COVID-19 pandemic within the Brazilian regional; the difference may be due to the pre-existent social inequalities between regions and uncoordinated implementation of non-pharmaceutical interventions across the country. (25, 26)

The study's results ought to be considered in light of certain limitations. Specifically, the retrospective design, missing data, and potential reporting bias may have had an impact on the findings. Additionally, the study was restricted to evaluating maternal outcomes exclusively, and the ecological VOC case definition may be susceptible to VOC period misclassification.

Notwithstanding these limitations, the study benefited from a comprehensive database including regional and participant-level data from Brazil. This allowed for an

assessment of the impact of the Gamma, Delta, and Omicron variants on maternal outcomes across diverse Brazilian regions.

Conclusion: The Omicron variant was associated with a lower risk of severe maternal outcomes compared to the Delta and Gamma period predominance era. However, the risk of severe maternal outcome among symptomatic pregnant and postpartum women remained significant during the omicron variant era.

Author contributions

CMC and RCP conceptualized the study. CMC, AM, LT and CS were responsible for designing the data form, extract de data from the public database, data management and quality assessment. CMC, CS, LT, CT and RCP conducted the statistical analysis. CHM, and AM, JGC wrote the first draft of the manuscript. All the authors read and approved the final version of the manuscript.

Data availability

The data has been extracted from the Brazilian public database and is accessible at https://opendatasus.saude.gov.br.

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Conflicts of Interest

The authors have no conflicts.

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Figures Title/legends

Figure 1: Study flowchart

Figure 2: Risk estimate for severe maternal outcomes among laboratory-confirmed COVID-19 cases during the Delta and Gamma era compared to the Omicron era in Brazil and its regions.

Figure one: Study flowchart

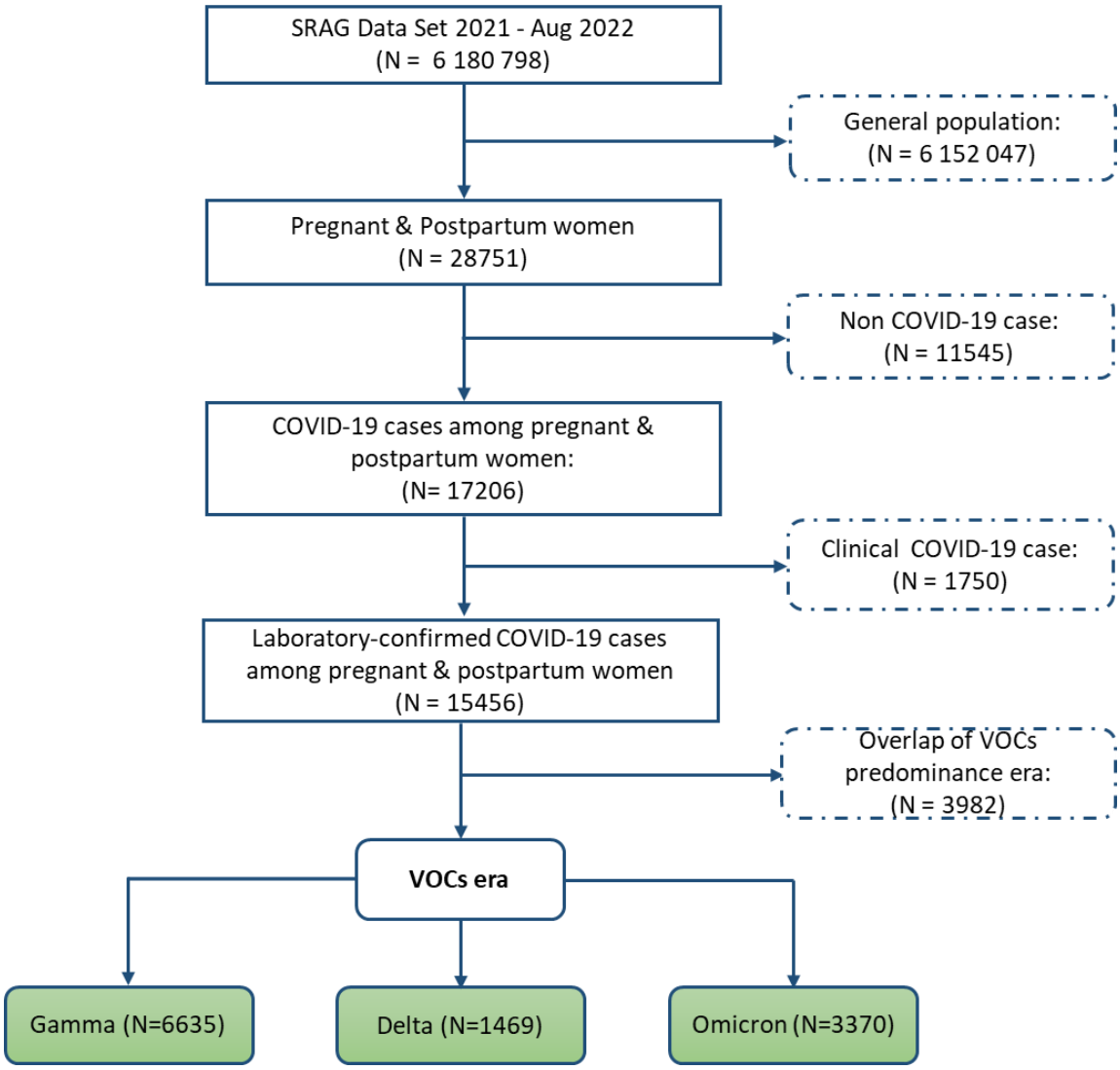
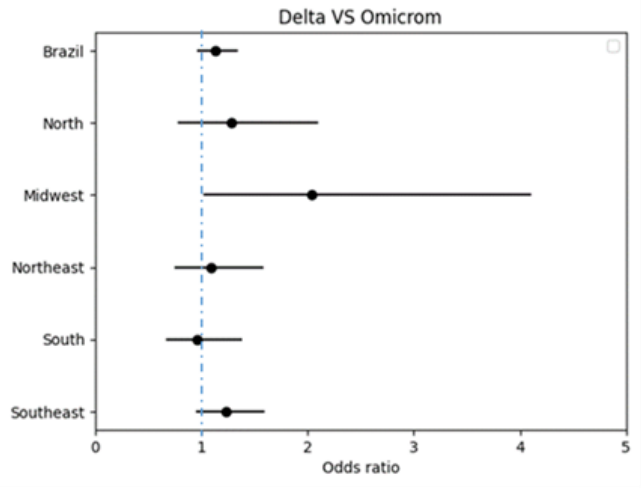
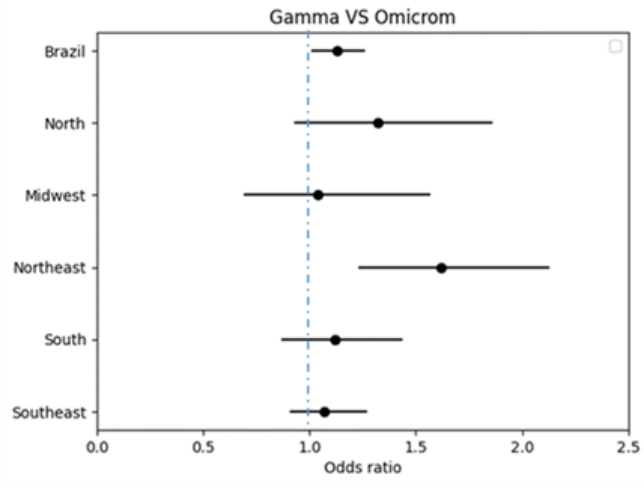


Figure 2: Risk estimate for severe maternal outcomes among laboratory-confirmed COVID-19 cases during the Delta and Gamma era compared to the Omicron era in Brazil and its regions.





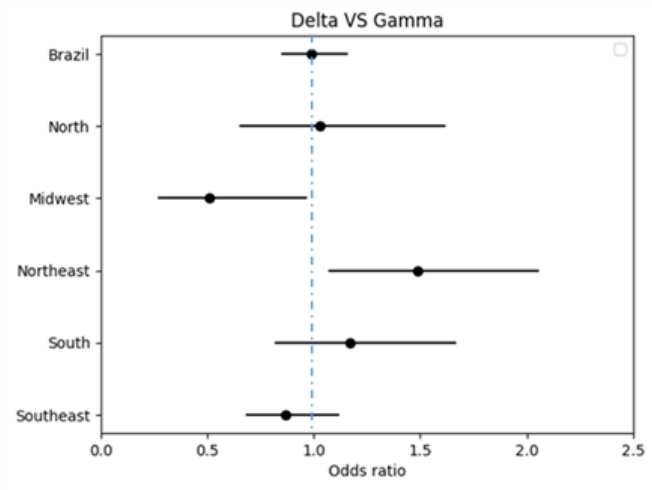


Table 1: Sociodemographic and obstetrical characteristics of Brazilian pregnant and postpartum women with laboratory-confirmed SARS-CoV-2 infection during de Gama, Delta and Omicron predominance era.

Characteristics	SARS -CoV-2 VOCs			p-value
	Gamma N (%)	Delta N (%)	Omicron N (%)	
***Age** (Years)*				0.42
≤19	418 (6.3)	102 (6.94)	229 (6.8)	
20-24	1057 (15.93)	212 (14.43)	503 (14.93)	
25-29	1514 (22.82)	337 (22.94)	767 (22.76)	
30-34	1590 (23.96)	354 (24.1)	813 (24.12)	
35 -39	1323 (19.94)	301 (20.49)	667 (19.79)	
≥ 40	733 (11.05)	163 (11.1)	391 (11.6)	
Ethnicity [a]				0.79
White	2690 (46.52)	595 (46.59)	1354 (46.61)	
Black	307 (5.31)	75 (5.87)	171 (5.89)	
Others	2786 (48.18)	607 (47.54)	1380 (47.5)	
Region				0.70
North	538 (8.11)	136 (9.26)	277 (8.22)	
Northeast	1177 (17.74)	268 (18.24)	606 (17.98)	

Southeast	2823 (42.55)	622 (42.34)	1427 (42.34)	
South	1223 (18.43)	241 (16.41)	606 (17.98)	
Midwest	874 (13.17)	202 (13.75)	454 (13.47)	
Schooling [b]				0.61
None or Primary incomplete	25 (0.88)	4 (0.66)	10 (0.71)	
Primary	236 (8.34)	55 (9.11)	136 (9.59)	
Secondary	2040 (72.06)	423 (70.03)	1005 (70.87)	
College or more	530 (18.72)	122 (20.2)	267 (18.83)	
COVID-19 Vaccination status [c]				0.99
At least 1 dose	855 (20.57)	190 (21.13)	439 (20.88)	
Unvaccinated	3302 (79.43)	709 (78.87)	1663 (79.12)	
Gestational period [d]				0.85
1st Trimester	456 (6.87)	95 (6.47)	235 (6.97)	
2nd Trimester	1397 (21.06)	323 (21.99)	694 (20.59)	
3rd Trimester	3000 (45.21)	664 (45.2)	1531 (45.43)	
Post-partum	1567(23.62)	333 (22.67)	791 (23.47)	

Underline medical condition				
Asthma [e]	216 (8.77)	41 (7.75)	109 (8.74)	0.87
Diabetes [f]	504 (19.59)	106 (19.03)	222 (17.27)	0.46
Kidney disease [g]	53 (2.21)	17 (3.27)	30 (2.48)	0.67
Cardiovascular disease [h]	463 (18.23)	93 (17.16)	223 (17.35)	0.80

Missing value: a) 1509, b) 6621, c) 4316, d) 388, e) 7234, f) 7060, g) 7342, h) 7107

Table 2: Clinical features of SARS-CoV-2 infection among Brazilian pregnant and postpartum women, by SARS-COV-2 Variant of Concern predominance era.

Characteristics	SARS -CoV-2 VOCs predominance era			
	Gamma N (%)	Delta N (%)	Omicron N (%)	p-value
Fever	3438 (60.46)	762 (61.25)	1754 (61.05)	0.81
Cough	4636 (77.24)	1037 (78.68)	2337 (76.82)	0.63
Dyspnoea (Shortness of breath)	4033 (69.30)	900 (69.34)	2045 (69.02)	0.96
Diarrhoea	607 (12.39)	128 (11.99)	298 (12.02)	0.89
Vomiting	596 (12.16)	131 (12.15)	321 (12.92)	0.89
Fatigue	1699 (33.95)	386 (35.25)	862 (34.15)	0.85
Sore throat	1362 (26.71)	300 (26.57)	698 (26.97)	0.99
Hyposmia/Anosmia (Loss of smell)	910 (18.65)	221 (20.77)	471 (23.70)	0.47
Ageusia (Loss of taste)	838 (17.17)	193 (18.14)	422 (17.15)	0.82
Desaturation/Oxygen saturation <95%	3067 (55.73)	712 (57.51)	1553 (55.44)	0.53
Abdominal pain	490 (10.21)	108 (10.28)	258 (10.64)	0.94

Table 3: Risk estimates for severe maternal among COVID-19 infection laboratory-confirmed cases, by the SARS-COV-2 VOCs, in Brazil, adjusted for age, gestational period, Brazilian region, education and COVID-19 vaccine status.

Maternal outcomes	**Omicron (N of events)**	**Gamma (N of events)**	**Gamma** Vs **Omicron**		**Delta (N of events)**	**Delta** VS **Omicrom**		**Gamma Vs Delta**	
	Bad/Good	**Bad/Good**	**OR (95% CI)**	**aOR (95% CI)**	**Bad/Good**	**OR (95% CI)**	**aOR (95% CI)**	**OR (95% CI)**	**aOR (95% CI)**
ICU admission	332/2480	2130/3621	0.23 (0.20-0.26)	0.35 (0.23-0.34)	469/789	0.23 (0.19-0.26)	0.19 (0.10-0.42)	1.01 (0.89-1.14)	1.51 (1.06 -2.16)
Maternal death	110/2689	881/4858	0.24 (0.20-0.29)	0.31 (0.19-0.52)	153/1103	0.30 (0.23-0.38)	0.49 (0.20-1.16)	0.77 (0.65-0.93)	0.74 (0.46-1.18)

Table 4: Association of clinical features of SARS-CoV-2 infection at admission and maternal death by SARS-COV-2 VOCs' predominant era in Brazil.

Symptoms	SARS -CoV-2 VOCs predominance era			p-value
	Gamma	Delta	Omicron	
	OR (95% CI)	OR (95% CI)	OR (95% CI)	
Fever	1.18 (1.0 - 1.4)	1.17 (0.78 - 1.75)	**2.09 (1.37 - 3.2)**	**<0.01**
Cough	1.14 (0.94 - 1.38)	1.25 (0.79 - 1.99)	1.46 (0.94 - 2.27)	**<0.01**
Sore throat	1.07 (0.87 - 1.32)	0.83 (0.51 - 1.36)	**0.45 (0.24 - 0.84)**	0.23
Dyspnoea (Shortness of breath)	**3.75 (2.98 - 4.71)**	**3.53 (2.13 - 5.85)**	**11.53 (6.99 - 19.01)**	**<0.01**
Respiratory discomfort	**2.85 (2.37 - 3.43)**	**2.4 (1.58 - 3.66)**	**6.76 (4.33 - 10.55)**	**<0.01**
Desaturation/Oxygen saturation <95%	**3.91 (3.22 - 4.75)**	**4.19 (2.69 - 6.54)**	**13.79 (8.67 - 21.95)**	**<0.01**
Diarrhoea	0.85 (0.64 - 1.13)	0.76 (0.36 - 1.62)	3.31 (1.69 - 6.46)	0.44
Vomiting	0.84 (0.62 - 1.13)	1.23 (0.63 - 2.41)	1.57 (0.82 - 3.02)	0.97
Abdominal pain	0.84 (0.61 - 1.16)	1.43 (0.74 - 2.73)	1.58 (0.83 - 3.04)	0.99
Fatigue	1.02 (0.85 - 1.22)	1.1 (0.71 - 1.71)	**1.78 (1.08 - 2.92)**	**0.01**
Hyposmia/Anosmia	0.78 (0.61 - 1.01)	0.56 (0.3 - 1.05)	2.21 (0.99 - 4.95)	0.73
Ageusia (Loss of taste)	**0.68 (0.52 - 0.89)**	**0.35 (0.16 - 0.78)**	2.35 (1.04 - 5.27)	0.11

Table 5: Association of Clinical features of SARS-CoV-2 infection at admission and ICU admission among pregnant and postpartum women by SARS-COV-2 VOCs predominance era in Brazil

Symptoms	SARS -CoV-2 VOCs predominance era			
	Gamma	Delta	Omicron	p-value
	OR (95% CI)	OR (95% CI)	OR (95% CI)	
Fever	**1.25 (1.1 - 1.42)**	**1.37 (1.04 - 1.8)**	**1.63 (1.23 - 2.16)**	**<0.01**
Cough	**1.35 (1.17 - 1.56)**	**1.53 (1.12 - 2.1)**	**1.2 (0.91 - 1.59)**	**<0.01**
Sore throat	**0.79 (0.67 - 0.93)**	0.95 (0.68 - 1.31)	**0.7 (0.5 - 0.99)**	**<0.01**
Dyspnoea (Shortness of breath)	**4.2 (3.58 - 4.93)**	**4.71 (3.4 - 6.53)**	**4.88 (3.67 - 6.5)**	**<0.01**
Respiratory discomfort	**3.01 (2.63 - 3.45)**	**3.26 (2.46 - 4.34)**	**3.82 (2.87 - 5.08)**	**<0.01**
Desaturation/Oxygen saturation <95%	**4.03 (3.51 - 4.63)**	**5.12 (3.82 - 6.87)**	**6.23 (4.63 - 8.38)**	**<0.01**
Diarrhoea	**0.72 (0.57 - 0.89)**	0.81 (0.5 - 1.31)	1.33 (0.73 - 2.44)	0.30
Vomiting	**0.73 (0.58 - 0.91)**	1.02 (0.63 - 1.65)	1.43 (0.91 - 2.27)	0.21
Abdominal pain	**0.67 (0.53 - 0.86)**	1.0 (0.61 - 1.62)	1.43 (0.91 - 2.27)	0.06

Fatigue	**1.37 (1.2 - 1.57)**	**1.74 (1.29 - 2.33)**	**1.88 (1.35 - 2.62)**	**<0.01**
Hyposmia/Anosmia	**0.74 (0.61 - 0.89)**	0.7 (0.48 - 1.02)	1.0 (0.49 - 2.04)	0.44
Ageusia (Loss of taste)	**0.67 (0.55 - 0.81)**	**0.52 (0.34 - 0.79)**	0.9 (0.43 - 1.9)	0.02

5. DISCUSSÃO GERAL

As situações de emergências em saúde pública (por exemplo a pandemia da COVID-19 e epidemia da Ebola), eventos climáticos extremos, conflitos e crises econômicas, intensificam as fragilidades preexistentes dos sistemas de saúde, comprometendo o acesso equitativo e universal de cuidados de saúde assentes na qualidade e princípios éticos. (108)

A pandemia da COVID-19 acentuou a situação de vulnerabilidade em saúde, saúde materna e perinatal em especial, em diferente contexto ao nível mundial, colocando em situação de risco um dos direitos fundamentais e inalienável das mulheres e dos seres humanos. (109) Os serviços de saúde constituem um dos determinantes cruciais na proteção da mulher durante o ciclo gravídico puerperal dos diversos fatores de riscos modificáveis e não modificáveis inerentes a saúde materna e perinatal. (6)

No entanto, durante a pandemia da COVID-19 os serviços de saúde tiveram falhas no desempenho do seu atributo chave, a provisão de serviços de qualidade, que incluem os serviços preconcepção (que inclui a oferta de serviços de planejamento familiar, manejo de condições médicas preexistentes), consulta pré-natal, assistência ao parto e pós-parto. (108, 110)

A baixa oferta de serviços de saúde básicos e essenciais (redução significativa de consultas pré-natais e de planejamento familiar, em cerca de 39% e 44% respectivamente) associados a falha na proteção dos riscos financeiros relacionados a gastos a saúde (em 2020 os gastos aumentaram em torno de 5.6% a 13.5%) foram fatores determinantes para o aumento da vulnerabilidade em saúde materna, principalmente nas populações minoritárias, com baixo poder aquisitivo, deslocados internos e refugiados. (43, 108, 111)

Em países de baixa e média renda como é o caso de Moçambique e Brasil, a vulnerabilidade tornou-se evidente devido ao sistema de saúde previamente frágil ou fragilizado pela pandemia (redução de acesso aos serviços de saúde - enceramento ou redução da disponibilidade de atendimento pré-natal e serviços de planejamento

familiar) e ausência de estratégias efetivas (implementação ou propagação de não embasada em evidências científicas) para a neutralização dos efeitos deletérios da pandemia da COVID-19 na saúde materna e perinatal.

No Brasil, o Sistema Único de Saúde (SUS), estabelecido em 1990, representa um marco significativo na busca pelo cumprimento do terceiro Objetivo de Desenvolvimento Sustentável, que se relaciona ao Acesso Universal aos Cuidados de Saúde. (112, 113) O SUS abrange aproximadamente 75% da população brasileira. No entanto, devido às vastas dimensões territoriais do país, fragilidades estruturais, crises políticas e políticas de austeridade, bem como à fraca colaboração entre os setores público e privado, criou-se um ambiente propício para a distribuição não equitativa de infraestrutura e recursos humanos no setor de saúde, colocando em risco os avanços alcançados no acesso universal aos cuidados de saúde e a sustentabilidade do SUS. (78, 113, 114)

Igualmente, as adaptações fisiológicas inerentes a gestação, a susceptibilidade aumentada a morbidade materna não grave (ansiedade, depressão, exposição da violência física e por parceiro íntimo), limitações econômicas impostas pela pandemia, implementação de estratégias em saúde dúbias para mitigação dos efeitos da pandemia, deficiente medidas de prevenção de infeções e desfechos adversos associados a infecção pelo SARS-CoV-2, baixo rastreio de agravos de condições de saúde pré-existentes, resultaram em aumento das complicações maternas graves e mortalidade materna no Brasil.

Os dados do nosso estudo (coorte prospectiva na gestação realizada em Maputo) sugeriram que o consumo do álcool e não ter parceiro foram os fatores de maior vulnerabilidade a infeção pelo SARS-CoV-2 e a prevalência da infeção em gestante foi maior que na população geral Moçambicana. A alta prevalência da infeção pelo SARS-CoV-2 observada na população obstétrica moçambicana pode ser atribuída, em parte, à estratégia implementada pelo nosso estudo, que envolveu a testagem universal. Não foram observados casos de morte materna associada à COVID-19 em nossa coorte. Entretanto, evidências da literatura apontam para uma diminuição de 15,3% na razão de mortalidade materna em Moçambique entre os anos de 2019 e 2021. Esse cenário contraria as projeções iniciais e os dados recentes de estudos

epidemiológicos realizados em Moçambique e outros países de baixa renda. (115, 116) Em Moçambique, estimava-se um aumento em cerca de 8% na mortalidade materna devido à redução na prestação de serviços (115). Os progressos na redução da mortalidade materna observados em Moçambique, mesmo durante a pandemia, justificam uma análise detalhada para investigar as estratégias implementadas pelos diversos intervenientes do Sistema Nacional de Saúde de Moçambique (SNS).

O SNS de Moçambique foi estabelecido como uma estrutura unificada após a independência do país em 1975, guardando semelhanças com o Sistema Único de Saúde Brasileiro (SUS). Compreende diversos subsistemas, incluindo o Subsistema Público, gerido pelo Estado moçambicano, o Subsistema Privado, de fins lucrativos e sem fins lucrativos, o Subsistema de Saúde Militar e Paramilitar, e Organizações socioprofissionais, como a Ordem dos Médicos, a Ordem dos Enfermeiros e a Associação Médica de Moçambique. No Subsistema Público, os serviços de prevenção e promoção da saúde são oferecidos gratuitamente, enquanto o acesso aos serviços curativos requer o pagamento opcional de uma taxa simbólica, equivalente a cerca de 10 centavos de real brasileiro. (117)

Desde sua criação, o Sistema de Saúde de Moçambique enfrentou diversos desafios, incluindo altas taxas de analfabetismo, emigração de profissionais qualificados, guerra civil, escassez de instituições públicas de formação de profissionais de saúde, e instabilidade política e militar, especialmente na região central do país. Mais recentemente, desde 2017, o país enfrenta conflitos armados na região norte, com aumento significativo do número de deslocados internos. (117, 118)

Os serviços de saúde em Moçambique foram inicialmente estruturados com base na formação de profissionais de saúde de diferentes níveis educacionais e habilidades, como enfermeiros elementares, básicos e médios, agentes de medicina curativa, agentes de medicina preventiva e técnicos de cirurgia. Além disso, o Ministério da Saúde incorporou parteiras tradicionais, praticantes de medicina tradicional e agentes polivalentes elementares como extensão do SNS, promovendo seu mapeamento e treinamento em áreas como medicina preventiva, promoção da saúde e fornecimento de kits básicos.

Em 2017, o Ministério da Saúde definiu diretrizes para a formação e capacitação de enfermeiros de nível superior (universitário) em diversas áreas, com o objetivo de melhorar a qualidade da assistência no país, incluindo enfermagem geral, saúde materna, enfermagem pediátrica, técnicos superiores em anestesia, cirurgia geral, nutrição e saúde pública.

Apesar dos avanços na formação e capacitação de profissionais de saúde, o Sistema de Saúde de Moçambique enfrenta grandes desafios na busca pelo alcance das metas dos Objetivos de Desenvolvimento Sustentável relacionados ao acesso universal a cuidados de saúde de qualidade (Objetivo 3). Atualmente, a densidade de profissionais de saúde por habitante em Moçambique permanece abaixo dos parâmetros recomendados. Por exemplo, a proporção de médicos é de cerca de 6 por 100.000 habitantes, enquanto no Brasil essa proporção é de 238 médicos por 100.000 habitantes, e a média global é de 370 médicos por 100.000 habitantes. (119) Similarmente, o número de enfermeiros também é inferior à média global, com 29 enfermeiros por 100.000 habitantes, em comparação com uma média global de 400 enfermeiros por 100.000 habitantes. (120)

Em 2022, a Rede Hospitalar de Moçambique abrange 1778 unidades de saúde, compreendendo 1710 unidades de nível primário, 54 de nível secundário, 7 de nível terciário e 7 de nível quaternário. Contudo, a relação população por unidade de saúde ainda supera as recomendações da Organização Mundial da Saúde, com uma média de 17.782 habitantes por unidade de saúde.(121)

O acesso aos serviços de saúde, especialmente aos cuidados primários, apresenta variações significativas em todo o país. Estudos indicam que cerca de dois terços da população moçambicana precisam caminhar mais de 60 minutos para acessar os serviços de saúde primários. Enquanto na Cidade de Maputo a cobertura dos serviços de saúde alcança aproximadamente 69,8%, na Província de Cabo Delgado, na Região Norte, esse número é inferior a 7%. (122) Além disso, os indicadores de acesso aos Serviços de Saúde Sexual e Reprodutiva (SSR) diminuíram no início da pandemia, com reduções de 28% nas consultas de planejamento familiar e 26% nas primeiras consultas pré-natais, e um aumento significativo nos partos fora do ambiente hospitalar, em torno de 74%.(123)

Durante o mesmo período, o investimento em saúde per capita por ano em Moçambique foi metade do recomendado pela OMS e vinte vezes inferior ao investimento em saúde realizado pelo Brasil, com aproximadamente 34,28 USD, 80 USD e 700 USD per capita por ano, respectivamente. (119)

Apesar da recente implementação do sistema de vigilância de eventos vitais, coordenado pelo Instituto Nacional de Saúde e John Hopkins University, a interpretação destes indicadores deve ser realizada com cautela, considerando o contexto de Moçambique onde número significativo partos (36%) e mortes (71%) ocorrem ao nível da comunidade, deficiência de sistemas fidedignos de coleta de informações dados estatísticos de mortalidade (incluindo as causas da morte). (124)

Contudo, as características do Sistema Nacional de Saúde de Moçambique e os desafios atinentes a manutenção em longo prazo do sistema de vigilância da mortalidade materna ressaltam a importância de reflexão sobre as estratégias utilizadas para melhorar esse indicador.

Em 2020, os dados globais de vigilância da mortalidade materna indicam uma estagnação deste indicador vital, e a cada 2 minutos uma mulher morre por causas relacionadas a gestação e parto, e cerca de 95% das mortes ocorrem em países de baixa e média renda. (125)

No entanto, os dados provenientes de Moçambique sugerem que o país está fazendo progressos significativos na consecução das metas estabelecidas pelos Objetivos de Desenvolvimento Sustentável (ODS). Por outro lado, os dados do Brasil indicam que o progresso em direção às metas de desenvolvimento sustentável foi comprometido, especialmente no que diz respeito à cobertura universal em saúde e à redução da taxa de mortalidade materna para menos de 30 mortes por 100 000 nascidos vivos. (40)

As ações para melhoria da qualidade de saúde e bem-estar materno e acelerar a redução da morbidade e mortalidade materna, depende de investimento no sistema de saúde, no manejo das causas imediatas, diretas de incapacidade e morte materna. Igualmente, dos determinantes não biomédicos da saúde e bem-estar materno. (6, 126)

Assente na definição da vulnerabilidade na saúde materna em situação de emergência em saúde pública, o nosso trabalho avalia a ocorrência dos desfechos maternos e perinatais adversos, os fatores relacionados a prevenção de causas diretas (complicações de aborto – através da aferição de disponibilidade de métodos contraceptivos) e indiretas (aceitação e fatores relacionados a aceitação de dose adicionais da vacina da COVID-19) de morbidade e mortalidade materna e perinatal em situação de crise em saúde pública, a pandemia da COVID-19. (127, 128)

A vacinação em gestantes e puérperas iniciou de forma tardia, devido a exclusão das gestantes e puérperas em estudos iniciais sobre a segurança e efetividade da vacina da COVID-19 e falta de políticas públicas que incluíssem este grupo vulnerável como prioritário em campanhas de vacinação contra a COVID-19. A recomendação inicial da OMS sobre a vacinação em gestantes e mulheres lactantes foi em 10 de fevereiro de 2021 e atualizada em 02 de Junho de 2021.(129) A nota técnica sugeria que as mulheres gestantes e lactentes deveriam ter acesso a vacina contra a COVID-19 e que as mulheres deveriam decidir de forma informada sobre o uso da vacina da COVID-19. Até a data da atualização da nota técnica da OMS (Junho de 2021), em Moçambique o uso de vacina da COVID-19 em Gestante era proibido, revelando uma defasagem na resposta aos efeitos deletérios da pandemia. (129) No Brasil, a vacinação em gestante iniciou em Maio de 2021, este processo pode ter sido comprometido pela propagação de desinformações sobre os efeitos adversos da vacina no grupo de gestante e puérperas e a politização da religião.(130) A elevada hesitação em relação à administração de doses adicionais da vacina contra a COVID-19 entre gestantes brasileiras deve ser encarada com preocupação devido a provável politização da religião. Embora o risco de contrair a doença seja menor com a variante Ômicron em circulação, a gravidade dos casos ainda é considerável. Além disso, a hesitação em relação à vacinação pode aumentar devido à diminuição no número de casos graves ou óbitos associados à COVID-19.

Os nossos estudos ilustram e reforçam o papel dos determinantes sociais (exposição a desinformação), fatores individuais e familiares (status marital e consumo de álcool) na morbidade e mortalidade materna. A educação em saúde é uma das estratégias cruciais para redução de eventos maternos adversos (incluído a morbidade materna grave e mortalidade materna), principalmente em situações de emergência em saúde

pública. Por exemplo, dados da literatura indicam que as pacientes com níveis adequados de informações em saúde foram menos susceptíveis a ansiedade e depressão associada a pandemia. (131)

No entanto, o aumento das taxas de prematuridades observada no período da pandemia não se deve exclusivamente a infeção pela COVID-19, mas também devido a influência de fatores potencializados pela pandemia da COVID-19. Por exemplo, parto prematuro iatrogênico, aumento da prevalência de condições obstétricas não potencialmente ameaçadora da vida (depressão, ansiedade, exposição de violência), e agravo de condições medicas pré-existentes (hipertensão arterial crônica, anemia, infeção pelo HIV). (132-138) O aumento do risco de parto prematuro observado em nosso estudo foi leve. Por outro lado, esse mesmo padrão não foi identificado em um estudo individual realizado na Austrália, nem na revisão sistemática conduzida por Chmielewska e colegas (2021). Essas discrepâncias podem estar associadas à maior patogenicidade e gravidade da doença causada pela variante Gamma no Brasil, em comparação com outras regiões do mundo. Além disso, a revisão sistemática realizada por Chmielewska e colegas não incluiu estudos que avaliassem o impacto da variante Gamma nos desfechos perinatais. (96, 139)

As estratégias de mitigação dos efeitos de crises em saúde públicas na saúde da mulher e perinatal devem incluir estratégias holísticas, que englobam os diferentes aspectos interconectados, mutuamente influentes e sinérgicos que possam reduzir a vulnerabilidade materna e afetam a resiliência materna durante o ciclo gravídico puerperal (e além desse período), de modo a garantir que as mulheres sobrevivam durante o período da gestações, tenham uma experiência positiva da gestação (parto e puerpério) e prosperem na sociedade na qual estão inseridas, em consequência de manejo adequado de complicações relacionadas ao ciclo gravido-puerperal que causam incapacidade a mulher além das 6 semanas do puerpério previamente estabelecida.

A redução da mortalidade materna está intrinsecamente ligada à eficácia do sistema de saúde, que deve ser capaz de prover a cobertura universal dos serviços de saúde, enfrentar e mitigar os desafios impostos pelas transições demográficas, climáticas, econômicas e obstétricas. Isso implica em fornecer serviços de saúde de qualidade,

que atendam às necessidades das mulheres em idade reprodutiva, promovendo sua saúde de maneira equitativa e garantindo a confiabilidade e valorização desses serviços pela população. Para reverter o cenário atual, onde mulheres em países de baixa e média renda frequentemente recebem cuidados inadequados, é fundamental garantir que durante as consultas médicas, as gestantes recebam todas as medidas preventivas e curativas recomendadas, conforme evidenciado por estudos como o *Better Birth*. (109, 140) No entanto, para alcançar efetivamente a redução da mortalidade materna, é necessário adotar uma abordagem abrangente, abordando todos os aspectos das chamadas "três demoras", onde a mulher desempenha um papel fundamental nesse processo.(23)

Jornada do Aluno no Programa de Pós-graduação

A trajetória no Programa de Pós-graduação em Tocoginecologia teve início em 2018 com a entrada no programa de mestrado, que se revelou desafiador devido à minha escassa experiência em pesquisa. Contudo, o mestrado foi fundamental para construir bases sólidas na área da pesquisa clínica. Posteriormente, o projeto de pesquisa do doutorado, inicialmente voltado para intervenções no manejo de morbidades maternas não graves, precisou ser reformulado devido à pandemia de COVID-19, direcionando-se para questões de saúde sexual e reprodutiva visando a minimização dos impactos da pandemia.

Dentre os diversos projetos desenvolvidos, destaca-se a implementação da coorte prospectiva em Moçambique, que proporcionou aprendizados valiosos. O estabelecimento de cooperação entre pesquisadores moçambicanos e brasileiros foi fundamental, possibilitando a realização do projeto no país africano. Além disso, essa colaboração agregou experiência em todas as etapas da pesquisa, desde sua concepção até a redação de artigos científicos e relatórios para o Ministério de Saúde de Moçambique.

A implementação da estratégia de testagem para gestantes sintomáticas e assintomáticas, em um contexto de baixa capacidade diagnóstica para COVID-19, foi um desafio superado com a busca por recursos e empréstimos de insumos ao Instituto

Nacional de Saúde de Moçambique. Durante esse período, a formação de uma equipe de pesquisa dedicada também enfrentou dificuldades devido à sobrecarga dos profissionais de saúde e aos riscos associados à implementação da pesquisa em meio à pandemia.

Por outro lado, a busca por recursos para a pesquisa resultou no financiamento do Fundo Nacional de Investigação de Moçambique, viabilizando a continuidade do projeto em Maputo. A execução do estudo também estreitou os laços de ensino e pesquisa com a Universidade Eduardo Mondlane.

Ao longo da pós-graduação, participei de grupos de pesquisa multidisciplinares focado em temas de saúde sexual e reprodutiva. Adicionalmente, a participação em workshops e cursos internacionais contribuiu para a publicação de mais de 20 artigos em periódicos científicos renomados, como o *Lancet Global Health e Scientific Report*.

A oportunidade de realizar revisões por pares em periódicos científicos contribuiu significativamente para minha integração na comunidade científica. Além disso, essa experiência me levou a participar de consultas e grupos de trabalho abordando temas cruciais de alcance global, como a interação entre mudanças climáticas, saúde e direitos sexuais e reprodutivos. Essas iniciativas foram promovidas por instituições renomadas, tais como a Organização Mundial da Saúde e o Instituto Karolinska.

Portanto, a jornada acadêmica do candidato reflete não apenas um percurso de aprendizado e aprimoramento de habilidades técnicas, mas também um compromisso com a pesquisa de relevância global e a busca por soluções inovadoras para desafios complexos na área da saúde sexual e reprodutiva.

6. CONCLUSÃO

6.1. Em situações de emergência em saúde pública, como a pandemia da COVID-19, é crucial promover um esforço colaborativo em diversos níveis (global e regional) para desenvolver conhecimento que permita a formulação de políticas públicas embasadas em evidências. Isso é especialmente importante para atender às necessidades do grupo de mulheres em idade reprodutiva, incluindo aquelas no ciclo gravídico-puerperal, visando assegurar a prestação de serviços de saúde de alta qualidade. A colaboração entre pesquisadores da Rede Brasileira de Estudo da COVID-19 na Gestação (REBRACO) e pesquisadores da Faculdade de Medicina da Universidade Eduardo Mondlane em Maputo, Moçambique, facilitou a realização de pesquisa e a produção de conhecimento sobre a COVID-19 em Moçambique e Brasil.

6.2. As vendas da maioria dos anticoncepcionais modernos reduziram ao longo do ano de 2020; no entanto, o aumento das vendas do implante, do sistema intrauterino de levonorgestrel no sector privado sugerem desigualdade no acesso à contracepção.

6.3. As mulheres grávidas ou puérperas mostraram-se mais hesitantes em aceitar doses de reforço da vacina COVID-19 quando comparadas as mulheres não grávidas. O rendimento familiar, as crenças religiosas, as preocupações com a segurança das vacinas e a percepção de pouca importância das vacinas foram barreiras significativas à aceitação a doses de reforço da vacina. O impacto destes fatores foi mais evidente entre as mulheres grávidas ou puérperas, enfatizando o efeito prejudicial da desinformação entre esta população vulnerável.

6.4. A prevalência de COVID-19 na população obstétrica moçambicana foi maior que na população em geral, e metade das mulheres grávidas e puérperas com infecção por COVID-19 eram assintomáticas. Não ter companheiro e consumo de álcool foram fatores de maior vulnerabilidade à infecção por SARS-COV-2. Além disso, as gestantes tiveram maior vulnerabilidade à COVID-19 comparada as puérperas. Os dados sugerem que as mulheres grávidas têm uma maior frequência de infecção pela COVID-19, reforçando a necessidade de testagem universal, acompanhamento adequado para esta população e aumento das instalações de terapia de suporte para casos de COVID-19 em Moçambique. Além disso, garantir aconselhamento durante os cuidados pré-natais sobre as medidas preventivas da

COVID-19. No entanto, são necessários estudos prospectivos e robustos adicionais para avaliar esses achados**.**

6.5. Nossa análise mostra que a pandemia aumentou a variação regional e disparidade racial no número de nascimentos prematuros no Brasil em 2020 e 2021 em comparação com os anos prévios a pandemia. Embora não tenhamos observado um aumento expressivo de nascimentos prematuros, a interrupção dos serviços de saúde sexual e reprodutiva podem ter influenciado os desfechos gestacionais. Portanto, a monitorização da taxa de nascimentos prematuros pode ser uma estratégia essencial para avaliar a qualidade dos cuidados maternos e perinatais e pode ajudar os profissionais de saúde, os gestores do sistema de saúde e políticos a desenvolverem estratégias para mitigar este problema de saúde pública.

6.6. O período de predominância da variante Omicron foi associado ao menor risco de desfechos maternos graves em comparação com o período de predominância das Variantes Delta e Gamma. No entanto, o risco de desfechos maternos graves entre as gestantes e puérperas com sintomas da COVID-19 permaneceu significativo. A presença de sintomas como febre, tosse e dispneia foi associada a um maior risco de admissão na unidade de terapia intensiva e de morte materna.

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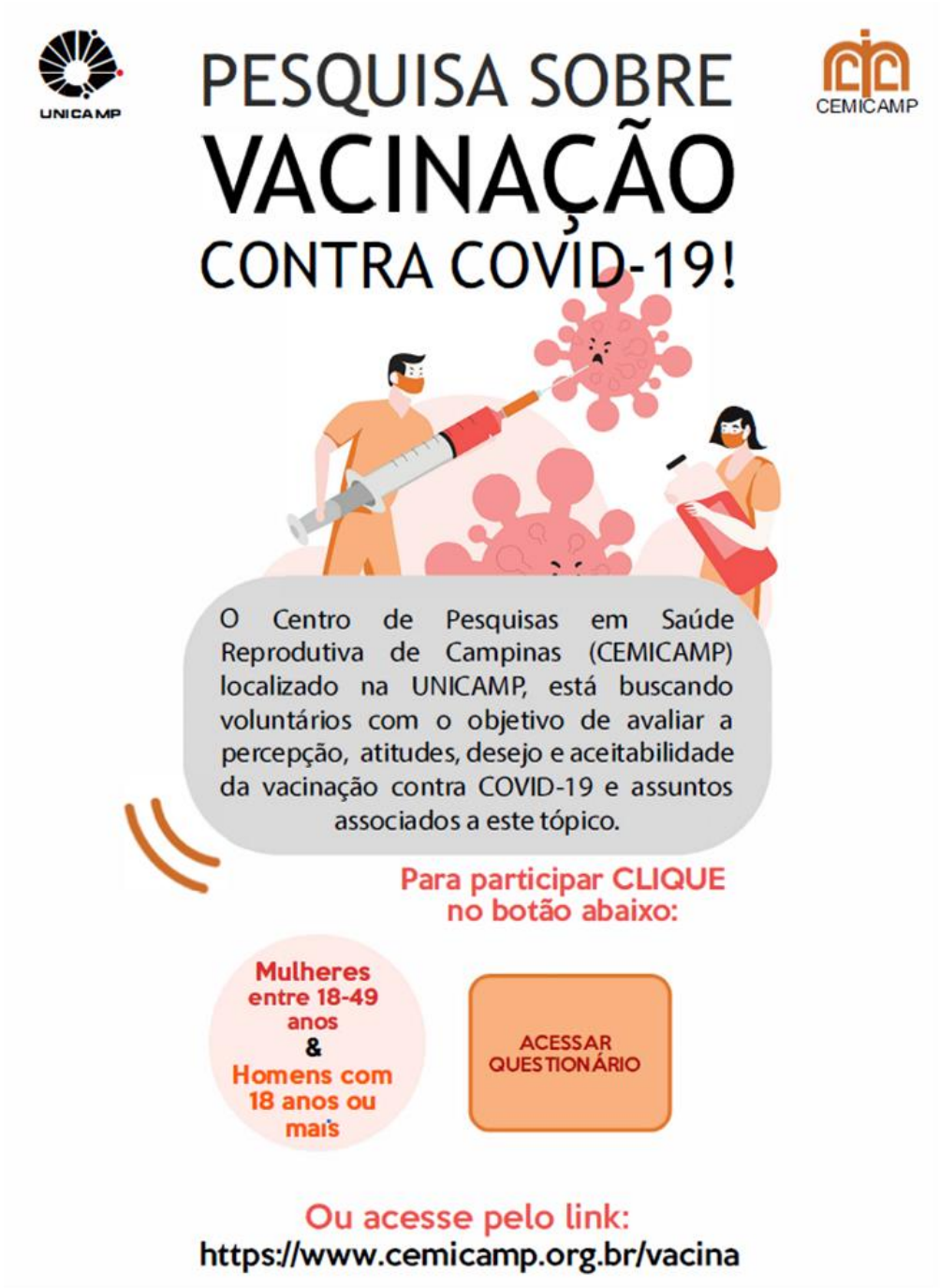
8. APÊNDICES

I. Convites e fichas de coleta de dados do estudo sobre aceitação e factores associados a doses adicionais de vacina da COVID-19 em Mulheres Brasileiras em idade reprodutiva (gestantes e não gestantes) e homens.

CONVITE (eletrônico)



CONVITE (afixados nos ambulatórios)

UNICAMP

CEMICAMP

PESQUISA SOBRE VACINAÇÃO CONTRA COVID-19!

O Centro de Pesquisas em Saúde Reprodutiva de Campinas (CEMICAMP) localizado na UNICAMP, está buscando voluntários com o objetivo de avaliar a percepção, atitudes, desejo e aceitabilidade da vacinação contra COVID-19 e assuntos associados a este tópico.

Para participar escaneie o QR code abaixo:

Mulheres entre 18-49 anos & Homens com 18 anos ou mais

Ou acesse pelo link:
https://www.cemicamp.org.br/vacina

II. QUESTIONÁRIO

"Este formulário contém algumas questões que solicitam dados pessoais seus. Você deseja respondê-las?

[1] ***sim;***

[2] ***não"***

I. DADOS SOCIODEMOGRÁFICOS

1) Idade em anos completos no momento da entrevista: --------

2) Sexo (Por favor, assinale uma resposta)

[1] Feminino

[2] Masculino

[3] Outro

3) Se respondeu feminino [1] à pergunta 2, você está gravida?

[1] Sim

[2] Não

4) A qual grupo você pertence? (Por favor, assinale uma resposta)

[1] Mulher grávida

[2] Mulher não grávida

[3] Parceiro mulher grávida

[4] Parceiro mulher não gravida

[5] Outro

5) Cor da pele: (Por favor, assinale uma resposta)

[1] Branca

[2] Preta

[3] Parda

[4] Amarela

[5] Indígena

6) Estado marital (Por favor, assinale uma resposta)

[1] Casada (o)

[2] Vive junto

[3] Solteira (o) com parceiro (a)

[4] Solteira(o) sem parceiro (a)

[5] Viúva (o)

[6] Separada(o) / Divorciada(o)

7) Renda familiar (Insira o valor total, mensal em reais (considerando todos os membros da família que moram na mesma casa):

[1] Até um salário mínimo (R$ 1.100,00)

[2] De R$ 1.100,00 a R$ 2.999,00

[3] De R$ 3.000,00 a R$ 5.000,00

[4] De R$ 5.000,00 a R$ 7.000,00

[5] Mais de R$ 7.000,00

8) Tipo de habitação

[1] Área Urbana com acesso a água e esgoto

[2] Área Urbana sem acesso a água e esgoto

[3] Área Rural com acesso a água e esgoto

[4] Área Rural sem acesso a água e esgoto

[5] Outro

9) Qual é a cidade e estado onde você vive? (Exemplo Campinas, SP)

10) Situação Ocupacional no momento:

[1] Empregado(a) com carteira de trabalho assinada

[2] Empregado(a) sem carteira de trabalho assinada

[3] Trabalha por conta própria (autônomo)?

[4] Não remunerado (a)

[5] Desempregado (a)

[6] Estudante

[7] Aposentado

[8] Outros

11) Escolaridade

[1] Ensino Fundamental incompleto

[2] Ensino Fundamental completo

[3] Ensino Médio incompleto

[4] Ensino Médio completo

[5] Ensino Superior incompleto

[6] Ensino superior completo

[7] Pós-graduação

12) Religião

[1] Católica

[2] Protestante (Presbiteriana, Batista, Metodista)

[3] Evangélica (Crente, Assembleia, Congregação, Universal)

[4] Espirita

[5] Nenhuma

[6] Outros…

13) Histórico obstétrico (Se respondeu **feminino [1]** à pergunta 2)

[1] Número de gestações (para as grávidas, incluindo a atual)

[2] Número de partos:

[3] Número de abortos:

[4] Número de filhos nascidos vivos:

14) Você tem alguma doença crônica?

[1] Sim

[2] Não

[3] Não sabe

Qual das seguintes doenças crônicas? (Se respondeu sim [1] ou não sabe [3] para a pergunta 14) *(Por favor, pode assinalar mais de uma resposta)*

[1] Hipertensão;

[2] Diabetes;

[3] Câncer;

[4] Uso de imunossupressores;

[5] Asma;

[6] Doença pulmonar obstrutiva crônica;

[7] Outro

15) Você recebeu algum apoio (assistência social ou auxílio emergencial) do governo durante a pandemia?
[1] Sim

[2] não

16) Você tem acesso à internet?
[1] Sim

[2] Não

II. HISTÓRICO DA COVID-19 E VACINAÇÃO CONTRA COVID-19 & INFLUENZA

17) Você já teve COVID?
[1] Sim

[2] Não

[3] Não sabe

18) Você acredita que em algum momento da pandemia você teve COVID-19, apesar de não ter feito o teste de COVID-19?
[1] Sim

[2] Não

19) Você teve necessidade de internação por causa da COVID-19? *(Se respondeu sim à pergunta 17)*
[1] Sim

[2] Não

20) Você já foi vacinada(o)?
[1] Sim

[2] Não

[3] Tive chance de ser vacinada (o) mas decidi não tomar

21) Quantas doses? *(Se resposta sim [1] à pergunta 20)*
[1] 1

[2] 2

[3] 3

[4] 4

22) Quão fácil ou difícil foi ter acesso a vacina contra a COVID-19 *(Assinale uma resposta) (Se resposta sim [1] à pergunta 20)*

Muito difícil	Difícil	Normal	Fácil	Muito fácil

23) Qual foi o motivo para você tomar a vacina contra a COVID-19? *(Por favor, pode assinalar mais de uma resposta) (Se resposta sim [1] à pergunta 20)*
[1] é importante para a minha saúde

[2] obrigatório no meu local de trabalho/ escola/ faculdade

[3] para proteger os meus familiares e amigos

[4] meu familiar/ amigo teve COVID-19

[4] pertenço ao grupo de risco (tenho doença crônica)

[5] Trabalho com o público

[6] Para proteger o meu bebê (para as gestantes)

24) Quais foram os motivos para não tomar a vacina contra a COVID-19? (*Se respondeu não [2] e foi oferecida a vacina, mas decidi não tomar [3] à pergunta 20*) *(Por favor, pode assinalar mais de uma resposta)*
[1] acho que não é segura

[2] não tenho informações suficientes sobre a eficácia da vacina

[3] estou preocupada(o) com os efeitos colaterais

[4] acho que não irá funcionar

[5] não estou em risco de contrair a COVID-19

[6] é contra os meus princípios religiosos

[7] desconheço os efeitos secundários da vacina

[8] sou contra a vacina

[2] outros

25) Você tomou a vacina da gripe / influenza em 2020?
[1] Sim

[2] Não

26) Você tomou a vacina da gripe / influenza em 2021?
[1] Sim

[2] Não

27) Algum membro da sua família e ou amigos teve COVID-19?
[1] Sim

[2] Não

28) Durante a pandemia, você teve que se isolar devido à suspeita de COVID-19/ apresentando sintomas de gripe?
[1] Sim

[2] Não

29) Durante a pandemia, quantas vezes você teve que se auto isolar? (Por favor, assinale uma resposta) *(Se resposta sim [1] à pergunta 28)*
[1] 1 vez

[2] 2 vezes

[3] 3 vezes

[4] 4 ou mais vezes

30) Que tanto a pandemia da COVID-19 impactou no seu dia a dia? (Por favor, assinale uma resposta)
[1] não teve impacto

[2] impactou pouco

[3] teve um impacto moderado

[4] impactou muito

III. CONHECIMENTO E ATITUDE SOBRE A PANDEMIA DA COVID-19 E A VACINA CONTRA A COVID-19.

31) Onde você procura informações e esclarecimentos sobre a COVID-19? *(Por favor, pode assinalar mais de uma resposta)*
[1] Mídia (rádio, televisão, jornais)

[2] Redes sociais (whatsapp, facebook, Youtube, Intagram, Twitter)

[3] Profissionais de saúde

[4] Amigos e familiares

[5] Líderes religiosos

[6] Ministério da Saúde

[7] Governo (Federal, estadual e Municipal)

[8] Cientista envolvidos no estudo da vacina contra a COVID-19

[9] outros

32) Onde você procura informações e esclarecimentos sobre a vacina contra a COVID-19? *(Por favor, pode assinalar mais de uma resposta)*
[1] Mídia (rádio, televisão, jornais, panfletos, cartazes)

[2] Redes sociais (whatsapp, facebook, Youtube, Intagram, Twitter)

[3] Profissionais de saúde, na unidade básica de saúde, posto de saúde

[4] Amigos e familiares

[5] Líderes religiosos

[6] Ministério da Saúde

[7] Governo (Federal, estadual e Municipal)

[8] Cientistas envolvidos no estudo da vacina contra a COVID-19

[9] outros

33) Você acha que as informações sobre a vacina contra a COVID-19 foram adequadamente divulgadas?
[1] Sim

[2] Não

34) Se for necessário, você gostaria de receber uma ou mais doses adicionais da vacina da COVID-19?
[1] Sim

[2] Não

35) Por favor indique as razões de não tomar doses adicionais da vacina contra a COVID-19. (Se respondeu não [2] à pergunta 34)
[1] Ainda não fui chamada para a quarta dose

[2] Por causa dos efeitos colaterais da vacina contra a COVID-19

[3] desconheço os efeitos secundários da vacina (não tenho informações suficientes sobre os efeitos colaterais da vacina)

[4] não tenho informações suficientes sobre a eficácia da vacina

[5] tive efeitos colaterais a vacina

[6] Não sou a favor a vacina

[7] É contra os meus princípios religiosos

[8] Não estou em risco de contrair a COVID-19

[9] outros

Por favor indique as razões de tomar doses adicionais da vacina contra a COVID-19. (**Por favor, pode assinalar mais de uma resposta**) **se respondeu sim [1] à pergunta 34)**

[[1] é importante para a minha saúde

[2] obrigatório no meu local de trabalho/ escola/ faculdade

[3] para proteger os meus familiares e amigos

[4] pertenço ao grupo de risco (tenho doença crônica)

[5] Trabalho com o público

[6] Para proteger o meu bebê (para as gestantes)

III PERCEPÇÃO SOBRE A VACINA DA COVID-19 (**Indique o grau de concordância com as seguintes questões**) **(Por favor, assinale uma resposta)**

36) Eu acredito que a vacina da COVID-19 é efetiva (funciona)

Concordo completamente	Concordo	Não sei	Não concordo	Discordo completamente

37) Eu penso que a vacina é segura

Concordo completamente	Concordo	Não sei	Não concordo	Discordo completamente

38) Eu considero a vacina contra a COVID-19 importante

Concordo completamente	Concordo	Não sei	Não concordo	Discordo completamente

39) Eu concordo com o uso massivo da vacina da COVID-19, incluindo em gestantes e mulheres no pós-parto?

Concordo completamente	Concordo	Não sei	Não concordo	Discordo completamente

40) Eu penso que a COVID-19 é mais letal do que a gripe

Concordo completamente	Concordo	Não sei	Não concordo	Discordo completamente

41) Eu penso que é importante que as mulheres grávidas tomem a vacina para a sua proteção

Concordo completamente	Concordo	Não sei	Não concordo	Discordo completamente

42) Eu penso que é importante que as mulheres grávidas tomem a vacina para proteger as suas famílias

Concordo completamente	Concordo	Não sei	Não concordo	Discordo completamente

43) Eu penso que é importante que todas as pessoas tomem a vacina para a sua proteção.

Concordo completamente	Concordo	Não sei	Não concordo	Discordo completamente

44) Eu penso que é importante que todas as pessoas tomem a vacina para protegerem as suas famílias.

Concordo completamente	Concordo	Não sei	Não concordo	Discordo completamente

45) Eu penso que as pessoas devem tomar a vacina da COVID-19 para que a vida volte ao normal

Concordo completamente	Concordo	Não sei	Não concordo	Discordo completamente

46) Eu penso que as minhas crenças religiosas são compatíveis com o uso da vacina da COVID-19

Concordo completamente	Concordo	Não sei	Não concordo	Discordo completamente

47) Eu me sinto bem informado sobre a vacina da COVID-19

Concordo completamente	Concordo	Não sei	Não concordo	Discordo completamente

48) Eu estou satisfeita (o) com as ações do governo no enfrentamento da pandemia

Concordo completamente	Concordo	Não sei	Não concordo	Discordo completamente

49) O tempo curto no desenvolvimento da vacina é preocupante

Concordo completamente	Concordo	Não sei	Não concordo	Discordo completamente

50) Estou preocupada (o) com os efeitos colaterais da vacina da COVID-19

Concordo completamente	Concordo	Não sei	Não concordo	Discordo completamente

51) Quão preocupada (o), você ficaria em pegar COVID-19 se não tomasse a vacina?

Muitíssimo completamente	Muito preocupado	Preocupado	Pouco preocupado	Sem preocupação

52) Há algum comentário adicional que você gostaria de fazer sobre a COVID-19 e a vacinação contra a COVID-19? (Se sim, por favor descreva abaixo)

Obrigado por participar da nossa pesquisa.

9. ANEXOS

9.1. Produção cientifica adicional.

9.1.1. Artigo publicado na revista *Scientific Reports*

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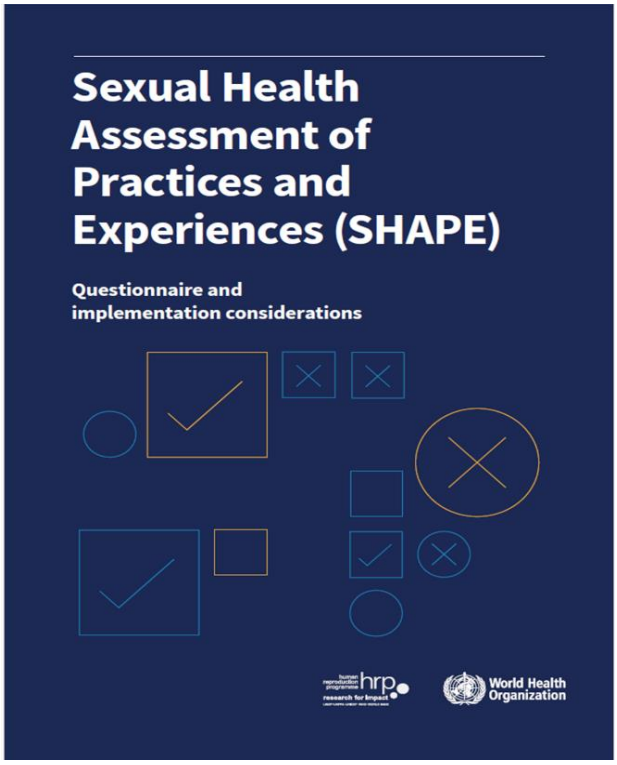
Article | Open access | Published: 11 July 2022

The COVID-19 pandemic in Brazilian pregnant and postpartum women: results from the REBRACO prospective cohort study

Renato T. Souza, Jose G. Cecatti, Rodolfo C. Pacagnella, Carolina C. Ribeiro-Do-Valle, Adriana G. Luz, Giuliane J. Lajos, Guilherme M. Nobrega, Thayna B. Griggio, Charles M. Charles, Silvana F. Bento, Carla Silveira, Fernanda G. Surita, Maria J. Miele, Ricardo P. Tedesco, Karayna G. Fernandes, Sérgio H. A. Martins-Costa, Frederico J. A. Peret, Francisco E. Feitosa, Rosiane Mattar, Evelyn Traina, Edson V. Cunha Filho, Janete Vettorazzi, Samira M. Haddad, Carla B. Andreucci, REBRACO Study Group + Show authors

Scientific Reports **12**, Article number: 11758 (2022) | Cite this article

9.1.2. Manual publicado no website da Organização Mundial da Saúde



Acknowledgements

The World Health Organization (WHO) would like to thank the many individuals who contributed to the development of this document.

The multi-year process to develop Sexual Health Assessment of Practices and Experiences (SHAPE) questionnaire was co-led by Lianne Gonsalves and Vanessa Brizuela from the WHO Department of Sexual and Reproductive Health and Research, in Geneva, Switzerland, which includes the UNDP-UNFPA-UNICEF-WHO-World Bank Special Programme of Research, Development and Research Training in Human Reproduction (HRP).

Coordination of the study titled "Cognitive testing of a survey instrument to assess sexual practices, behaviours, and health-related outcomes" – known as the CoTSIS Study – was led by Vanessa Brizuela and Lianne Gonsalves, both of WHO/HRP, Switzerland, and Erin Hunter of Clemson University, United States of America (USA) (formerly of the University of Sydney, Australia). They were closely supported by Kirsten Black and Elizabeth Fine both from the University of Sydney, Australia. Lale Say and Anna Thorson of WHO/HRP provided guidance throughout project planning and design. Manjulaa Narasimhan of WHO/HRP provided guidance for the questionnaire's publishing and dissemination.

Sincere thanks are due to all research collaborators who participated in the CoTSIS Study. Following are the **CoTSIS Study research team members from the 19 participating countries**, listed alphabetically by country: **Australia** – Sharyn Burns, Roisin Glasgow-Collins, Jacqueline Hendriks, Claudia Hodges, Hanna Saltis (Collaboration for Evidence, Research and Impact in Public Health, Curtin University); **Bangladesh** – Fahmida Akter, Md. Shoeb Ali, Md. Khaledul Hasan, Tania Jahir, Md. Sharful Islam Khan, Rizwana Khan, Shabnam Koli, Md. Mahbubur Rahman, Nahian Soltana, Fahmida Tofail (International Centre for Diarrhoeal Disease Research, Bangladesh - icddr,b); **Botswana** – Mbabi Bapabi, Emily Hansman, Chelsea Morroni, Neo Moshashane, Aamirah Mussa, Kehumile Ramontshonyana (Botswana Sexual and Reproductive Health Initiative, Botswana–Harvard AIDS Institute Partnership); **Brazil** – Silvana Bento, Montas Laporte, María Makuch, Charles Mpoca, Aline Munezero, Karla Padua, Vilma Zotareli (Centro de Pesquisas em Saúde Reprodutiva de Campinas); **Canada** – Elissa Aikema, Kathleen Deering, Brontë Johnson, Emma Kuntz, Carmen Logie, A.J. Lowik, Frannie Mackenzie, Kat Mortimer, Sophie Myers, Mika Ohtsuka, Chelsey Perry, Travis Salway, Colleen Thompson, Larissa Watasuki (Centre for Gender & Sexual Health Equity); **Colombia** – Juliana Fonseca, Rocío Murad, Danny Rivera, Daniela Roldán, Diana Zambrano (Asociación Profamilia); **Ghana** – William Akatoti, Emmanuel Anaba, Emelia Atta, Caroline Badzi, Adom Manu, Emefa Modey, Kezia Obeng, Deda Ogum Alangea, Godfred Sai, Kwasi Torpey (Department of Population, Family and Reproductive Health, School of Public Health, University of Ghana); **Guinea** – Mamadou Dioulde Balde, Sadan Camara, Aissatou Diallo, Ramata Diallo, Alama Diawara, Siaka Faro, Maria Kourani Kamano, Djiba Keita, Alpha Oumar Sall, Anne Marie Soumah, Amadou Oury Toure (Centre for Research in Reproductive Health in Guinea); **Indonesia** – Ifta Choiriyyah, Fahdilla Noviyanti, Rizka Rachmawati, Siswanto Wilopo (Center for Reproductive Health, University of Gadjah Mada); **Italy** – Roberta Galizia, Carlo Lai, Filippo Maria Nimbi, Chiara Simonelli, Renata Tambelli (Dipartimento di Psicologia Dinamica, Clinica e Salute, Sapienza Università di Roma); **Kenya** – Kenneth Juma, Beatrice Maina, Peterrock Muriuki, Emmanuel Otukpa (African Population and Health Research Center); **Malaysia** – Mohamad Aznuddin Abd Razak, Noor Ani Ahmad, Fazila Haryati Ahmad, Nazirah Alias, Norsyamilina Che Abdul Rahim, Mohd Shaiful Azlan Kassim, Lee Lan Low, Kartiekasari Syahidda Mohammad Zubairi, Muhammad Solihin Rezali, Norhaftzah Sahril, Nik Adilah Shahein, Norliza Shamsuddin, (Institute for Public Health, National Institutes of Health, Ministry of

9.2. Aprovação ética dos projetos de pesquisa

REPÚBLICA DE MOÇAMBIQUE
MINISTÉRIO DA SAÚDE
COMITÉ NACIONAL DE BIOÉTICA PARA A SAÚDE
IRB00002657

Exmo. Senhor
Dr. Jahit Sacarlal
Faculdade de Medicina

Ref:373/CNBS/20 **Data 27 de Julho de 2020**

Assunto: Aprovação do Comité Nacional de Bioética para Saúde (CNBS) ao protocolo de estudo intitulado: "*Aspectos clínico e epidemiológico da infecção pelo SARS-CoV-2 (COVID 19) na população obstétrica moçambbicana e nos seus recém-nascidos – Coorte prostectiva*"

O Comité Nacional de Bioética para Saúde (CNBS) analisou as correcções efectuadas no protocolo de estudo intitulado: "***Aspectos clínico e epidemiológico da infecção pelo SARS-CoV-2 (COVID 19) na população obstétrica moçambbicana e nos seus recém-nascidos – Coorte prostectiva***", Registado no CNBS com o número 61/CNBS/2020, conforme os requisitos da Declaração de Helsínquia.

Não havendo nenhum inconveniente de ordem ética que impeça a continuação do estudo, o CNBS dá a sua devida aprovação aos seguintes documentos:

- Protocolo de estudo, *versão 02 de 14 de Julho de 2020;*
- Consentimento Informado, *Versão 2 de 15 de Julho 2020;*
- Assentimento Informado , *versão 02 de 15 de Julho de 2020.*

Todavia, o CNBS informa que:

1- Qualquer alteração a ser introduzida no protocolo, incluindo os seus anexos deve ser submetida ao CNBS para aprovação.
2- A presente aprovação não substitui a autorização administrativa.
3- Não houve declaração de conflitos de interesse por nenhum dos membros do CNBS.
4- A aprovação terá a validade de um ano, terminando esta a 27 de Julho de 2021. Os investigadores deverão submeter o pedido de renovação da aprovação um mês antes de terminar o prazo.
5- Recomenda-se aos investigadores que mantenham o CNBS informado do decurso do estudo.
6- A lista actualizada dos membros do CNBS esta disponível na secretaria do Comité.

Sem mais do momento, queiram aceitar as nossas mais cordiais saudações.

O Presidente

Dr. João Fernando Lima Schwalbach

C/c: CIBS-FM&HCM

Endereço:
Ministério da Saúde - 2º andar dto
Av. Eduardo Mondlane / Salvador Allende
Maputo - Moçambique

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Comissão de Pesquisa
CAISM/UNICAMP

PARECER CIRCUNSTANCIADO DE PROJETO DE PESQUISA ANALISADO PELA COMISSÃO DE PESQUISA/CAISM/UNICAMP

IDENTIFICAÇÃO		
1. Título do Projeto:. REBRACO - REde BRAsileira em estudos do COVID-19 em Obstetrícia		
2. Pesquisador Responsável: Profa. Dra. Maria Laura Costa do Nascimento		
3. Instituição do Pesquisador: FCM-UNICAMP		
4.LocalondeserárealizadaaPesquisa: Hospital da Mulher Prof. Dr. JoséAristodemo Pinotti - Centro de Atenção Integral à Saúde da Mulher– CAISM – da Universidade Estadual de Campinas.		
5. Nº de inscriçãonoCEP/FCM: /.	**6.** Grupo:	**7.** Data de apresentaçãoaoCEP: / /2020.

APRESENTAÇÃO DO PROJETO:

8. RESUMO Introdução: a Doença do Coronavírus-19 (COVID-19) é uma doença respiratória viral grave que alcançou alta relevância no panorama global nos meses iniciais de 2020. Causada pelo Coronavírus da Síndrome Respiratória Aguda Grave 2 (SARS- CoV-2), demonstrou características epidemiológicas clínicas de rápida disseminação e capacidade de infectar a população geral, adquirindo caráter pandêmico. O conhecimento sobre as repercussões deste vírus é parco na população obstétrica e sua ampliação é necessária, tanto para o enfrentamento da atual pandemia de COVID-19 como para futuras repercussões na saúde materna e perinatal. **Objetivos:** avaliar os aspectos clínicos, epidemiológicos e laboratoriais relacionados à infecção por SARS-CoV-2 na gestação, suas repercussões (maternas e perinatais) e coletar informações relevantes para prover respostas rápidas no enfrentamento da pandemia COVID-19. **Materiais e métodos:** foram definidos 5 subprojetos de atividades que auxiliarão na caracterização da infecção por SARS-CoV-2 na gestação e suas repercussões maternas e neonatais. Primeiro, para a descrição da prevalência da infecção por SARS-CoV-2 na população obstétrica, será realizado um estudo de corte transversal por um período de 3 meses em 3 centros (CAISM, HU/FMJ e HES). Todas as parturientes que derem entrada no Pronto Atendimento (PA) desses hospitais realizarão testes virológicos e sorológicos para SARS-CoV-2. Segundo, serão avaliados os desfechos maternos e perinatais associados à manifestação clínica da doença causada pelo SARS-CoV- 2 (COVID-19), através de um estudo de coorte prospectiva incluindo gestantes com diagnóstico de síndrome gripal e/ou suspeita de COVID-19 atendidas no PA dos 18 centros por um período de 3 meses, estimando-se cerca de 1000 mulheres. As participantes serão testadas para COVID-19 e serão seguidas até ao final da gestação. Durante o seguimento será realizada a avaliação e monitoria dos agravos maternos e do concepto (clínicos, laboratoriais, manejos, disfunções orgânicas e óbitos). O seguimento ambulatorial das participantes da coorte será feito com o auxílio da ferramenta de inteligência artificial – PRENACEL. No terceiro subprojeto, será realizado um estudo de coorte transversal, em que serão coletadas amostras biológicas das participantes com teste sorológico e/ou virológicos positivo para SARS-CoV-2 nos 3 centros (CAISM, HU/FMJ e HES). Em seguida, serão realizadas a análise anatomopatológica e pesquisa viral dos diferentes tecidos e líquidos biológicos maternos e neonatais (sangue, placenta, sangue do cordão umbilical, leite materno, urina, fezes, secreção respiratória inferior, swab de naso e orofaringe) e neonatais (swab da naso e orofaringe). Quarto, um comitê de gestão de monitoramento e avaliação (M&A) será implementado para realizar o levantamento de informações relevantes ao atendimento de casos e fará o planejamento de

UNICAMP - CAMPUS CAMPINAS

PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: Crenças, atitudes e comportamento relacionado a aceitação da vacina da COVID-19 em mulheres brasileiras em idade reprodutiva (gestantes e não gestantes) e seus parceiros.

Pesquisador: Luis Guillermo Bahamondes

Área Temática:

Versão: 1

CAAE: 57410722.3.0000.5404

Instituição Proponente: CEMICAMP - CENTRO DE PESQUISAS EM SAUDE REPRODUTIVA DE

Patrocinador Principal: FUNDACAO DE AMPARO A PESQUISA DO ESTADO DE SAO PAULO

DADOS DO PARECER

Número do Parecer: 5.380.503

Apresentação do Projeto:

As informações contidas nos campos "Apresentação do Projeto", "Objetivo da Pesquisa", "Avaliação dos Riscos e Benefícios" e "Comentários e Considerações sobre a Pesquisa" foram obtidas dos documentos apresentados para apreciação ética pelo CEP e das informações inseridas pelo PESQUISADOR RESPONSÁVEL pelo estudo, na Plataforma Brasil.

Introdução:

A SARS-CoV-2 (COVID-19) é uma infeção sistêmica com predomínio respiratório, incialmente diagnosticada em dezembro de 2019, evolui rapidamente para o nível pandêmico (1, 2). O Brasil, foi um dos países

9.3 Relatório de similaridade

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(State University of Campinas)
FACULDADE DE CIÊNCIAS MÉDICAS
(Faculty of Medical Sciences)
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Campinas, 13 de março de 2024

PARECER NºP067/2024

O documento “Impacto da pandemia da covid-19 na saúde sexual e reprodutiva em moçambique e no brasil: uma avaliação epidemiológica na perspectiva das metas dos objetivos de desenvolvimento sustentável” passou pela checagem de similaridade do sistema Turnitin. O resultado apontou 20% de semelhança. Taxa de semelhança baixa, dentre os apontamentos do sistema, há trechos inerentes ao discurso científico que, obrigatoriamente, se repetem entre as produções e devem ser desconsiderados para avaliação de originalidade no Programa de Pós-Graduação da FCM-Unicamp.

Orientador (a): Prof. Dr. Rodolfo de Carvalho Pacagnella

Aluno (a): Charles M’Poca Charles

Cleusa Telles

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Itens	Apontamentos do Sistema Turnitin	Sugestão
1.	A checagem da tese resultou em 20% de similaridade, considerada baixa.