SAMIRA EL MAERRAWI TEBECHERANE HADDAD

REDE NACIONAL DE VIGILÂNCIA DE MORBIDADE MATERNA GRAVE: EXPLORANDO ASPECTOS METODOLÓGICOS DA ABORDAGEM DO NEAR MISS MATERNO

BRAZILIAN NETWORK FOR SURVEILLANCE OF SEVERE MATERNAL MORBIDITY: EXPLORING METHODOLOGICAL ASPECTS OF MATERNAL NEAR MISS APPROACH

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Orientador: Prof. Dr. JOSE GUILHERME CECATTI

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Tese de Doutorado apresentada ao Programa de Pós-Graduação de Tocoginecologia da Faculdade de Ciências Médicas da Universidade Estadual de Campinas para obtenção do Título de Doutora em Ciências da Saúde, área de concentração em Saúde Materna e Perinatal.

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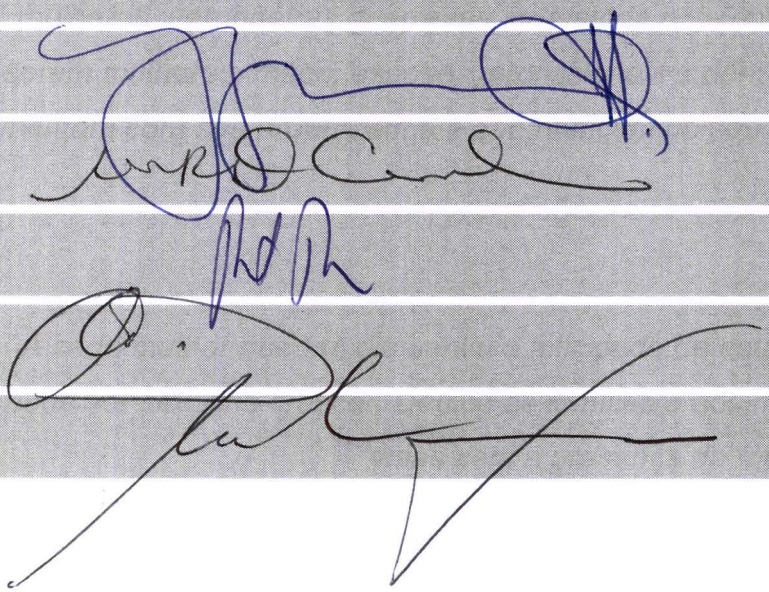

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Dedico este trabalho...

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SUMÁRIO

SÍMBOLOS, SIGLAS E ABREVIATURAS

AAS – Amostragem Aleatória Simples

ANOVA – *Analysis of variance*

AUC – *Area under the curve*

AUROC – *Area under the curve ROC*

CAISM – Centro de Atenção Integral à Saúde da Mulher

CEMICAMP – Centro de Estudos em Saúde Reprodutiva de Campinas

CEP – Comitê de Ética em Pesquisa

CNPq – Conselho Nacional de Pesquisa

CPR – *Cardio Pulmonary Resuscitation*

DECIT – Departamento de Ciência e Tecnologia do Ministério da Saúde

DEFF – Design effect

ICC – *Intraclass correlation coefficient*

ICU – *Intensive Care Unit*

IRB – *Institutional Review Board*

LB – *Livebirths*

MD – *Maternal death*

MDG – *Milenium Development Goal*

MMG – Morbidade Materna Grave

MMR – *Maternal mortality ratio*

MSI – *Maternal Severity Index*

NM – *Near Miss*

NPV – *Negative predictive value*

OMS – Organização Mundial de Saúde

P – *Prevalence*

PLTC – *Potentially life threatening condition*

PPV – *Positive predictive value*

PSU – *Primary sampling unit*

ROC – *Receiver operating characteristic*

SIM – Sistema de Informação de Mortalidade

SINASC – Sistema de Informações de Nascidos Vivos

SOFA – *Sequential Organ Failure Assessment*

SMM – *Severe Maternal Morbidity*

SMR – *Standardized Mortality Ratio*

SRS – *Simple random sampling*

SUS – Sistema Único de Saúde

UNFPA – *United Nations Fund for Population Activities*

WHO – World Health Organization

RESUMO

Introdução: A saúde materna é um dos focos das Metas de Desenvolvimento do Milênio das Nações Unidas para 2015. As mais recentes estimativas sugerem que o número de mulheres que morrem de complicações durante a gestação e parto caiu 47% de 1990 a 2010. Para alcançar a redução planejada de 75% até 2015, a taxa anual deveria cair em 5,5%. Porém, um pouco além da metade do que seria necessário foi conseguido. Para que as metas sejam atingidas, intervenções efetivas são identificadas como necessárias. Além de melhorias com investimentos estruturais locais, uma das bases para a organização de ações efetivas é a obtenção de dados fidedignos e o desenvolvimento de sistemas de informação em saúde. Até um passado recente, não havia padronização de conceitos para morbidade materna grave. Em 2009, condições ameaçadoras da vida foram definidas pela Organização Mundial da Saúde (OMS). Como resultado, critérios clínicos, laboratoriais e de manejo específicos orientam a identificação de casos de near miss. A criação de uma rede de vigilância no Brasil utilizando os novos critérios de near miss poderia trazer um panorama desta condição em um país de média renda e população heterogênea. Com tais informações, novas estratégias para melhoria da assistência à saúde materna e perinatal poderiam ser desenvolvidas, com potencial redução real de mortes. **Objetivos:** Avaliar a homogeneidade amostral dos casos incluídos na Rede, validar os critérios de near miss da OMS, desenvolver um modelo de predição de mortalidade baseado na gravidade dos casos e, a partir deste modelo, avaliar o desempenho dos centros da Rede na prestação de cuidados obstétricos. **Métodos:** A Rede Nacional de Vigilância de Morbidade Materna Grave foi um estudo de corte

transversal multicêntrico implantado em 27 hospitais entre todas as regiões do país, com coleta prospectiva de dados pelo período de um ano, utilizando os novos critérios de near miss da OMS. A partir de 9555 casos incluídos no período, foram calculados os coeficientes de correlação intraclasse (ICC) e efeitos do desenho por cluster das variáveis do estudo. Também, testes de acurácia diagnóstica foram utilizados para validar dos critérios da OMS. Um modelo de regressão logística bivariada foi utilizado para avaliar a correlação entre os critérios de near miss e variáveis distais na ocorrência de morte e desenvolver uma ferramenta para predição de mortalidade, o Maternal Severity Index (MSI). A partir deste modelo, foi analisada a razão entre as mortes observadas e aquelas esperadas de acordo com a gravidade dos casos e avaliados os níveis de desempenhos dos centros na prestação de cuidado obstétrico. **Conclusão:** Os ICC para as variáveis de desfecho da Rede são considerados pequenos, o que indica adequada heterogeneidade amostral. Seus valores podem ser utilizados para o cálculo do tamanho amostral de estudos futuros na área. O uso dos critérios de near miss da OMS para identificação de casos de morbidade materna grave foi validado. O índice de gravidade materna (MSI) pode ser utilizado como ferramenta para predição de mortalidade e avaliação de desempenho e adequação de cuidado em instituições que prestem atendimento a mulheres com condições ameaçadoras a vida.

Palavras-chave: Near miss; Mortalidade materna; Morbidade materna grave – Redes de informação; Vigilância epidemiológica; Gravidez – Complicações e sequelas. .

ABSTRACT

Introduction: Maternal health is one of the focuses of the United Nations' Millennium Development Goals for 2015. The most recent estimates suggest that the number of women who died from complications during pregnancy and childbirth fell 47% from 1990 to 2010. To achieve the planned reduction of 75% by 2015, the annual rate should fall by 5.5%. However, a little more than half of what is required has been obtained. To achieve the goals, effective interventions are identified as necessary. In addition to improvements in local structural investments, one of the bases for the organization of effective actions is obtaning reliable data and the development of health information systems. Until recently, there was no standardazed concept for severe maternal morbidity. In 2009, the World Health Organization (WHO) defined life-threatening conditions. As a result, specific clinical, laboratory and management criteria guide the identification of near miss cases. The development of a surveillance network in Brazil using the new criteria for maternal near miss could bring an overview of this condition in a middle-income country with heterogeneous population. With such information, new strategies to improve maternal and perinatal care could be developed, with potential real reduction of deaths. **Objectives**: To evaluate the homogeneity of the sample included in the network, to validate the WHO near miss criteria, to develop a predictive model of mortality based on severity of cases and,

from this model, to evaluate the performance of the Network facilities in providing obstetric care. **Methods**: The Brazilian Network for Surveillance of Severe Maternal Morbidity was a multicenter cross-sectional study implemented in 27 hospitals from all regions of the country, with prospective data collection for a one year period, using the new WHO maternal near miss criteria. From 9555 cases included in the period, the intraclass correlation coefficients (ICC) and cluster design effects for the variables of the study were calculated. Also, diagnostic accuracy tests were used to validate the WHO criteria. A bivariate logistic regression model was used to evaluate the correlation between the near miss criteria and distal variables in the occurrence of death and to develop a tool for prediction of mortality, the Maternal Severity Index (MSI). From this model, the ratio between the number of observed and expected deaths was analyzed according to the severity of cases and the performance levels of the centers in providing obstetric care was assessed. **Conclusion**: The ICC for the outcome variables of the network are considered small, what indicates adequate sample heterogeneity. Their values can be used to calculate the sample size of further studies in the area. The use WHO maternal near miss criteria to identify cases of severe maternal morbidity has been validated. The maternal severity index (MSI) can be used as a tool for assessing the performance and appropriateness of care in facilities providing care for women with life threatening conditions

Keywords**:** Near miss; Maternal mortality; Severe maternal morbidity - Information networks; Epidemiological surveillance; Pregnancy – Complications and sequelae.

1. INTRODUÇÃO

Mortalidade e Carga de Doença (*Burden of disease*) no mundo

As doenças, os agravos à saúde e as causas de morte podem ser classificadas em três grandes grupos: Grupo I, doenças comunicáveis, condições maternas, perinatais e nutricionais; Grupo II, doenças não comunicáveis; e Grupo III, agravos à saúde. A principal causa de morte no mundo são as doenças cardiovasculares, seguidas por doenças infecciosas e parasitárias, câncer, doenças respiratórias e agravos não intencionais. Entre as vinte principais causas, três estão relacionadas com o período neonatal, 20% do total ocorrem em crianças abaixo de cinco anos, sendo 37% até o primeiro mês de vida, e 1,9% correspondem a condições maternas (WHO, 2008).

As causas do Grupo I ocorrem em quase sua totalidade em populações mais pobres, em países de média e baixa renda. Tipicamente, o aumento do nível econômico reflete-se na transição epidemiológica, quando as doenças não comunicáveis se tornam mais incidentes e prevalentes em populações de maior faixa etária (WHO, 2008). A mortalidade materna e infantil são indicadores de

saúde que evidenciam a grande diferença entre pobres e ricos, entre países e dentro deles (WHO, 2010a).

Burden of disease ou "carga da doença" é a avaliação abrangente da ocorrência de morte e redução da saúde devido à doença ou agravo em particular. Ela quantifica a diferença entre o estado de saúde pós-agravo e a situação ideal de saúde onde todos vivem até a velhice, livres de doença e incapacidade (WHO, 2008). A avaliação geral da carga da doença combina a medida dos anos potencias de vida perdidos por uma morte prematura e os anos de vida saudável perdidos em virtude de incapacidades ou dificuldades causadas pela condição (Murray et al., 1994).

Embora as duas principais causas de morte, doença cardíaca isquêmica e doença cerebrovascular, permaneçam entre as seis principais causas de *burden of disease*, os transtornos depressivos lideram o *ranking* de anos de vida saudável perdidos e, entre as 10 principais causas, três estão diretamente ligadas ao período neonatal. Entre as mulheres, as causas maternas contabilizam duas das dez principais causas de perda de vida saudável, sendo 8% do total nas regiões mais pobres do mundo (WHO, 2008).

Considerando-se que a maior parte dos transtornos depressivos ocorre entre as mulheres em idade reprodutiva, que problemas com o neonato estão entre as principais causas mundiais de morte e *burden of disease* (WHO, 2008), que a morte de uma mãe pode agravar o estado de saúde dos seus filhos e que todos estes fatores podem ser consequentes a afecções no período gestacional e

parto, a saúde materna e a infantil ganham destaque entre as doenças mundiais. O impacto social, econômico e de saúde desse cenário tornou a redução da morte materna e do recém-nascido a mais urgente prioridade para o desenvolvimento do milênio. Alia-se à definição de prioridade o fato de sua ocorrência ser potencialmente evitável na maior parte dos casos e refletir os danos advindos da desigualdade entre populações (WHO, 2008; WHO, 2010b).

Mortalidade Materna e Infantil no mundo

Na Declaração do Milênio das Nações Unidas assinada em 2000, chefes de estado se comprometeram a combater questões primordiais para o desenvolvimento mundial. Oito áreas principais foram identificadas e cada uma delas possui metas e indicadores específicos. As Metas de Desenvolvimento do Milênio estabelecem melhorias a serem alcançadas até o ano de 2015 (WHO, 2010b).

Além de questões econômicas, sociais e de meio ambiente, a saúde é o foco direto de três das oito metas. A Meta 4 estabelece a redução da mortalidade infantil, a Meta 5 a melhoria da saúde materna e a Meta 6 o combate a doenças como HIV/AIDS e malária, entre outras. Entre 1990 e 2015, a mortalidade infantil deveria ser reduzida em dois terços e a mortalidade materna em 75%. Avanços foram alcançados desde o início dos esforços, porém em sua maioria de forma insatisfatória e desigual (WHO, 2010b).

As mais recentes estimativas sugerem que o número de mulheres que morrem de complicações durante a gestação e parto caiu 47% de 1990 a 2010, resultando em um total absoluto de 287.000 mortes de mulheres por ano. Para alcançar a redução planejada de 75% no período, a taxa deveria ser reduzida em 5,5% ao ano. Porém, a subtração dos casos ocorreu a uma velocidade média de 3,1% ao ano, um pouco além da metade do que seria necessário para alcançar a meta. O declínio por regiões do mundo variou em 5,7% ao ano no Leste da Ásia a 0,8% na mesma área excluindo-se a China. As Américas como um todo e o Brasil especificamente colaboraram com aproximadamente 2,5% de redução anual, chegando o país a uma razão de mortalidade materna de 56 para cada 100.000 nascidos vivos em 2010, segundo a Organização Mundial de Saúde (WHO, 2012).

Incertezas nas estimativas de mortalidade geral variam de 1% para países de alta renda, a 15-20% para a África Subsaariana, mostrando grande variação na disponibilidade de dados (WHO, 2011a).

Mortalidade Materna e Infantil no Brasil

No Brasil, a distribuição da morte materna assemelha-se àquela encontrada no mundo. A grande extensão territorial propicia disparidades no grau de desenvolvimento econômico-social e desigualdades cultural e populacional. Tal heterogeneidade também se evidencia na incidência de complicações maternas e nas diferenças de enfrentamento destas complicações (Souza et al., 2007; Brasil, 2010).

De 2000 a 2008, a razão de mortalidade materna brasileira passou de 73,3 para 68,7 mortes para cada 100 mil nascidos vivos. No entanto, o indicador foi calculado apenas para os estados que atingiram índice final de cobertura e regularidade do Sistema de Informação de Mortalidade (SIM) igual ou superior a 80% e cobertura do Sistema de Informação de Nascidos Vivos (SINASC) igual ou superior a 90%, o que corresponde a todos os estados das regiões Sudeste, Sul e Centro-Oeste, com exceção de Minas Gerais, Mato Grosso e Goiás (Brasil, 2010).

O Departamento de Informática do Sistema Único de Saúde - DATASUS, órgão da Secretaria Executiva do Ministério da Saúde, é o principal responsável no país pela regulamentação, fomento e avaliação dos sistemas de informação em saúde. Dentre as suas atividades estão o desenvolvimento, pesquisa e incorporação de tecnologias de informática para a implementação de sistemas e disseminação de informações necessárias às ações de saúde. Também é de sua responsabilidade a manutenção do acervo das bases de dados ao sistema de informações e aos sistemas internos de gestão institucional.

Quando os dados de mortalidade do SUS foram avaliados, constatou-se que não houve interligação entre os dados dos sistemas, havendo, por exemplo, discrepâncias entre os números de morte materna entre o SIM e o Sistema de Informação Hospitalar (SIH) (Sousa et al., 2007). Quanto à análise de morbidade materna através do SIH e correlação com SIM e SINASC, mais uma vez observou-se falta de conexão entre os sistemas, possíveis inconsistências

de informações e problemas no preenchimento da causa de morte e a relação com a gravidez (Sousa et al., 2008a).

Para a mortalidade abaixo de cinco anos, o Ministério da Saúde estimou através de métodos diretos e indiretos uma taxa de 32 óbitos por 1000 nascidos vivos no ano 2000 e 20,5 em 2008. Em 2010, segundo a OMS, 62% das mortes de crianças abaixo de 5 anos foram por causas relacionadas à prematuridade, anormalidades congênitas, asfixia ao nascimento e sepse neonatal (WHO, 2011c).

Estratégias para redução da mortalidade

Para doenças não comunicáveis e mais prevalentes no mundo, como acidente vascular cerebral, sepse e doença coronariana isquêmica, diversos estudos e iniciativas são conduzidos há anos com o objetivo de reduzir desfechos graves e sequelas. Esses estudos permitiram a reunião das melhores evidências científicas, com o delineamento de fatores de risco, critérios clínicos e laboratoriais específicos para diagnóstico e classificação de gravidade, fluxogramas de atendimento de urgência, referência, manejo hospitalar e, ainda, orientações quanto à estrutura de saúde necessária para garantir suporte adequado para esses casos (Adams et al., 2007; Mensah et al., 2007; Dellinger et al., 2008).

A identificação precoce dessas condições a partir de critérios bem estabelecidos e o seguimento das recomendações desenvolvidas foram

capazes de reduzir a mortalidade e as sequelas por doenças cardiovasculares e sepse, ainda que estas doenças continuem com incidência crescente em todo o mundo. Porém, melhores resultados poderiam ser alcançados, também, com a ampla adesão e estruturação dos sistemas de saúde para a implementação desses protocolos (Rogers et al., 2000; Kumar et al., 2011; Tromp et al., 2011).

Com relação à saúde materna, as estratégias atuais ainda se encontram nos estágios iniciais de organização. Diversos estudos foram conduzidos no Brasil e em todo o mundo com o objetivo de monitorar a mortalidade materna e identificar os casos mórbidos (Mantel et al., 1998; Cochet et al., 2003; Amaral et al., 2011; Souza et al., 2010a, Souza et al., 2010b; Paxton et al., 2005; Price at al., 2008; Sousa et al., 2008b; Cecatti et al., 2007). No entanto, a ausência de definições claras e uniformes dessas condições dificultou a comparação entre os dados obtidos das mais diversas fontes, prejudicando, assim, a elaboração de estratégias para redução dos desfechos graves (Say et al., 2004).

Combatendo a mortalidade materna

Para que as Metas de Desenvolvimento do Milênio sejam atingidas, intervenções efetivas através da organização dos sistemas de saúde são identificadas como necessárias. Além de melhorias em infraestrutura, capacitação de recursos humanos e investimentos com insumos, uma das bases para a organização de ações efetivas é a obtenção de dados fidedignos e o desenvolvimento de sistemas de informação em saúde (WHO, 2010b; Islam, 2009; Canada, 2004).

Em concordância com os esforços de instituições internacionais para a redução da mortalidade materna, o Governo Federal brasileiro lançou em 2004 o Pacto Nacional pela Redução da Mortalidade Materna e Neonatal. Esta estratégia foi adotada tendo como fundamento a ampla mobilização de gestores e da sociedade civil na promoção de políticas e ações integradas para melhoria da saúde materna e infantil.

Um dos objetivos do Ministério da Saúde é a implementação de redes assistenciais, visando articulação da atenção primária, média e de alta complexidade. As redes assistenciais são entendidas como fundamentais, sendo necessária a operacionalização dos serviços e da atenção em um processo de compromisso e responsabilização entre sociedade civil e os três níveis da gestão do Sistema Único de Saúde (Brasil, 2004).

A Rede Cegonha está atualmente em processo de implantação no âmbito do Sistema Único de Saúde do Brasil. Esse projeto consiste em uma rede de cuidados que visa assegurar à mulher o direito ao planejamento reprodutivo e a atenção humanizada à gravidez, parto, puerpério e ao abortamento, bem como à criança o direito ao nascimento seguro, crescimento e desenvolvimento saudáveis (Brasil, 2012a). Esta rede tem como objetivos principais garantir um novo modelo de atenção ao parto, acesso, acolhimento e resolutividade do sistema de saúde e a redução da mortalidade materna e neonatal (Brasil, 2012b).

Morbidade materna grave e *Near miss*

A partir de estudos sobre mortalidade materna, foi observado que a morte é precedida por um estado de disfunção grave e/ou falência orgânica, ou seja, uma condição ameaçadora à vida. Esta, por sua vez, é consequente de um estado de menor disfunção, potencialmente ameaçador à vida. Assim, o processo de morte foi entendido como um *continuum* de agravamentos a partir da gestação normal (WHO, 2011b; Geller et al., 2004a).

Neste sentido, devido à baixa ocorrência de morte em países de alta renda e à percepção de que algumas mulheres apresentam condição ameaçadora à vida e sobrevivem (*near miss*), houve maior tendência na condução de estudos sobre morbidade materna grave (Cochet et al., 2003; Geller et al., 2004b).

Até um passado recente, não havia padronização de conceitos e critérios diagnósticos para morbidade materna grave (Pattinson et al., 2003; Geller et al., 2004b; Tunçalp et al., 2012). Os diversos estudos na área eram conduzidos com a utilização de parâmetros variáveis de morbidade extremamente grave, como admissão em unidade de terapia intensiva (UTI) ou diagnósticos clínicos de condições patológicas (Mantel et al., 1998, Waterstone et al., 2001; Mhyre et al., 2011; Donati et al., 2012).

A percepção de que a homogeneidade de nomenclatura e definições era essencial para um adequado monitoramento levou à reunião de entidades e profissionais de saúde para a realização dessa tarefa (Geller et al., 2002; Pattinson et al., 2009).

Em 2009, condições ameaçadoras da vida e suas precedentes condições potencialmente ameaçadoras à vida foram definidas pela Organização Mundial da Saúde. Como resultado, critérios clínicos, laboratoriais e de manejo específicos orientam a identificação de casos de *near miss*. Além disso, diagnósticos de afecções potencialmente ameaçadoras à vida são listados como os mais envolvidos nas complicações graves durante a gestação e o parto (Say et al., 2009).

Near miss é definido como uma mulher que quase morreu, mas sobreviveu a uma complicação durante a gestação, parto ou nos primeiros 42 dias de puerpério (Say et al., 2009). Por apresentar uma maior proporção de casos com relação à ocorrência de óbitos e por permitir que as próprias mulheres relatem o seu processo de adoecimento, a avaliação do *near miss* pode possibilitar o entendimento dos determinantes de morte em mulheres gravemente enfermas, já que o desfecho é a única condição que as diferencia (WHO, 2011b; Say et al., 2009).

Com isso, a análise do processo de cuidado dos casos de *near miss* pode gerar informações para o desenvolvimento de estratégias que interrompam a cadeia de eventos que culminam com a morte materna, reduzindo as ocorrências globais (Mantel et al., 1998).

Após essa definição, estudos em morbidade materna grave passaram a adotar os novos critérios de *near miss* como identificadores de gravidade (Jayaratnam

et al., 2011, Souza et al., 2011) e testes de validação desse conjunto de critérios foram inicialmente conduzidos.

Uma primeira avaliação retrospectiva da utilização dos critérios de *near miss* foi realizada em uma população de pacientes obstétricas admitidas em UTI, utilizando o escore SOFA total máximo (Sequential Organ Failure Assessment) como padrão ouro para comparação. O SOFA é um escore de disfunção orgânica de uso tradicional para população geral, que mostrou alto desempenho na identificação de gravidade de casos de morbidade materna grave (Oliveira-Neto et al., 2012).

Os resultados desse estudo mostraram que os critérios de *near miss* da OMS obtiveram sensibilidade e especificidade de 99,2 e 86%, respectivamente, para a identificação de falência orgânica em pelo menos um dos sistemas (Cecatti et al., 2011).

A Rede Nacional de Vigilância de Morbidade Materna Grave

O Departamento de Tocoginecologia da Faculdade de Ciências Médicas da Universidade de Campinas iniciou desde 2002 uma linha de pesquisa direcionada para a mortalidade e morbidade materna. A transição do estudo da morte para a morbidade materna seguiu a tendência mundial. O Centro de Atenção Integral à Saúde da Mulher (CAISM) é um hospital terciário de referência para a região de Campinas, no estado de São Paulo, uma das regiões mais desenvolvidas do Brasil. Neste local, a ocorrência absoluta de

mortes é relativamente pequena em relação ao número de casos mórbidos, sendo estes mais acessíveis e fidedignos para o estudo da qualidade da assistência obstétrica.

Levando-se em consideração a experiência adquirida com os estudos nesse campo (Cecatti et al, 2007) e o conceito de que um sistema de pesquisa epidemiológica baseado na identificação precoce de casos pode permitir um nível mais adequado de monitorização, cuidado e prevenção de mortes (Pattinson et al., 2003), foi desenvolvida a proposta da Rede Nacional de Vigilância de Morbidade Materna Grave (Cecatti et al., 2009).

Entre os anos de 2009 e 2010, vinte e sete hospitais distribuídos por todas as regiões do Brasil fizeram a coleta prospectiva de dados utilizando os novos critérios de *near miss* e condições potencialmente ameaçadoras à vida. Este estudo de corte transversal multicêntrico utilizou de forma pioneira os critérios da OMS para identificação prospectiva de casos de morbidade materna grave.
Uma forma de integrar, validar, analisar e disseminar as informações é necessária para comparar a importância dos determinantes de mortes prematuras, de perda de saúde e do surgimento de incapacidade nas diferentes populações. Estatísticas e dados de saúde confiáveis são a base para avaliação, monitoramento e desenvolvimento de estratégias e políticas de saúde (WHO, 2008).

Em comparação com a organização atual da evidência para combate da mortalidade mundial por doenças não comunicáveis, a Rede Nacional de

Vigilância de Morbidade Materna Grave foi desenvolvida como uma estratégia científica para avaliação dos determinantes de mortalidade materna através da utilização de critérios padronizados (Haddad et al., 2011).

A criação de uma rede de vigilância utilizando os novos critérios de *near miss* poderia delinear um panorama geral desta condição em um país de média renda e população heterogênea. Além disso, poderia permitir a validação prospectiva desses critérios recém-definidos para utilização futura em diferentes populações. Tais informações poderiam permitir análises comparativas do cuidado obstétrico prestado em diferentes locais e, com isso, o posterior desenvolvimento de estratégias efetivas para combate da mortalidade materna e infantil nacional e mundialmente.

2. OBJETIVOS

2.1. Objetivo geral

Explorar aspectos metodológicos da abordagem ao *near miss* materno da Rede Nacional de Vigilância de Morbidade Materna Grave no Brasil.

2.2. Objetivos específicos:

- Calcular os coeficientes de correlação intraclasse das variáveis do estudo, os efeitos do desenho por cluster e analisar a homogeneidade da amostra obtida;
- Validar os critérios de *near miss* da OMS pela correlação dos critérios, em conjunto e separados, com a ocorrência de morte; e desenvolver um instrumento de predição de mortalidade a partir dos critérios de *near miss* e variáveis relacionadas com gravidade;
- Avaliar a utilização do modelo de predição de mortalidade como ferramenta de avaliação de desempenho de instituições e sistemas de saúde obstétricos, a partir dos centros e dados do estudo da Rede Nacional de Vigilância de Morbidade Materna Grave.

3. PUBLICAÇÕES

O estudo da Rede Nacional de Vigilância de Morbidade Materna Grave é uma iniciativa científica com objetivo de criar um sistema de informação em saúde para identificação de casos de morbidade materna grave, utilizando como parâmetro diagnóstico os novos critérios de *near miss* e condições potencialmente ameaçadores à vida, definidos pela Organização Mundial de Saúde. Além deste corte transversal, o projeto teórico global da Rede contempla a avaliação das possíveis repercussões tardias da morbidade materna grave, estando o projeto da Rede apresentado no Anexo 4.

A execução prática do projeto foi dividida em duas fases. A primeira fase está apresentada no Anexo 5 e corresponde ao método do estudo e à implantação da estrutura operacional da Rede. E a segunda fase corresponde, além das análises dos determinantes da morbidade, aos objetivos desta tese de doutorado, que são a avaliação dos aspectos metodológicos da abordagem do *near miss* como instrumento de vigilância e qualidade da atenção à saúde materna.

Artigo 1:

Haddad SM, Sousa MH, Cecatti JG, Parpinelli MA, Costa ML, Souza JP, for the Brazilian Network for Surveillance of Severe Maternal Morbidity Group. Intraclass correlation coefficients in the Brazilian Network for Surveillance of Severe Maternal Morbidity Study. *BMC Pregnancy Childbirth.* 2012 (aceito).

Artigo 2:

Souza JP, Cecatti JG, **Haddad SM**, Parpinelli MA, Costa ML, Katz L, Say L, on behalf of the Brazilian Network for Surveillance of Severe Maternal Morbidity Group. The WHO Maternal Near-Miss Approach and the Maternal Severity Index (MSI): validated tools for assessing the management of severe maternal morbidity. *PlosOne* 2012; 7(8):e44129.

Artigo 3:

Haddad SM, Cecatti JG, Souza JP, Parpinelli MA, Sousa MH, Costa ML, on behalf of the Brazilian Network for Surveillance of Severe Maternal Morbidity Group. Applying the near miss approach for the evaluation of obstetric care: a worked example from a multicenter surveillance study. *Bulletin of the World Health Organization.* 2012 (submetido).

3.1. Artigo 1

ORIGINAL ARTICLE

Intraclass correlation coefficients in the Brazilian Network for Surveillance of Severe Maternal Morbidity Study

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Abstract

Background: The purpose of the study was to evaluate intraclass correlation coefficients (ICC) of variables concerning personal characteristics, structure, outcome and process in the Brazilian Network for Surveillance of Severe Maternal Morbidity study conducted to identify cases of severe maternal morbidity/near miss using the World Health Organization criteria.

Method: It was a cross-sectional, multicenter study involving 27 hospitals providing care for pregnant women in Brazil. The size of clusters and the mean size of the primary sampling unit were described. Estimated prevalence rates, ICC, their respective 95% confidence intervals, the design effect and the mean size of the clusters were presented for each variable.

Results: Overall, 9,555 cases of severe maternal morbidity (woman admitted with potentially life threatening conditions, near miss or death) were included in the study. ICC ranged from <0.001 to 0.508, with a median of 0.035. ICC was < 0.1 for approximately 75% of the variables. For process-related variables, median ICC was 0.09, with 0.021 for those related to outcome. These findings confirm data of previous studies, and this homogeneity may be considered minor, thus increasing the reliability of these findings.

Conclusions: These results may be used to design new cluster trials in maternal and perinatal health and to help calculate sample sizes.

Keywords*:* intraclass correlation coefficient; maternal near miss; severe maternal morbidity; maternal and perinatal health.

Background

Cluster studies are widely used in epidemiological research to evaluate health interventions and the implementation of public policies. In these cases, selection units or randomization units consist of population groups such as specific geographical areas or healthcare units such as hospitals or healthcare sectors rather than individuals [1,2].

In single-stage cluster sampling, all the subjects belonging to each group are included to obtain the data of interest. Unlike simple random sampling (SRS) in which each individual has an equal likelihood of being selected within the general population, the data obtained from clusters may not be sufficiently representative so as to allow generalization. This is due to the greater homogeneity in the characteristics of the population under observation as opposed to the heterogeneity found in the general population [2].

The reliability of estimates obtained from studies using cluster sampling may be analyzed by measuring inter- and intra-cluster variance. One way of performing these measurements is by calculating the intraclass correlation coefficient (ICC), □, for the variables evaluated in the study [3]. An additional way of doing so is by calculating the design effect (DEFF).

The ICC is a coefficient that measures the homogeneity of the elements within clusters. The ICC of a variable indicates to what extent the variance in a parameter can be explained by the variation between clusters [4,5]. Its value depends on the type of variable, the size of the clusters and the prevalence of the condition [6]. Coefficients closest to zero suggest intraclass heterogeneity, which indicate that the variable is distributed at random among the clusters. Likewise, values close to 1 indicate homogeneity in the sample and the variance of cluster units is greater than that of single elements [2].

The design effect (DEFF) indicates the extent to which the variance in parameter estimation is a result of the study design, in this case the cluster sampling, compared to what would be obtained if sampling had been carried out by the SRS method [7]. For example, a DEFF value of 3 indicates that the variance of the parameter estimation is three times greater than would be found if the study had been based on a random sample of equal size. The components involved in calculating the DEFF are the ICC and the mean size of the cluster, as demonstrated in the formula DEFF = 1 + (cluster size – 1) x ICC [8]. The larger the ICC and the larger the cluster, the higher the DEFF value [9].

The routine adoption of ICC calculation in cluster studies may improve interpretation of the results and facilitate the development of new studies in the field. These values could be used as a correction factor for the calculation of sample size in future cluster studies, thus avoiding underestimates, since, in studies in which SRS is used, the sample size required to achieve sufficient statistical power is generally smaller [4].

The Brazilian Network for Surveillance of Severe Maternal Morbidity study was developed with the objective of identifying cases of severe maternal morbidity/near miss (woman admitted with potentially life threatening conditions, near miss) or death in 27 hospitals distributed throughout Brazil. The participating centers were selected using the following criteria: the availability of each center to participate in the surveillance study, the geographical region of the country in which the hospital was situated and a requirement that the hospital in question performed at least 1,000 deliveries per year. Therefore, the participating centers constituted the primary sampling units, while the subjects at each center represented the units of analysis [10].

The objective of the present report is to evaluate the intraclass correlation coefficients of the variables associated with outcome, process, personal characteristics and structure, based on the data collected by the Brazilian Network for Surveillance of Severe Maternal Morbidity, as well as the design effects.

Methods

The Brazilian Network for Surveillance of Severe Maternal Morbidity, established in 2009, conducted a cross-sectional, multicenter study involving 27 hospitals providing care for pregnant women in Brazil. The objective of this network was to identify cases of severe maternal morbidity/near miss, using the criteria established by the World Health Organization (WHO) to characterize these conditions [11]. According to this definition, a maternal near miss is a woman who experienced a very serious complication during pregnancy and almost died but survived at least until the 42nd day of postpartum period [11].

The selection of clusters was based predominantly on the location of the hospitals in order to ensure broad coverage throughout the country, and on a minimum of 1,000 deliveries per center per year to enable the calculated sample size to be reached. The sample size calculation was based on an prevalence of 8 cases of near miss for every 1,000 deliveries [12], a maternal death ratio of 140 for every 100,000 liveborn infants, with confidence level of 95%, and considering a precision level of 8/1,000 for near miss and 8.5/1,000 for maternal death; it was added approximately 25% based on the fact that this definition of near miss had not yet been tested. In result, around 75,000 deliveries would have to be monitored to identify approximately 600 cases of near miss and 100 maternal deaths. The study was evaluated and approved locally by the respective Institutional Review Board of each participating hospital and also by the National Council for Ethics in Research.

Over the course of one year, all the pregnant women admitted to these institutions were monitored. Women found to have any of the morbidity criteria were included in the analysis. The data of interest to the study were collected from the women's charts immediately after they were discharged from hospital [13]. After data collection was complete in June 2010, procedures were initiated to verify and correct any inconsistencies to ensure the quality of the data obtained.

These procedures included daily check of all data inputted in the database, appointment of possible inconsistence to researchers, correction of errors and programmed check of all dataset at the end of study.

Data analysis

Initially, the cluster size and the mean size of the primary sampling unit (PSU) obtained from the total sample of 9,555 women were described. The estimated prevalences of each one of the dichotomized variables, the intraclass correlation coefficients (ICC), their respective 95% confidence intervals (95%CI), the design effects (DEFF) and the mean size of the clusters for each one of the variables were calculated. The software programs used for the analysis were SPSS, version 17.0 [14] and Stata, version 7.0 [15], taking into consideration the cluster sampling plan (centers) in the data analysis. The information on health facilities and live births for the whole country came from official data [16,17].

Sampling plan used in the Brazilian Network for Surveillance of Severe Maternal Morbidity study

A single-stage cluster sampling was used, with 27 primary sampling units (PSU) corresponding to the 27 participating centers (hospitals). The sampling plan did not involve stratification of the PSU or weighting of the data. The unit of analysis (subject) was the registration of each woman admitted with potentially life threatening conditions, near miss or death.

Prevalence – ratio estimator (r) [2]

$$r = \frac{y}{x} = \frac{\sum y_\alpha}{\sum x_\alpha} = \frac{\sum_{\alpha=1}^{a} \sum_{\beta=1}^{X_\alpha} y_{\alpha\beta}}{\sum_{\alpha=1}^{a} x_\alpha}$$

in which $y = \sum_{\alpha} y_{\alpha} = \sum_{\alpha} \sum_{\beta} y_{\alpha\beta}$ (α for cluster and β for individual) is the total number of subjects in the sample possessing a certain category (for example "Yes") for the variable $y_{\alpha\beta}$ (dichotomized); for example, *y*: the total number of subjects in the sample with "prenatal care at the same facility", and $x = \sum_{\alpha} x_{\alpha}$ is the size of the available sample (valid) for that variable, where x_{α} is the sample size for the cluster 'α'.

For this study, the ratio estimator is:

$$r = \frac{y}{x} = \frac{\sum_{\alpha=1}^{27} y_{\alpha}}{\sum_{\alpha=1}^{27} x_{\alpha}}$$

Intraclass correlation coefficient – ICC (Roh)

According to Kish [2], the intraclass correlation coefficient is:

$Roh = \frac{s_a^2 - s_b^2/b}{\hat{s}^2}$, where s_a^2 is the variance between clusters; s_b^2 is the variance within clusters; b is the size of clusters and $\hat{s}^2$ is the estimate of $S_{\cdot}^2$ (the variance in individual level). The estimate $\hat{s}^2$ is obtained by: $\hat{s}^2 = s_a^2 + \frac{b-1}{b} s_b^2$

Stata's equivalent computing formula [15] is:

$$ICC = \frac{(F-1)a/n}{1+(F-1)a/n}$$

where ‘F’ is the Snedecor’s F-value from the ANOVA table and ‘a’ is the number of groups. The variance estimate for ICC is obtained by an extensive asymptotic formula, and because this it was not showed.

Design effect - DEFF [2]

$$Deff = \frac{\text{var}_{actual}(r)}{\text{var}_{SRS}(r)} = \frac{s_a^2/a}{s^2/n}$$

where $\text{var}_{\text{actual}}(r)$ is the estimated variance according to the complex design being studied and $\text{var}_{SRS}(r)$ is the variance in the estimator considering the design as if it were calculated using a SRS of the same size, *n*.

- Variance estimator of *r* under the design being studied:

- $\text{var}_{actual}(r) = \dfrac{\dfrac{1}{(a-1)}\sum_{\alpha=1}^{a}(r_\alpha - r)^2}{a}$ Variance estimator of *r* under SRS:

$$\text{var}_{SRS}(r) = \frac{r.(1-r)}{(n-1)}$$

where r is the ratio estimator under the SRS.

Recalculation of the sample size

Using the ICC from the main outcome as a correction factor [18]:

$$n^* = a/ICC \cdot (Deff-1+ICC)$$

Where ‘a’ is the number of clusters, ‘Deff’ the design effect and ‘ICC’ the intraclass correlation coefficient of the main outcome.

Results

Of the 82,388 deliveries performed in the participating institutions during the study period, 82,144 liveborn infants and 9,555 cases of maternal morbidity were included in the study. The mean size of each cluster was 354 and the distribution of cases per center and region and of the liveborn infants per region is shown in Table 1.

The ICCs ranged from <0.001 to 0.508, with a median of 0.035. The ICC was below 0.1 for approximately 75% of the variables. In this block of variables, the median ICC was 0.021, while in the other 25%, median ICC was 0.195. The ICCs for the variables related to the process are shown in Table 2, with values ranging from 0.001 to 0.508 (median 0.09), while DEFF values varied from 1.5 to 292.63 (median 20.52).

Table 3 shows the variables related to outcome, with ICCs that ranged from < 0.001 to 0.375 (median 0.021) and DEFF values of 0.94 to 289 (median 6.24). ICC values were < 0.05 for approximately 74% of the variables associated with outcome, while the proportion of variables for which ICC was < 0.07 was almost 80%.

Tables 4 and 5 show the ICC values with their respective 95% confidence intervals, prevalence rates, DEFF values and the mean size of the clusters for the variables referring to population/obstetric characteristics and structure, respectively. With the exception of some variables related to structure, particularly those associated with delays in the service or healthcare system, ICC values were very low.

Based on the fact that the sample size calculation did not take into account the ICC for the primary outcome of interest, because it was not available from other studies at the time of project development, the sample size was recalculated using the ICC for the variable near miss / deaths as the correction factor.

This was an exercise to evaluate if our sample would have been sufficient for analysis considering the cluster design. This variable was used because it is the main outcome of interest

in this study and its value was 0,077. Using the formula for recalculating the sample size in such sitations [18], results indicate that a sample size of 7,072 would be needed to identify the near miss / death cases and it corresponds to 74% of the total number of subjects included in the Network.

Discussion

The values of the intraclass correlation coefficients found in this study can be considered low, close to zero, for the majority of the variables. Intraclass heterogeneity was greater in the variables related to outcome in comparison with the others.

In selecting the clusters, stratification by region was not performed. Proportionally more of the centers were situated in the southeast of the country (48%), and consequently a greater number of liveborn infants were also born in this region (46%). This distribution is in conformity with the actual distribution of healthcare institutions and the proportionality of liveborn infants per region of the country. According to the Ministry of Health's National Register of Healthcare Institutions, approximately 45% of the institutions registered are situated in the southeastern region [16] and, in 2008, 38.5% of all liveborn infants were born in this region [17]. Proportionality was also maintained in comparison with the other regions.

Although the surveillance of cases of severe maternal morbidity/near miss was prospective, the data were collected from the patients' charts immediately following the women's discharge from hospital. Therefore, for some variables, the number of individuals for whom data is available is less than the total number of cases, since it was impossible to recover some of the missing data. This possible loss of part of the data for some of the variables was predicted and taken into consideration in planning the study. Severely ill women may not be able to consent to participate in studies of this type because they may be unconscious, may die or may find themselves in various different situations of emotional fragility. Therefore, data collection

following hospital discharge was completely anonymous and avoided the need to obtain informed consent, what allowed a larger number of research subjects to be included, factors that are important in studies of serious conditions with a relatively low prevalence rate.

Previous studies have shown that ICC values are generally higher for variables related to process compared to those for variables related to outcome, since for the same intervention (measure of process), responses may differ between the different individuals under therapeutic management (outcome measurement). Furthermore, higher healthcare levels tend to increase the degree of homogeneity [18-21]. The explanation for this is that when the level of care is higher, there is a greater likelihood that management techniques will be standardized and institutional protocols will be used. In these cases, when one of the objectives is to evaluate compliance with established guidelines, homogeneity may be interpreted as a leveling of institutions with respect to certain recommendations.

This tendency is also seen in the present results, which were obtained from secondary and tertiary care hospitals, the majority of which were teaching hospitals. In this type of institution, the majority of procedures are performed in conformity with evidence-based healthcare protocols. Indeed, the mean ICC value for the variables related to process was 2.6 times higher than the mean ICC value for the variables related to outcome.

The variable with the highest ICC was "Major type of healthcare insurance used for hospital admission" with a value of 0.508. This homogeneity was expected, since only 3 of the 27 centers accepted private patients, all the other centers being exclusively public healthcare services.

Some of the variables related to process were obtained from a specific section of the study focusing on delays during patient care. In addition to obtaining data from the women's charts, this study also involved another step in which the investigators were instructed to make a subjective analysis of the chain of healthcare services provided, based on the data available on

the charts. In addition, after all the variables had been completed, the data for each subject were reanalyzed by the principal investigators and standard procedures for the classification of delays were implemented for all the cases in all the clusters. Therefore, the greater homogeneity found for these variables may be explained by this "standard correction" adopted for all the centers.

Previous studies in the primary care sector have reported ICC values < 0.05 for variables related to outcome and ICC values > 0.05 for variables related to the process [21]. In the field of maternal and perinatal healthcare, Taljaard *et al*. calculated ICC values based on data obtained from secondary/tertiary services [19]. The ICC of some variables analyzed in this study can be compared with ours as reported in table 6.

The findings of those investigators showed that, in general, ICC values for the variables related to the process tended to be >0.07, with values <0.07 for the variables related to outcome. The present findings are in agreement with this observation. Furthermore, these values can probably be considered as a good parameter of variance for calculating sample size in new studies in this area, similar to the 0.08 value used by van de Ven *et al*. [22].

Pagel et al. [23] estimated ICC of data from five community-based cluster-randomized controlled trials, all evaluating community interventions to improve maternal and newborn health outcomes. The mean cluster size of these studies ranged from 3,934 to 27,953 people. Of 9 key perinatal indicators, only maternal death has the possibility of comparison with our calculations and its ICC ranged from 0.00 to 0.00051.

All those comparisons show what was already known. The smaller the cluster size, the higher the ICC, and the opposite occurs regarding the prevalence of the condition. Mortality events are rare in community based population and the prevalence rises with morbidity association. Pagel et al. [23] established as a limitation of their findings that the ICC estimates for rare outcomes as maternal mortality are not likely to be reliable. Taljaard et al. [19] collected data from hospital based population, as our study, and obtained ICC similar to our findings.

This study is based on pregnant women who had at least one of the potentially life threatening conditions. So, prevalence of any factor that is associated with these conditions will be higher in the study sample than in the general obstetric population. This could potentially inflate ICC estimation as ICC generally tends to increase with higher prevalence. The ICCs of this study also depend on other factors such as the hospitals' characteristics. Caution in applying these ICCs to other settings should be used and this could be considered as a possible limitation of the study.

The absence of previous studies using these new near miss criteria standardized by the WHO [11] made it impossible to obtain the respective ICC values for the variables of interest related to outcome. Therefore, in this study sample size was calculated based exclusively on previous prevalence rates of the condition.

Considering the mean general characteristics of women in this study, most of whom received care in public hospitals linked to universities, and that the ICC values showed sample heterogeneity, studies conducted in middle income countries with similar characteristics to Brazil probably can use the ICC values of this study as the basis for their calculations.

Conclusions

The Brazilian Network for Surveillance of Severe Maternal Morbidity conducted a pioneering, cross sectional, multicenter study in the application of the new WHO near miss criteria to identify severe cases in obstetrics. This paper reports the intraclass correlation coefficients for the study variables. The results found are in agreement with those of previous studies and the homogeneity of the data obtained from the variables related to outcome may be considered minor, increasing the reliability of the study estimates. These values may be used to plan new cluster studies in maternal and perinatal health, mainly studies associated with severe maternal morbidity/near miss, and will be useful for calculating sample size.

List of abbreviations

(ANOVA): analysis of variance; (DEFF): design effect; (ICC): intraclass correlation coefficient; (PSU): primary sampling unit; (SRS): simple random sampling; (WHO): World Health Organization.

Competing of interests

The authors declare that there are no competing interests.

Authors' contribution

JPD and JGC were responsible for the original idea of the study. SMH, JGC and MAP were responsible for its implementation. All of them plus the whole group were responsible for care of women, data collection, data consistency and cleaning. MHS, SMH and JGC were responsible for planning and performing analysis. SMH and MHS wrote the first draft of the manuscript which was finalized with output of all others who read and approved the final version.

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Table 1. **Distribution of cases and live births (LB) by cluster and according to geographical region of the country**

Region	Center	n_c (or x_α #)	LB in the Network	LB in Brazil*
Southeast n_{se}**= 2,794 (29.2%)**	1	48	37,865 (46.1%)	1,130,407 (38.5%)
	2	59		
	3	66		
	4	74		
	5	96		
	6	112		
	7	154		
	8	155		
	9	172		
	10	186		
	11	253		
	12	369		
	13	1050		
Northeast n_{ne}**= 5,148 (53.9%)**	1	118	33,172 (40.4%)	888,268 (30.3%)
	2	210		
	3	263		
	4	281		
	5	294		
	6	465		
	7	566		
	8	920		
	9	945		
	10	1086		
South n_s**= 939 (9.8%)**	1	98	4,532 (5.5%)	371,497 (12.7%)
	2	841		
Midwest n_{mw}**= 609 (6.4%)**	1	609	2,527 (3.1%)	222,658 (7.6%)
North n_n **= 65 (0.7%)**	1	65	4,048 (4.9%)	321,998 (11.0%)
Total (n)	27	9555	82,144	2,934,828

Mean size of clusters (n_a)= 354

Denominator of the expression of the ratio estimator

* Data from SINASC (Brazil, 2011) [16]

Table 2. Estimates of prevalence, intraclass correlation coefficients, their respective 95% CI, design effect, and mean size of clusters for variables related to the process

Variable	P (%)	ICC	95%CI for ICC	DEFF	n_a
• Prenatal care at the same institution	22.1	0.103	0.033–0.174	44.72	316
• Access of women to the center (Spontaneous demand)	47.9	0.195	0.078–0.312	118.12	333
• Major type of healthcare insurance used for prenatal care (Public)	88.5	0.115	0.039–0.191	30.27	279
• Major type of healthcare insurance used for hospital admission (Public)	98.9	0.508	0.323–0.693	31.66	354
Procedure related to abortion					
• Procedure performed: D&C	77.8	0.054	0.001–0.148	1.50	9
• Procedure performed: Oxytocin	33.3	0.339	0.136–0.542	9.39	9
• Procedure performed: Vacuum aspiration	7.0	0.001	<0.001–0.068	2.26	9
• Procedure performed: Prostaglandins	22.2	0.118	<0.001–0.245	1.91	9
• Procedure performed: Other	7.0	0.155	0.011–0.298	1.53	9
Related to PLTC criteria					
• Any therapeutic management	76.1	0.272	0.125–0.419	225.19	354
• Transfusion of blood derivatives	16.4	0.079	0.024–0.133	37.50	354
• Central venous access	3.8	0.090	0.028–0.151	21.23	354
• Admission to ICU	22.1	0.288	0.136–0.439	199.58	354
• Prolonged hospital stay	30.0	0.098	0.032–0.164	81.88	354
• Intubation unrelated to anesthesia	3.1	0.047	0.013–0.081	12.99	354
• Return to operating room	3.3	0.021	0.005–0.038	11.75	354
• Hysterectomy/ laparotomy	6.2	0.043	0.011–0.074	20.44	354
• Use of magnesium sulfate	48.3	0.363	0.192–0.534	292.63	354
• Another major surgical procedure	0.8	0.008	0.001–0.016	6.35	354
Related to near miss criteria					
• Any management near miss criteria	6.1	0.075	0.023–0.127	20.52	354
• Continuous use of vasoactive drug	2.6	0.028	0.007–0.049	8.93	354
• Hysterectomy due to infection or hemorrhage	1.8	0.031	0.008–0.054	8.05	354
• Transfusion of ≥5 U red cells	2.6	0.053	0.015–0.091	11.42	354
• Intubation and ventilation ≥ 60 min unrelated to anesthesia	3.1	0.047	0.013–0.082	13.94	354
• Dialysis for acute renal failure	0.7	0.009	0.001–0.017	3.60	354
• Cardiopulmonary resuscitation (CPR)	1.3	0.018	0.004–0.033	8.41	354
• At least one of these conditions was already present when the woman was admitted	32.0	0.132	0.046–0.218	6.91	34
Related to delay in care					
• Delay related to patients and/or their family members (Yes/ No)	39.3	0.090	0.028–0151	27.26	310
• Search for a health service	5.3	0.174	0.067–0.281	54.03	310
• Geographic difficulty in accessing health service	2.4	0.352	0.183–0.520	113.16	310

• Refused treatment/care	5.1	0.014	0.002–0.025	7.72	310
• Prenatal care absent or inadequate	32.1	0.043	0.012–0.075	14.98	310
• Delay in care related with health professional	17.3	0.328	0.164–0.492	134.27	331
• Delay in diagnosis	5.5	0.218	0.091–0.346	72.81	331
• Delay in starting treatment	6.7	0.321	0.159–0.483	105.23	331
• Inadequate management	13.6	0.300	0.144–0.456	121.82	331
• Delay in referring or transferring the case	3.3	0.055	0.015–0.095	20.77	331

P: prevalence of each category; ICC: Intraclass Correlation Coefficient; 95% CI: 95% confidence interval; DEFF: Design effect; n_a: Mean size of clusters; PLTC: potentially life threatening condition; NM: near miss.

Table 3. Estimates of prevalence, intraclass correlation coefficients, their respective 95% CI, design effect and mean size of clusters for variables related to outcome

Variable	P (%)	ICC	95% CI for ICC	DEFF	n_a
• Any hemorrhagic complication	24.8	0.165	0.062–0.268	129.54	354
• Abruptio placentae	5.7	0.016	0.003–0.029	9.55	354
• Placenta previa/acreta	2.2	0.017	0.004–0.031	6.24	354
• Complicated ectopic pregnancy	3.1	0.034	0.009–0.059	17.72	354
• Uterine rupture	0.3	0.005	<0.001–0.011	2.12	354
• Severe post abortion hemorrhage	1.3	0.015	0.003–0.028	5.92	354
• Postpartum hemorrhage	12.5	0.248	0.110–0.387	200.97	354
✓Atony	63.0	0.375	0.134–0.617	77.37	44
✓Retained placenta	11.8	0.114	0.005–0.224	12.94	44
✓Tears	8.8	0.130	0.008–0.251	10.04	44
✓Coagulopathy	4.6	0.102	0.002–0.203	13.51	44
✓Uterine inversion	0.6	0.035	<0.001–0.079	1.65	44
✓Other obstetric cause	11.2	0.370	0.130–0.610	43.77	44
• Other severe hemorrhage	1.0	0.023	0.005–0.041	6.16	354
• Any complication due to hypertension	70.2	0.183	0.072–0.294	124.72	354
• Severe preeclampsia	51.2	0.231	0.099–0.363	188.23	354
• Eclampsia	4.5	0.023	0.005–0.040	14.62	354
• Severe hypertension	18.3	0.334	0.169–0.499	289.00	354
• HELLP syndrome	6.2	0.028	0.007–0.049	15.43	354
• Acute fatty liver	0.2	0.005	0.001–0.010	1.59	354
• Any other complication	17.2	0.103	0.034–0.172	31.93	354
• Pulmonary edema	1.7	0.020	0.004–0.036	4.45	354
• Seizures	1.4	0.009	0.001–0.016	3.66	354
• Thrombocytopenia	3.9	0.022	0.005–0.039	6.77	354
• Thyrotoxic crises	0.1	0.007	0.001–0.013	1.55	354
• Shock	3.1	0.034	0.009–0.059	9.95	354
• Acute respiratory failure	4.0	0.051	0.014–0.087	19.37	354
• Acidosis	1.6	0.021	0.005–0.038	12.54	354
• Cardiopathy	1.7	0.013	0.002–0.023	5.71	354
• Stroke	0.2	0.001	0.001–0.003	1.10	354
• Coagulation defects	2.0	0.012	0.002–0.021	4.69	354
• Disseminated intravascular coagulation	0.6	0.012	0.002–0.021	2.60	354
• Thromboembolism	0.9	0.010	0.001–0.018	4.95	354
• Diabetic ketoacidosis	0.2	0.004	0.001–0.008	0.94	354
• Jaundice/ liver dysfunction	1.4	0.014	0.003–0.026	2.46	354
• Meningitis	<0.1	<0.001	0.001–0.002	0.94	354
• Severe sepsis	3.5	0.064	0.019–0.109	18.09	354
✓Postpartum endometritis	19.5	0.131	0.011–0.252	3.95	13
✓Post abortion endometritis	11.0	0.043	0.001–0.115	2.13	13
✓Pulmonary focus	29.3	0.055	0.001–0.133	2.03	13
✓Urinary focus	25.0	0.013	0.001–0.067	1.08	13
✓Other	15.2	0.042	0.001–0.113	1.15	13

• Acute renal failure	2.2	0.027	0.006–0.047	8.68	354
• Complication possibly associated with Influenza A 'H1N1'	2.2	0.056	0.016–0.097	20.62	354
• Any clinical maternal near miss criteria	5.5	0.037	0.010–0.065	15.44	354
• Cyanosis	1.3	0.023	0.005–0.040	12.63	354
• Gasping	0.4	0.009	0.001–0.017	4.21	354
• Respiratory rate <6 or RR>40	2.0	0.016	0.003–0.029	8.42	354
• Shock	2.6	0.031	0.008–0.054	9.24	354
• Oliguria unresponsive to fluids or diuretics	0.9	0.010	0.001–0.018	4.43	354
• Coagulation problems	1.0	0.012	0.002–0.021	4.88	354
• Loss of consciousness for 12h or more	0.7	0.005	<0.001–0.010	4.25	354
• Absence of consciousness and absence of pulse rate/heartbeat	0.7	0.006	0.001–0.011	4.96	354
• Stroke	0.3	0.002	0.001–0.005	1.16	354
• Uncontrolled seizures – total paralysis	0.2	0.001	<0.001–0.004	2.22	354
• Jaundice in presence of preeclampsia	0.3	0.001	<0.001–0.002	1.36	354
• Any laboratory near miss criteria	5.2	0.047	0.013–0.082	12.08	354
• O_2 saturation < 90% for longer than 60 min	1.9	0.016	0.003–0.029	8.30	354
• PaO_2/FiO_2 < 200 (Yes/ No)	1.1	0.015	0.003–0.028	8.37	354
• Creatinine ≥ 300 mmol/l or ≥ 3.5 mg/dl	1.0	0.007	0.001–0.013	3.03	354
• Bilirubin ≥ 100 mmol/l or ≥ 6 mg/dl	0.5	<0.001	<0.001–0.002	1.25	354
• pH < 7.1	0.8	0.009	0.001–0.016	5.32	354
• Lactate > 5	0.8	0.098	0.032–0.165	18.31	354
• Platelet < 50,000	2.1	0.025	0.006–0.044	5.32	354
• Absence of consciousness plus glucose and ketoacids in urine	0.2	0.004	<0.001–0.009	3.49	354
• Condition of woman at discharge (Medical discharge)	94.1	0.011	0.002–0.020	6.54	354
• Unsafe abortion	0.6	0.025	0.006–0.045	7.43	310
• **Maternal Death**	1.5	0.018	0.004–0.033	7.93	354
• **Maternal Death + NM**	9.5	0.077	0.023–0.130	21.09	354

P: prevalence of each category; ICC: Intraclass Correlation Coefficient; 95% CI: 95% confidence interval; DEFF: Design effect; n_a: Mean size of clusters; NM: near miss.

Table 4. Estimates of prevalence, intraclass correlation coefficients, their respective 95% CI, design effect and the mean size of clusters with respect to personal and obstetric data

Variable	P (%)	ICC	95% CI for ICC	DEFF	n_a
• Age (<30 years)	65.6	0.013	0.002–0.024	4.00	354
• Skin color (White)	42.5	0.285	0.127–0.443	146.55	264
• Schooling (Primary)	46.5	0.051	0.012–0.091	17.45	256
• Marital status (Has a partner)	53.2	0.176	0.066–0.286	101.96	298
• Weight (<75 kg)	52.3	0.055	0.010–0.101	21.45	167
• Height (<1.60 m)	48.6	0.054	0.007–0.101	13.51	151
• Body Mass Index (Low BMI)	15.4	0.053	0.006–0.100	18.47	146
• Number of pregnancies (One)	41.9	0.010	0.001–0.019	9.01	352
• Number of deliveries (None)	48.2	0.010	0.002–0.019	8.87	352
• Number of abortions (None)	77.6	0.005	<0.001–0.011	2.59	352
• Number of previous C-sections (None)	76.0	0.011	0.002–0.021	6.87	347
• Number of live births (None)	51.3	0.016	0.003–0.028	11.27	341
• Time since last delivery (≤2 years)	25.5	0.022	0.001–0.043	4.23	99
• Previous uterine surgery	2.0	0.067	0.017–0.117	20.52	299
• Number of prenatal visits (<6)	46.4	0.018	0.003–0.034	5.34	276
• Pregnant at admission	95.0	0.043	0.011–0.074	20.70	354
• Gestational age at admission (<37 weeks)	53.4	0.069	0.020–0.117	37.71	327
• Mode of onset of labor (no labor)	49.4	0.113	0.038–0.188	88.44	349
• Gestational age at resolution (<37 weeks)	45.7	0.055	0.015–0.095	31.28	309
• Mode of delivery (C-section before labor)	49.6	0.111	0.037–0.184	87.28	352
• Mode of onset of abortion (Spontaneous)	63.6	0.044	<0.001–0.141	1.52	8
• Total number of fetuses (None)	6.0	0.128	0.044–0.212	52.87	325
• Fetal presentation at birth (Cephalic)	91.3	0.011	0.001–0.020	4.77	273
• Some pathological or risky condition prior to this current pregnancy	48.9	0.115	0.038–0.191	47.12	305
• Chronic hypertension	17.7	0.046	0.012–0.079	15.98	305
• Obesity	24.1	0.110	0.036–0.184	65.40	305
• Low weight	0.3	0.004	<0.001–0.008	1.68	305
• Diabetes mellitus	2.5	0.023	0.005–0.041	7.84	305
• Smoking	5.7	0.065	0.018–0.111	44.05	305
• Cardiac diseases	2.9	0.025	0.006–0.045	9.23	305
• Respiratory diseases	2.8	0.018	0.004–0.033	9.67	305
• Renal diseases	1.2	0.038	0.010–0.067	11.74	305
• Sickle cell disease-thalassemia	0.8	0.005	<0.001–0.011	5.08	305
• HIV/AIDS	1.1	0.006	<0.001–0.013	3.16	305
• Thyroid disease	1.4	0.008	0.001–0.016	2.65	305
• Neurologic diseases/ epilepsy	1.2	0.011	0.001–0.020	4.35	305
• Collagenosis	0.6	0.028	0.007–0.050	8.93	305
• Cancer	0.3	0.006	<0.001–0.012	2.31	305
• Other	5.2	0.037	0.009–0.065	13.99	305
• Drug addiction	1.2	0.005	<0.001–0.010	4.07	305

P: prevalence of each category; ICC: Intraclass Correlation Coefficient; 95% CI: 95% confidence interval; DEFF: Design effect; n_a: Mean size of clusters.

Table 5. Estimates of prevalence, intraclass correlation coefficients, their respective 95% CI, design effect and mean size of clusters with respect to the variables related to structure

Variable	P (%)	ICC	95%CI for ICC	DEFF	n_a
• Delay related to service or healthcare system	15.6	0.247	0.108–0.387	106.64	328
• Lack of medication	1.3	0.021	0.005–0.038	9.77	328
• Difficulties with municipal/ hospital transport	1.3	0.031	0.007–0.055	9.27	328
• Difficulties with communication (hospital/ central regulation)	8.8	0.206	0.083–0.329	99.07	328
• Lack of blood derivatives	0.6	0.014	0.002–0.025	8.17	328
• Difficulty related to monitoring (intensive care unit)	4.6	0.230	0.097–0.363	64.99	328
• Lack of trained personnel	3.1	0.063	0.018–0.107	24.25	328
• Difficulty related to access to prenatal care	1.4	0.084	0.025–0.142	20.09	328

P: prevalence of each category; ICC: Intraclass Correlation Coefficient; 95% CI: 95% confidence interval; DEFF: Design effect; n_a: Mean size of clusters.

Table 6. Comparisom of Intraclass Correlation Coefficients of some variables between this study and that from Taljaard et al. [19]

ICC: Intraclass Correlation Coefficient; n_a: Mean size of clusters.

Variable	Haddad et al		Taljaard et al	
	ICC	n_a	ICC	n_a
• HIV positive	0.006	305	0.022	865
• Chronic respiratory conditions	0.018	305	0.042	861
• Diabetes mellitus	0.023	305	0.010	862
• Hysterectomy	0.031	354	0.002	862
• Eclampsia	0.023	354	0.007	862
• Maternal Death	0.018	354	0.0003	866

3.2. Artigo 2

The WHO Maternal Near-Miss Approach and the Maternal Severity Index Model (MSI): tools for assessing the management of severe maternal morbidity

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Abstract

Objectives: To validate the WHO maternal near-miss criteria and develop a benchmark tool for severe maternal morbidity assessments.

Methods: In a multicenter cross-sectional study implemented in 27 referral maternity hospitals in Brazil, a one-year prospective surveillance on severe maternal morbidity and data collection was carried out. Diagnostic accuracy tests were used to assess the validity of the WHO maternal near-miss criteria. Binary logistic regression was used to model the death probability among women with severe maternal complications and benchmark the management of severe maternal morbidity.

Results: Of the 82,388 women having deliveries in the participating health facilities, 9,555 women presented pregnancy-related complications, including 140 maternal deaths and 770 maternal near misses. The WHO maternal near-miss criteria were found to be accurate and highly associated with maternal deaths (Positive likelihood ratio: 106.8 (95% CI 99.56-114.6)). The maternal severity index (MSI) model was developed and found to able to describe the relationship between life-threatening conditions and mortality (Area under the ROC curve: 0.951 (95% CI 0.909 - 0.993)).

Conclusion: The identification of maternal near-miss cases using the WHO list of pregnancy-related life-threatening conditions was validated. The MSI model can be used as a tool for benchmarking the performance of health services managing women with severe maternal complications and provide case-mix adjustment.

Keywords: maternal near miss, quality of care, pregnancy-related complications, maternal intensive care

Background

In recent years, a global reduction in maternal mortality has been observed. However, over 1000 women die of pregnancy-related causes every day around the world and much has to be done for achieving the relevant target of the Millennium Development Goals (1). Despite the fact that most of the burden of maternal deaths is carried by low-income countries, maternal mortality is still a relevant public health problem among middle-income countries. In this context, strengthening health systems and services to provide optimal care for women during pregnancy and childbirth is crucial, particularly to those women experiencing acute pregnancy-related complications (2-5).

Confidential enquiries of maternal deaths have been used for many years to understand health systems and services failures in the provision of appropriate maternal health care. Based on these enquiries, lessons can be learned and used to strengthen health systems and improve quality of care (6). Despite the positive contribution of this approach, it has limitations, particularly in low mortality settings or at the health service level, where the amount of maternal deaths is generally insufficient to provide useful information. In the last 20 years, the concept of maternal near miss has been explored in maternal health as an adjunct to maternal-death confidential enquiries. Women who nearly died but survived complications have been studied as surrogates of maternal deaths. Among other positive characteristics, maternal near-miss cases can directly inform on problems and obstacles that had to be overcome during the process of health care. Maternal near-miss audits have been considered as useful approaches to improve maternal health care (7,8).

In 2008, the World Health Organization (WHO) has adopted a maternal near-miss definition and established standard criteria for the identification of women presenting pregnancy-related life-threatening conditions. Women surviving any of the life-threatening conditions listed in the Table 1 during pregnancy, childbirth, or postpartum are considered as maternal near-miss cases by WHO. The WHO definition enables a common ground for the implementation of maternal near-miss assessments across countries and allows international comparisons to be carried out (9).

Validation of the set of the WHO criteria for identifying women with life-threatening conditions

The WHO maternal near-miss definition and identification criteria have been developed using the collective wisdom of a group of international experts gathered by WHO in an evidence-informed process (9). A systematic review summarizing the range of previous related experiences provided the scientific basis for the development of the WHO definition and identification criteria (10). Intensive-care prognostic and severity assessment scores, such as the APACHE II, SAPS, MODS and particularly the SOFA score, were reviewed as possible sources of severity markers for identifying women with life-threatening conditions (11-13). A secondary analysis of a previous multicountry study was conducted to explore pragmatic identification criteria for maternal near misses (14). In addition, a small preliminary study was carried for piloting and pre-validating the criteria proposed by the WHO working group (15).

In spite of the evidence-informed process that led the development of the WHO criteria for identifying women with life-threatening conditions, an actual validation of such criteria is required. The validation of such criteria depends on the similarity between maternal deaths and maternal near-miss cases. From the conceptual standpoint, near-miss cases should be as similar to maternal deaths as possible. However, the development of criteria to identify near-miss cases is challenged by the absence of a gold-standard for near-miss cases. In addition, the identification of near-miss cases is always retrospective, i.e. the woman needs to survive the life-threatening complication in order to be considered as a near-miss case. In this context and considering a set of criteria as a diagnostic test, it is assumed that a set of criteria able to accurately "identify" maternal deaths would have as false positives the maternal near-miss cases. Truly-positive cases (maternal deaths) would be similar to false positive cases (maternal near-miss cases) except the vital status (14).

Development of a benchmarking tool

Populations of critically ill patients may differ in their mortality risks, depending on the severity of individual cases, the case-mix, and the quality of the therapeutic management, among other factors. Prognostic / risk-scoring systems have been used in the assessment of medical and surgical critically ill patients. Most of these systems are based on mathematical models and aim at determining the position of individual patients in the spectrum of severity. By providing a

judgment-free assessment of individual risks, these tools enable neutral case-mix adjustments for groups of patients. Some of these tools also enable an assessment of health service performance in the provision of care, as they allow an estimation of expected mortality considering the specific population case-mix. By comparing the observed mortality to the expected mortality in the population, a sense of appropriateness of care can be made (11,12,16,17). This is a benchmark approach, which uses the population that generated the model as the standard for comparison (17). Some attempts to use these generic systems in populations of severely-ill obstetric populations have been made, but the accuracy of these systems has been considered as suboptimal, possibly due to the mismatch between the reference population (general, non-obstetric) and the target population (obstetric) (18-22).

The WHO criteria are a package of 25 severity markers portraying a comprehensive range of life-threatening conditions. Each of these severity markers is associated with a specific relationship with mortality. In addition, women experiencing pregnancy-related complications can present more than one of these severity markers. Thus, combinations of severity markers would be associated with different mortality risks. For instance, a woman that presents postpartum hemorrhage and undergoes a hysterectomy due to uterine atony has a different risk of death as compared to a woman presenting several markers of severity denoting multiple organ dysfunctions. Similarly, depending on the case-mix, a population of women presenting life-threatening conditions may differ in its relationship with mortality in comparison to other populations of women presenting life-threatening conditions. Thus, a benchmark tool able to minimize severity bias by providing case-mix adjustment and enable comparisons to a reference population would improve the applicability of the maternal near-miss concept and enable more appropriate comparisons between populations.

Objectives

The present analysis aims at validating the WHO criteria for identification of women with pregnancy-related life-threatening conditions and developing a benchmark tool for severe maternal morbidity assessments.

Methods

Ethics Statement

This project has been reviewed and approved by the National Council for Ethics in Research (CONEP, Brazilian Ministry of Health) and by the Institutional Review Boards of each site (listed below). All data was obtained from medical records and did not identify participants. The National Council for Ethics in Research and the Institutional Review Boards of each site granted a waiver of individual informed consent.

The Review Boards of the following institutions reviewed and approved this project: Maternidade Cidade Nova Dona Nazarina Daou (Manaus, AM), Maternidade Climério de Oliveira (Salvador, BA), Hospital Geral de Fortaleza (Fortaleza, CE), Hospital Geral Dr. César Cals (Fortaleza, CE), Maternidade Escola Assis Chateaubriand (Fortaleza,CE), Hospital Materno Infantil de Goiânia (Goiânia, GO), Hospital Universitário da Universidade Federal do Maranhão (São Luis, MA), Maternidade Odete Valadares (Belo Horizonte, MG), Instituto de Saúde Elídio de Almeida (Campina Grande,PB), Hospital Universitário Lauro Wanderley da Universidade Federal da Paraiba (João Pessoa, PB), Centro Integrado de Saúde Amaury de Medeiros (Recife, PE), Instituto de Medicina Integral Prof. Fernando Figueira (Recife, PE), Hospital das Clínicas da Universidade Federal de Pernanmbuco (Recife, PE), Hospital das Clínicas da Universidade Federal do Paraná (Curitiba, PR), Hospital Maternidade Fernando Magalhães (Rio de Janeiro, RJ), Instituto Fernandes Figueira (Rio de Janeiro, RJ), Hospital das Clinicas da Universidade Federal do Rio Grande do Sul (Porto Alegre, RS), Faculdade de Medicina de Botucatu da Universidade Estadual Paulista (Botucatu, SP), Hospital da Mulher da Universidade Estadual de Campinas (Campinas, SP), Hospital e Maternidade Celso Pierro da Pontifícia Universidade Católica (Campinas, SP), Hospital Israelita Albert Einstein (São Paulo, SP), Faculdade de Medicina de Jundiaí (Jundiaí, SP), Hospital das Clínicas da Faculdade de Medicina de Ribeirão Preto da Universidade de São Paulo (Ribeirão Preto, SP), Santa Casa de Limeira (Limeira, SP), Santa Casa de São Carlos (São Carlos, SP), Casa Maternal Leonor Mendes de Barros (São Paulo, SP), Hospital São Paulo da Universidade Federal de São Paulo (São Paulo, SP).

Study design

Methodological details of the Brazilian Network for Surveillance of Severe Maternal Morbidity Study have been published elsewhere (23,24). Briefly, this is a multicenter, cross-sectional study implemented in 27 Brazilian referral maternity hospitals. A convenience sampling strategy was used to build the network of health facilities. Aiming at lessening the impact of the non-random sampling and optimizing the representativeness of Brazilian referral maternity hospitals, an adequate mix of health facilities was sought: public and private health facilities, university and non-university hospitals, at least one health facility from each of the five country macro-regions. The number of health facilities was determined based on the number of maternal deaths and maternal-near miss cases required to validate the use of the WHO criteria for pregnancy-related life-threatening conditions and carry out other relevant analysis. Based on previous studies (10,25), a total of approximately 75,000 deliveries would have to be screened in order to identify around 100 maternal deaths and 600 maternal near miss cases.

In each hospital, a research team was responsible for carrying out prospective surveillance on severe maternal morbidity. During the one-year data collection period (between July 2009 and June 2010), all women admitted to the participating health facilities were screened against the inclusion criteria by research assistants. The inclusion criteria were: presence of any of the conditions listed in the Table 1 (i.e. potentially life-threatening conditions, WHO life-threatening conditions), maternal deaths and referral to another health facility due to severe ill health.. The prospective surveillance was implemented by research assistants through daily visits to obstetric wards and other relevant facilities (e.g. intensive care units and emergency rooms). During the daily visit the attending staff was contacted and the medical charts of hospitalized women were screened for the study inclusion criteria. Medical records of eligible cases were retrieved for thorough review at hospital discharge, transfer to another hospital or death. Data was collected into a previously coded form and included demographic, medical and obstetric characteristics, primary determinants of life-threatening conditions (the first complication in the chain of events), duration of hospitalization (prior to delivery, following delivery and total time), the occurrence of life-threatening conditions, maternal and perinatal outcomes and information related to the occurrence of delays in the provision of care. All severity markers (i.e. WHO life threatening conditions) present in each case were recorded. Institutional capacity was assessed using an adapted version of the hospital complexity index developed for the WHO Global Survey project (26). The hospital complexity index was used to determine the range of services

available in each of the facilities and to summarise an institution's capacity to provide obstetric care. This index comprised eight categories reflecting the: standard of building/basic services, maternal intrapartum care and human resources; availability of general medical care, anaesthesiology, emergency obstetric services; and provision of screening tests and academic resources and clinical protocols. The original hospital complexity index was used by WHO in Latin America and Asia and adapted for use in Africa. We implemented minor adaptations to reflect the Brazilian context. An open-access, web-based, good-clinical-practice compliant database solution and study management system was used (OpenClinica, Akaza Research, LLC, 2009, Waltham, MA, USA, www.openclinica.org).

Data Quality

Several procedures were adopted to ensure high quality data and reliable information, including preparatory meetings, site visits, close monitoring of data collection and data entry, concurrent query management, inconsistency checks, double data collection for selected medical charts, and use of a detailed manual of operation. In the preparatory meetings, study coordinators and data collectors from each site were trained in the study procedures. The study protocol, manual of operation and study forms were thoroughly reviewed; training was provided on the use of the web-based data management system. During data collection the participating hospitals received continuous support including site visits. In the site visits, the study implementation was assessed and selected medical records were checked against data entered in the data management system. In addition, the web-based data management system used in this study is compliant with Good Clinical Practice (GCP) and regulatory guidelines (e.g. 21 CFR Part 11), allowing differentiated user roles and privileges, password and user authentication security, electronic signatures, SSL encryption, de-identification of Protected Health Information (PHI). Auditing to record and monitor access and data changes aligned with a set of validation and cross checking rules were implemented as part of the online data-management. Through this comprehensive package of data quality procedures reliable and high quality data were obtained.

Statistical Analysis

The Maternal Mortality Ratio (MMR) with 95% Confidence Intervals (CI) was determined based on the total of live births that took place in the participating hospitals during the data collection

period. The study maternal mortality data was compared with the WHO maternal mortality estimates for 2010 in Brazil (together with its range of uncertainty) (1). Sensitivity, specificity, positive and negative likelihood ratios were used to determine the accuracy of the WHO criteria in the identification of women with life-threatening conditions. Vital status at discharge was considered as the gold standard for identifying women with life-threatening conditions. The prevalence of women with life-threatening complications, maternal deaths and maternal near-miss cases was calculated. In addition, the prevalence and mortality estimates together with crude relative risks and 95% CI were calculated for each severity marker.

It was hypothesized that the number of severity markers present in each case would be correlated with mortality. The study population was categorized according with the total number of severity markers per case. In each category, the frequency of cases and mortality with 95% confidence interval was determined. The correlation between number of markers per case and mortality was determined by calculating the Pearson's correlation coefficient. In each case, the total number of severity markers is hereby defined as the maternal severity score.

Two binary logistic regressions models were developed and tested to describe the relationship between (severe) morbidity and mortality. In order to enable this, the study population was split in two: the subpopulation "A" (used for model development), and the subpopulation "B" (used for model testing). (27). The size of the subpopulation "B" was determined considering that the area under the Receiver Operating Characteristic curve (AUROC) would be used as an estimator of model validity. The following parameters were used in the subpopulation "B" sample size calculation: 0.05 as the probability of making a Type I error, 0.20 as the probability of making a Type II error, AUROC 0.500 as null hypothesis value, and 0.800 as the minimum expected AUROC. Based on these parameters, a total of 28 maternal deaths would be required in the subpopulation "B" for the comparison of the AUROC with the null hypothesis value. Considering the total number of maternal deaths included in the study database, 80% of the study population was randomly allocated to the population "A" and the remainder (20%) was allocated to the population "B".

The model I consisted in a univariate analysis including only the maternal severity score (i.e. the number of WHO severity markers). The model II tested the maternal severity score, distal predictors of maternal deaths (e.g. obstetric and demographic variables, direct and indirect causes of maternal deaths) and life-threatening conditions categorized as presented in the Table

1. In the multivariate analysis (model 2), a stepwise approach was used and only predictors that contributed significantly to the model were retained (the probabilities for stepwise were set as 0.05 (entry) and 0.10 (removal)). These logistic regression models estimate the probability of maternal death based on the presence or absence of severity markers and other relevant characteristics (27). The Hosmer-Lemeshow goodness-of-fit test was used to assess the ability of these models in adequately describing the data. The Nagelkerke R square test was used to estimate the proportion of variance in maternal mortality associated with the models' predictors. The area under the ROC curve was determined for the Maternal Severity score and the models I and II. The best performing model was selected to generate the Maternal Severity Index (MSI), hereby defined as the estimated probability of maternal death.

PASW Statistics 18, Release Version 18.0.0 (SPSS, Inc., 2009, Chicago, IL, www.spss.com) was the main statistical package used in this analysis. MedCalc® Version 11.6.1.0 (MedCalc Software,2011, Mariakerke, Belgium, www.medcalc.org) was used for AUROC sample size calculation.

Results

A total of 82,388 women were admitted to the 27 health facilities during the one-year data collection period. These women gave birth to 82,144 born-alive infants. The study population comprised 9,555 women presenting pregnancy related complications and meeting the study inclusion criteria. Of this population with pregnancy-related complications, 910 women presented at least one of the severity markers classified as life-threatening conditions by WHO, including 140 maternal deaths and 770 survivors. The MMR in the screened population was was 170 maternal deaths per 100,000 live births (95% CI 144-201 maternal deaths per 100,000 live births). The maternal deaths included in this study represent about 8% of all maternal deaths that are estimated to occur in Brazil in 2010 (range of uncertainty: 5-13%) (1). Table 2 shows the performance of the WHO set of criteria in two populations: all women giving birth during the data-collection period and those presenting pregnancy-related complications. All women that died presented at least one of the listed life-threatening conditions. Table 3 presents the relationship between markers of severity (WHO criteria) and maternal deaths. The prevalence of each of these life-threatening conditions ranged from 0.19 to 3.55 cases per 1000 deliveries and the condition specific mortality ranged between 12.9% and 85.0%. All life-threatening conditions were highly associated with maternal deaths, but heterogeneity was observed: 5 life-

threatening conditions presented relative risks between 10 and 20, 14 presented relative risks ranging from 20 to 60, and 6 presented relative risks over 60. The amount of severity markers per case (the maternal severity score) presented a very high positive correlation with mortality as illustrated in the Figure 1 and Table 4.

The logistic regression models were developed in the subpopulation "A", which included a total of 7,674 randomly selected cases (111 maternal deaths). The models were tested in the subpopulation "B", which included a total of 1881 cases (29 maternal deaths). The size of each subpopulation complied with the predetermined study sample size requirements. Table 5 summarizes the performance of the models and the maternal severity score.. The model II presented a better death prediction performance as evaluated by the Hosmer-Lemeshow test, Nagelkerke R^2 test, and the percentage of maternal deaths with a model-estimated death probability greater than 50%. Based on these findings, the model II was selected to become the MSI model. Table 6 presents the covariates that were retained in the model II (i.e. the MSI model) together with the coefficients that correspond to each covariate. The death probability can be obtained using the formula presented in the Table 5. A downloadable calculator has been developed to facilitate the use of the MSI (web appendix 1).

Discussion

The WHO criteria for pregnancy-related life-threatening conditions were found to be highly associated with maternal deaths. Survivors of the WHO pregnancy-related life-threatening conditions can be accurately classified as maternal near-miss cases. A severity score representing the total number of life-threatening conditions present in each case and a mathematical model describing the relationship between severity markers and maternal deaths have been developed.

Scoring systems have been used to evaluate severity and outcome of critically ill patients since many years. APACHE, SAPS, and SOFA systems are among the most used ones (11). Some of these systems are extensively used for intensive care benchmarking and quality of care assessment (16,17). Notwithstanding, these systems have been developed based on general critical care populations from developed countries. In these reference populations, obstetric patients were largely omitted or underrepresented, either because pregnant women were excluded, or because maternal deaths are rare events in the countries where these systems were

developed. Another issue that should be acknowledged is that the physiological changes of pregnancy affect some of the markers used by general severity scoring systems leading to overestimation of severity (18). Also, diseases that are exclusive to this period of life (e.g. eclampsia, HELLP syndrome, acute fatty liver of pregnancy, amniotic fluid embolism), have peculiar characteristics that may not have been adequately addressed by scores designed for general populations. Owing to this, the performance of these systems in obstetric population is challenged, particularly in developing countries. Limitations are observed in the discriminatory power and the calibration of generic scoring systems when applied to obstetric population (12, 15, 19-22).

The maternal severity score and the MSI model, developed in this study, may contribute for a better assessment of severity of obstetric populations and enable a benchmark approach to quality of care of women experiencing severe complications related with pregnancy. As part of the strengths of this analysis, the MSI model was developed in a large multicenter study, which had an appropriate sample both in terms of number of critically ill obstetric patients and maternal deaths. The study population was large enough to allow adequate model development and testing in different subsets of the study population as methodologically recommended (27). In the end, the MSI model was found to be robust, presenting good performance and discriminatory power. There are also two additional potential advantages that should be noted: the MSI model was developed based on the WHO criteria for pregnancy-related life-threatening conditions and the study database reflects the standard of care provided in obstetric referral hospitals from a developing country.

The WHO criteria for pregnancy-related life-threatening conditions are part of a strategy promoted by WHO for assessing and improving quality of maternal health care (8,9,28). These criteria are used in the identification of maternal near-miss cases in clinical audits and other near-miss studies. Together with routine implementation, there are several near-miss research projects being currently conducted around the world using these criteria. In addition to external validation, these initiatives may favor further dissemination of the maternal near miss concept and enable the use of the MSI model as a benchmark tool.

As in other severity models, the MSI model reflects the characteristics and standards of care received by the population that provided data for its development. Brazil is the largest country in Latin America and the world's fifth largest country (both by geographical area and population). It

is an upper-middle income country which overall MMR is estimated as 56 maternal deaths per 100,000 live births in 2010 by WHO (1). This study includes a substantial proportion of all maternal deaths that are estimated to have occurred in the country during the data-collection period (8%, range of uncertainty 5-13%). The fact that the MSI model has been developed in an obstetric population is relevant for the applicability of this tool in other populations. This is particularly important in the context of other scoring systems (e.g. the APACHE family) that were developed in generic populations of developed countries. We believe that the application of the MSI to obstetric populations of other developing countries is more direct as compared to extrapolating results from non-obstetric populations from developed countries. However, it should be noted that the standard of care provided by the participating facilities is being used as the reference for the MSI estimates. One would expect that there may be still some limitations and constraints in the quality of care provided by the participating facilities. Thus, the underlying aim of using the MSI as a benchmark is to the assess the health service performance against a standard and through interventions to improve quality achieve a superior performance.

This study has some limitations that are worth noting. First, the non-random nature of the facility sampling process may have introduced some level of selection bias, potentially impairing the country representativeness of this study. On the other hand, the convenience sampling approach was realistic and made this study feasible. Precautions have been taken to maximize country representativeness. An analysis based on the intra-cluster correlation coefficients provided some evidence supporting the success of these precaution measures (29). Second, this study is largely based on information obtained from medical records. In order to reduce the chances of recording bias, information from medical records was complemented with information obtained directly from the assisting staff (if relevant information was missing and in case of doubt). In addition, several procedures to optimize quality of data have been put in place. Third, the study population is essentially provided by referral hospitals which tend to concentrate the more severe cases: the MMR observed in this study is about three times the overall MMR estimated for the country. Another aspect that deserves noting is the relationship between the various covariates within the MSI model. The maternal severity score (i.e. the total number of severity markers present in each case) is positively correlated with maternal mortality and as the number of life-threatening conditions increase, the death probability increases. If a life-threatening condition is identified at hospital arrival or within the first 24 hours of hospital stay, there is an increase in the risk of death, possibly denoting the fact that the woman has arrived in the hospital already in a very severe condition. Cancer and a cardiovascular or respiratory failure substantially increase the

death risk. Two covariates (i.e. severe pre-eclampsia and hysterectomy) have negative coefficients denoting a "protective" association within the model. At the first glance this may seem counterintuitive, but these negative coefficients have to be considered in the context of severe maternal morbidity. Our interpretation to the negative coefficient associated to pre-eclampsia is that women presenting a severe health condition due to pre-eclampsia have the potential of a better outcome as compared to women in the same level of severity having other complications. This can be due to the fact that severe pre-eclampsia tend to be a transient complication and effective strategies to manage women with pre-eclampsia exist (e.g. fetal delivery, magnesium sulfate and anti-hypertensive drugs) and may have been used in the population that provided data to this model, resulting in reduced death risks. Similarly, hysterectomy plays a protective role in the outcome of women with uterine-related haemorrhage and infection.

There are several potential applications to both Maternal Severity Score and MSI. A primary application is determining the level of complexity and severity of a certain obstetric population. For example, a district hospital treating a population with an average maternal severity score = 0.5 is expected to require much more material and human resources than another district hospital treating a population with a maternal severity score = 0.1. These two hypothetical district hospitals receive two different case-mix and the maternal severity score can be used to put the health service in context and support decision making for resource allocation. Another primary application is the health impact evaluation, as part of quality of care assessment. The average MSI can provide an estimation of the expected number of maternal deaths for a selected population. For example, an hypothetical obstetric population being treated in an intensive care unit or in a high dependency facility in a tertiary hospital has an average MSI of 10%. It means that in a group of 100 women treated in this facility it would be expected the occurrence of 10 maternal deaths. If 20 maternal deaths have taken place in this population, one could conclude that there may be some opportunities being missed in this facility and a strategy to improve care is needed. The MSI allows also inter-hospital and over-time comparisons. Another possible applications is in research. In a randomized controlled trial, for instance, it is worthwhile determining if both trial arms are comparable in terms of severity. Severity can functions as a major confounder: trial results can differ because of unbalances in the severity of the study populations (e.g. populations containing more severe cases tend to present worse health outcomes in comparison to populations with less severe cases). The maternal severity score and

the MSI can be used for adjusting for the case-mix, through stratification or as a covariate in statistical modeling.

In summary, the maternal severity score provide an estimation of the overall severity associated with a specific women or a selected population. Similarly, the MSI provides an estimate of the death risk. For ease use, the web appendix contains a maternal severity score and maternal severity calculator. As a final remark, the estimates derived from the MSI model are to be used with caution. A MSI with 95% of death risk means that among 100 women with similar conditions, 95 women may die. However, the model is not able to differentiate if the specific woman is among the 5 that will survive. Thus, MSI estimates should not directly guide the management of critically ill patients.

Conclusion

The identification of maternal near-miss cases using the WHO list of pregnancy-related life-threatening conditions is valid, as these conditions are accurately associated with maternal deaths. The MSI model adequately describes the relationship between severity markers and maternal deaths. The MSI model can be used as a tool for benchmarking, population severity assessment and case-mix adjustment. The use of the MSI model within a maternal near-miss approach has the potential of contributing to the assessment and improvement of maternal health care, particularly that required by women experiencing severe maternal morbidity. Further studies assessing the performance of the MSI model in other populations are welcome.

Contributors

The Brazilian Network for Surveillance of Severe Maternal Morbidity Group provided data for this analysis. JPS designed the analysis plan in collaboration with JGC. JPS performed the analysis and drafted the manuscript. All authors provided valuable input into the manuscript.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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Table 1: The WHO set of severity markers (life-threatening conditions) used in maternal near-miss assessments

	Group A*	Group B*
Cardiovascular dysfunction	• Shock	• pH <7.1
	• Lactate >5	• Use of continuous vasoactive drugs
		• Cardiac arrest
		• Cardio-pulmonary resuscitation (CPR)
Respiratory dysfunction	• Acute cyanosis	• Gasping
	• Respiratory rate >40 or <6/min	• PaO2/FiO2 <200 mmHg
	• Oxygen saturation <90% for ≥60 minutes	• Intubation and ventilation not related to anesthesia
Renal dysfunction	• Oliguria non responsive to fluids or diuretics	• Creatinine ≥300 mmol/l or ≥3,5 mg/dl
		• Dialysis for acute renal failure
Coagulation/hematological dysfunction	• Clotting failure	• Acute thrombocytopenia (<50 000 platelets)
	• Transfusion of ≥5 units of blood/red cells	
Hepatic dysfunction	• Jaundice in the presence of pre-eclampsia	• Bilirubin>100 mmol/l or > 6,0 mg/dl
Neurological dysfunction	• Metabolic coma (loss of consciousness AND the presence of glucose and ketoacids in urine)	• Coma/ loss of consciousness lasting 12 hours or more
	• Stroke	
	• Status epilepticus/Uncontrollable fits/total paralysis	
Uterine dysfunction	• Hysterectomy due to infection or hemorrhage	

*A glossary with relevant operational definitions is available at reference 28. Stratification of the WHO life-threatening conditions is based on the SOFA score (reference 30). Group B reflects SOFA score categories 3 and 4 (i.e. markers of greater severity).

Table 2: Accuracy of the WHO set of severity markers in the prediction of maternal deaths among all women and women with pregnancy-related complications *

		All women (N=82388) Maternal deaths		**Women with complications** (N=9555) Maternal Deaths	
		+	**-**	**+**	**-**
Any WHO criterion	**+**	140	770	140	770
	-	0	81478	0	8645
Accuracy estimator					
Sensitivity (95% CI)		1.0 (0.97-1.0)		1.0 (0.97-1.0)	
Specificity (95% CI)		0.99 (0.99 - 0.99)		0.92 (0.91 - 0.92)	
Positive likelihood ratio (95% CI)		106.8 (99.56-114.6)		12.2 (11.4 - 13.1)	
Negative likelihood ratio (95% CI)		0.0		0.0	

*In this table maternal near-miss cases are the false positives

Table 3: Relationship between severity markers (WHO criteria) and maternal deaths

		Maternal Deaths +	Maternal Deaths -	Cases presenting the severity marker per 1000 deliveries*	Mortality	Relative Risk (95% CI)
Cardiovascular dysfunction						
Shock	+	74	176	3.01	29.60%	41.7 (30.7 - 56.7)
	-	66	9239			
Cardiac arrest	+	51	13	0.77	79.69%	85 (66.8 - 108.1)
	-	89	9402			
pH <7.1	+	51	22	0.88	69.86%	74.4 (57.6 - 96.1)
	-	89	9393			
Lactate >5	+	24	56	0.96	30.00%	24.5 (16.7 - 35.8)
	-	116	9359			
Use of continuous vasoactive drugs	+	101	143	2.93	41.39%	98.8 (69.9 - 139.8)
	-	39	9272			
Cardio-pulmonary resuscitation (CPR)	+	102	18	1.44	85.00%	211 (152.3 - 292.4)
	-	38	9397			
Respiratory dysfunction						
Acute cyanosis	+	55	68	1.48	44.72%	49.6 (37.2 - 66.2)
	-	85	9347			
Gasping	+	24	13	0.44	64.86%	53.2 (39.5 - 71.7)
	-	116	9402			
Respiratory rate >40 or <6/min	+	74	118	2.31	38.54%	54.7 (40.5 - 73.8)
	-	66	9297			
Oxygen saturation <90% for ≥60 minutes	+	80	106	2.24	43.01%	67.2 (49.7 - 90.8)
	-	60	9309			
PaO2/FiO2 <200 mmHg	+	53	48	1.21	52.48%	57 (43.1 - 75.4)
	-	87	9367			
Intubation and ventilation not related to anesthesia	+	123	172	3.55	41.69%	227.1 (138.6 - 372.1)
	-	17	9243			
Renal dysfunction						
Oliguria non responsive to fluids or diuretics	+	35	55	1.08	38.89%	35.1 (25.4 - 48.3)
	-	105	9360			
Creatinine ≥300 mmol/l or ≥3,5 mg/dl	+	21	77	1.18	21.43%	17 (11.2 - 25.9)
	-	119	9338			
Dialysis for acute renal failure	+	24	39	0.76	38.10%	31.2 (21.7 - 44.8)
	-	116	9376			
Coagulation/hematological dysfunction						
Clotting failure	+	33	63	1.15	34.38%	30.4 (21.7 - 42.5)
	-	107	9352			

Acute thrombocytopenia	+	30	170	2.41	15.00%	12.8 (8.7 - 18.6)
(<50 000 platelets)	-	110	9245			
Transfusion of ≥5 units of blood/red	+	50	199	2.99	20.08%	20.8 (15 - 28.7)
cells	-	90	9216			
Hepatic dysfunction						
Jaundice in the presence of pre-	+	7	22	0.35	24.14%	17.3 (8.9 - 33.7)
eclampsia	-	133	9393			
Bilirubin>100 mmol/l	+	13	37	0.60	26.00%	19.5 (11.8 - 32)
or > 6,0 mg/dl	-	127	9378			
Neurological dysfunction						
Coma/ loss of consciousness >12h	+	36	29	0.78	55.38%	50.5 (37.8 - 67.5)
	-	104	9386			
Metabolic coma	+	6	12	0.22	33.33%	23.7 (12.1 - 46.6)
	-	134	9403			
Stroke	+	10	15	0.30	40.00%	29.3 (17.6 - 48.8)
	-	130	9400			
Status epilepticus/ Uncontrollable	+	5	11	0.19	31.25%	22.1 (10.5 - 46.6)
fits/total paralysis	-	135	9404			
Uterine dysfunction						
Hysterectomy due to infection or	+	22	149	2.06	12.87%	10.2 (6.7 - 15.7)
hemorrhage	-	118	9266			

* N=82,388 deliveries.

Table 4: Relationship between the number of severity markers (maternal severity score) and mortality*

Number of severity markers	Total sample (N)	Maternal deaths (n)	Mortality (95% CI)
0	8645	0	0% (0% - 0%)
1	402	0	0% (0% - 0.9%)
2	148	3	2% (0.7% - 5.8%)
3	70	6	8.6% (4% - 17.5%)
4	61	14	23% (14.2% - 34.9%)
5	59	19	32.2% (21.7% - 44.9%)
6	46	16	34.8% (22.7% - 49.2%)
7	29	15	51.7% (34.4% - 68.6%)
8	18	10	55.6% (33.7% - 75.4%)
9	20	15	75% (53.1% - 88.8%)
10	20	13	65% (43.3% - 81.9%)
11	6	4	66.7% (30% - 90.3%)
12	13	11	84.6% (57.8% - 95.7%)
13	4	3	75% (30.1% - 95.4%)
14	7	5	71.4% (35.9% - 91.8%)
15+	7	6	85.7% (48.7% - 97.4%)

*The Pearson correlation coefficient between the maternal severity score and mortality is 0.96.

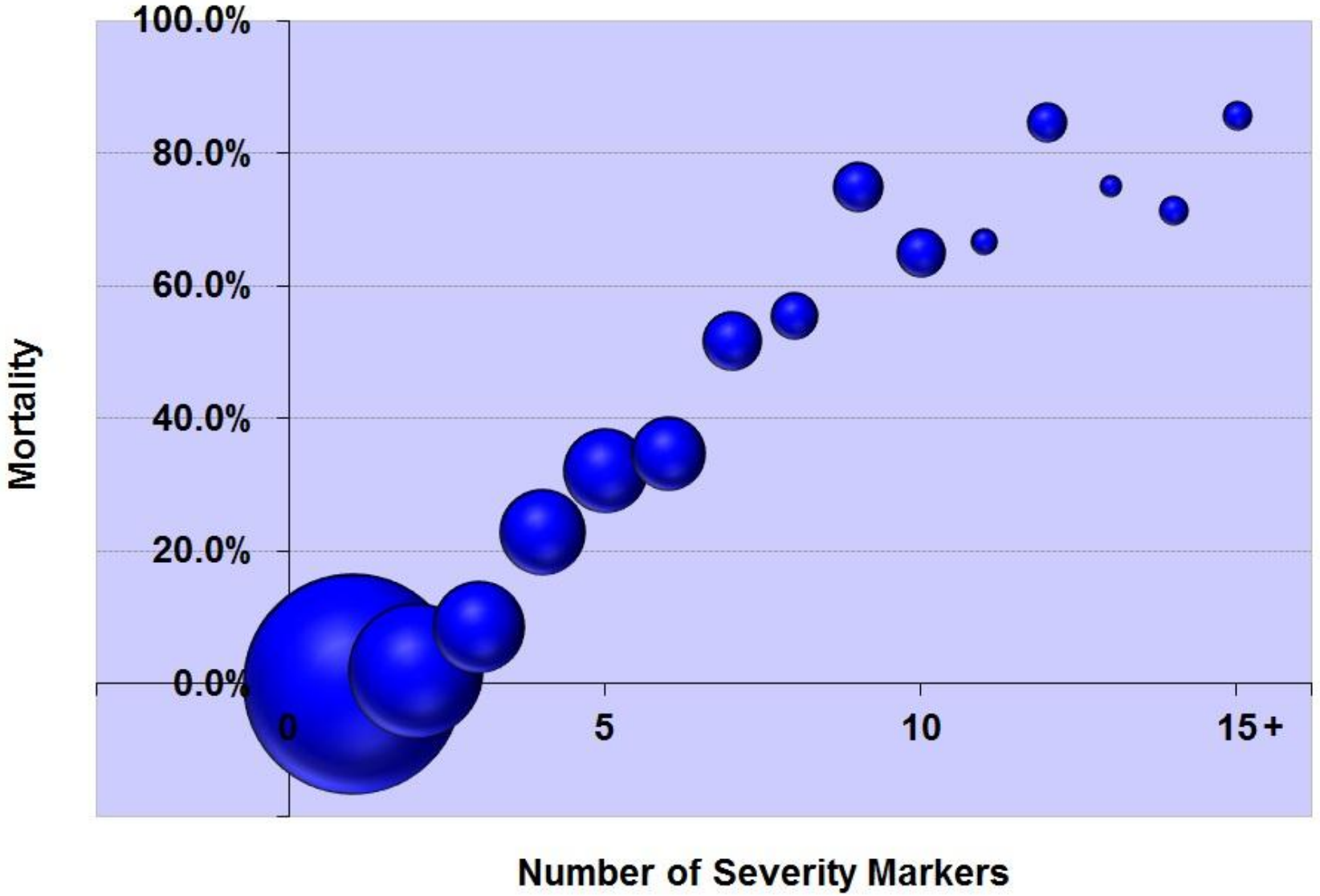

Figure 1: The relationship between the number of severity markers and mortality (the size of each bubble denotes the amount of cases)

Table 5: The performance of the models I and II and the maternal severity score

	Hosmer-Lemeshow test*	Nagelkerke R^2 test[£]	Percentage of maternal deaths with a model-estimated death probability > 50% (subpopulation "A")	Percentage of maternal deaths with a model-estimated death probability > 50% (subpopulation "B")	AUROC with 95% CI[@]
Model I	<0.001	0.629	45.9%	55.2%	0.955 (0.925-0.984)
Model II	0.402	0.745	66.7%	69.0%	0.954 (0.922 – 0.985)
Maternal Severity Score	N.A.	N.A.	N.A.	N.A	0.955 (0.925-0.984)

*The Hosmer-Lemeshow test indicates a poor fit if p value is less than 0.05
[£] The Nagelkerke R^2 values the proportion of variance in maternal mortality associated with the models' predictors. Higher R^2 values, better model performance.
[@]Area under the receiver operating characteristic curve with 95% confidence intervals calculated among women with life-threatening conditions of the subpopulation "B".
N.A.: not applicable

Table 6: The Maternal Severity Index (MSI)

Constant and covariates		Coefficients	
Constant		β	-7.540
Maternal severity score			
(x_1)	Number of life-threatening conditions* (n)	(β_1)	0.309
Associated conditions			
(x_2)	Life-threatening conditions identified in the first 24 hours of hospital stay	(β_2)	0.287
(x_3)	Severe pre-eclampsia	(β_3)	-0.579
(x_4)	Cancer	(β_4)	3.492
(x_5)	Any marker of cardiovascular failure#	(β_5)	4.209
(x_6)	Any marker of respiratory failure#	(β_6)	1.513
(x_7)	Histerectomy	(β_7)	-1.169

Determining the MSI

x_1 equals to the total number of life-threatening conditions present in the specific case and in the sequence x_2 to x_7, x equals 1 if the condition is present or x equals 0 if the condition is absent; then:

$$\text{Logit} = \beta + (x_1\beta_1) + (x_2\beta_2) + (x_3\beta_3) + (x_4\beta_4) + (x_5\beta_5) + (x_6\beta_6) + (x_7\beta_7)$$

and

$$\text{MSI} = e^{\text{Logit}}/(1 + e^{\text{Logit}})$$

* Listed in the Table 1

Life-threatening conditions listed in the group B of the corresponding organ

Maternal Severity Index (MSI) Calculator

Instructions:

(1) Enter the information at discharge of health facility or maternal death.

(2) Indicate (tick) all conditions that were present during the stay in the health facility.

Severity Status at arrival

☐ Any life-threatening condition identified in the first 24 hours of hospital stay

Associated conditions

☐ Severe pre-eclampsia

☐ Cancer

Life-threatening conditions

Cardiovascular dysfunction

☐ Shock
☐ Cardiac arrest
☐ pH <7.1
☐ Lactate >5
☐ Use of continuous vasoactive drugs
☐ Cardio-pulmonary resuscitation

Respiratory dysfunction

☐ Acute cyanosis
☐ Gasping
☐ Respiratory rate >40 or <6 breaths per minute
☐ Oxygen saturation <90% for ≥60 minutes
☐ PaO2/FiO2 <200 mmHg
☐ Intubation and ventilation not related to anesthesia

Renal dysfunction

☐ Oliguria non responsive to fluids or diuretics
☐ Creatinine ≥300 mmol/l or ≥3,5 mg/dl
☐ Dialysis for acute renal failure

Coagulation/hematological dysfunction

☐ Clotting failure
☐ Acute thrombocytopenia (<50 000 platelets)
☐ Transfusion of ≥5 units of blood/red cells

Neurological dysfunction

☐ Coma/ loss of consciousness lasting 12 hours or more
☐ Metabolic coma
☐ Stroke
☐ Status epilepticus/Uncontrollable fits/total paralysis

Hepatic dysfunction

☐ Jaundice in the presence of pre-eclampsia
☐ Bilirubin>100 mmol/l or > 6,0 mg/dl

Uterine dysfunction

☐ Hysterectomy due to infection or hemorrhage

Maternal Severity Score: 0

Maternal Severity Index: 0.1 %

Brazilian Network for Surveillance of Severe Maternal Morbidity. The WHO Maternal Near-Miss Approach and the Maternal Severity Index Model (MSI): tools for assessing the management of severe maternal morbidity. Plos One, 2012.

3.3. Artigo 3

Research

Applying the near miss approach for the evaluation of obstetric care: a worked example from a multicenter surveillance study

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Running title: the maternal near miss approach for evaluation of obstetric care

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Abstract

Objective: to assess the performance of care in facilities attending women with severe maternal morbidity and to identify associated factors.

Method: the Brazilian Network for Surveillance of Severe Maternal Morbidity was a multicenter cross sectional study conducted to identify cases of severe maternal morbidity, using criteria for potentially life-threatening conditions and maternal near miss from the WHO in 27 referral hospitals from all the Brazilian regions. All women presenting these conditions during a one-year period were included. Using the Maternal Severity Index (MSI) for mortality prediction based on the severity of complication, the expected number of maternal deaths was available, and the Standardized Mortality Ratio (SMR) for each study center was estimated. Analyses on the adequacy of care provided were then performed.

Findings: 17 hospitals were classified as providing adequate care and 10 as non-adequate care. There was a twofold increase in maternal mortality ratio for the group with non-adequate performance (225 versus 134/100.000 LB). The main factors associated with non-adequate performance were: geographic difficulty in accessing health services ($p<0.001$), delays related to quality of medical care ($p=0.012$), absence of blood derivatives ($p=0.013$), difficulties of communication between health services ($p=0.004$) and any delay during the whole process ($p=0.039$).

Conclusions: This is an example of how evaluation of the performance of health services is possible, using a benchmarking tool specific to Obstetrics. In this study the MSI was a useful tool for identifying differences in maternal mortality ratios and factors associated with non-adequate performance of care in the network.

Keywords: severe maternal morbidity, maternal near miss, maternal morbidity, severity score, quality of care assessment.

Introduction

The outcome of a critically ill patient is a result of a group of clinical and individual factors, including previous health status, physiologic reserve, disease diagnosis and also adequacy of care provided during the disease. Thus, it is difficult to individually analyze and predict morbidity and mortality outcomes in critically ill patients.[1] Stratification of patient groups according to clinical severity may facilitate interpretation of these results by comparing similar groups. [2]

Some scoring systems are capable of quantifying severity, e.g. the APACHE, SAPS, SOFA and MPM.[1] However, they were developed using general populations of critically ill patients in developed countries. Considering the severe pregnancy complications, several factors seem to reduce the capacity to classify severity and predict mortality among pregnant women with these models.

The different physiologic parameters, diseases unique to pregnancy and a population largely composed of young women who were previously healthy, contribute to the little applicability of these tools in Obstetrics.[3] As a result, traditional risk stratification models usually overestimate mortality among pregnant women, which may hinder analysis of the performance of care provided and interpretation of morbidity and mortality outcomes.[3]

"Benchmarking" may be understood as a reference point against which comparisons can be made, regarding the performance between facilities and/or best practice. The demand for this type of data is growing, not only due to initiatives to pay for performance, but also because of clinical, administrative and research applications. Performance feedback at an institutional or individual level may lead to an improvement in overall performance.[2]

Several initiatives for maternal and infant health have been implemented worldwide, aimed at achieving the Millennium Development Goals. [4-8] Nevertheless, advances made over the years are below those required for effective morbidity and mortality reduction. Structured health systems are identified as fundamental to obtain better results and accelerate progress for achieving these goals. [9,10]

The World Health Organization (WHO) used organ dysfunction criteria and parameters of extreme severity specific to Obstetrics to define life-threatening conditions associated with pregnancy, standardizing the maternal near miss criteria. [8] A maternal near

miss is an event in which a woman nearly died, but survived a severe complication occurring during pregnancy, childbirth or within 42 days of its termination. It represents the extreme degree of organ dysfunction/failure in the wide spectrum of morbidity and differs from death only by the final outcome.[8]

Until this definition, several studies used different parameters for severe morbidity, such as admission to intensive care units (ICU) or clinical diagnoses.[11-14] The first retrospective validation of these criteria was performed in a population of obstetric patients admitted to ICU, using the total maximum SOFA score as the gold standard and showing that the WHO near miss criteria obtained a sensitivity and specificity of 99.2 and 86.0%, respectively, for the identification of organ failure in at least one organ system. [15]

The Brazilian Network for Surveillance of Severe Maternal Morbidity was a prospective study aimed at identifying potentially life-threatening and maternal near miss cases.[16,17]. Assuming that a woman suffering from a near miss event is exactly like one who has died, except for the outcome, criteria would be validated if all maternal deaths were identified and if the false-positive cases represented exactly the near miss cases. The performance of the WHO near miss criteria was confirmed, with a sensitivity and specificity of 100 and 92%, respectively. [18] In this study a tool called Maternal Severity Index was also developed specifically to predict mortality for the obstetric population. This appears to be a first step in making a case-mix analysis and a comparison between obstetric services by matching similar populations.[18]

Strategies aimed at strengthening health systems are necessary. However, many systems still do not have the capacity to measure and understand their own weaknesses, making it difficult for healthcare policy managers to incorporate scientific strategies towards strengthening systems.[10] The maternal near miss approach may be a tool for assessment of quality of maternal care provided. As a result, standardization and comparison can be made between maternal morbidity groups from different locations and over time, identifying weaknesses.[7] Thus, the aim of this study was to simulate the evaluation of an obstetric health system, through analysis of the performance of care in the Brazilian Network for the Surveillance of Severe Maternal Morbidity, using the maternal near miss criteria approach.

Method

Study Population

The Brazilian Network for Surveillance of Severe Maternal Morbidity was a cross sectional multicenter study aimed at identifying severe maternal morbidity cases, using the new WHO definition.[8,16] From July 2009 to June 2010, 27 referral hospitals made a prospective surveillance to identify severe maternal morbidity/near miss cases. In this period, 9555 women had severe pregnancy complications, with 770 near miss cases and 140 maternal deaths.

The study was planned in details, with preparatory meetings to discuss methods and procedures with participants from all centers. After prospective data collection was completed, a rigorous checking system for data consistency was developed. Additional details on method and procedures are in other publications.[16,17] The study was approved by the local Institutional Review Board of each participating center and also nationally.

Each center was previously consulted regarding this analysis of performance and data publication. Approval was unanimous. To ensure confidentiality, each centers is not identified and received confidential information on the category it was classified in order to be able to adopt procedures to improve quality of care provided.

Development of a Model for Mortality Prediction

Previously, it was possible to build a model for mortality prediction, named Maternal Severity Index (MSI). [18] Briefly, two models for mortality prediction were developed. First, it was confirmed that the number of near miss markers could be related to mortality and this correlation was called Maternal Severity Score (MSS). Two models of bivariate logistic regression were then developed and tested to describe the relationship between severe morbidity and mortality. For this, the total study population was divided into two subpopulations “A” and “B” to develop and test the prediction model, respectively. The sample size of population “B” was obtained considering a probability of 0.05 for type I error, 0.20 for type II error and a minimum area under the ROC (receiver operating characteristic) curve of 0.80.

The first model was a univariate analysis including only MSS or the number of severity markers. The second used univariate analyses considering MSS, distal predictors of mortality (such as demographic, obstetric characteristics), and near miss criteria as independent variables and the outcome maternal death as the dependent variable. Variables significantly correlated with mortality were selected for multivariate analysis. Positive or negative correlation coefficients (β) were attributed to each variable included in the model. Calibration and discrimination of models were performed. Model 2 showed the best performance for mortality prediction. Therefore, it was chosen to be the Maternal Severity Index (MSI). To simplify the estimation of MSI, a calculator was developed.

Analysis of Performance of Network Centers

The mean MSI for each center was obtained and the Standardized Mortality Ratio (SMR) was calculated for each one (Figure 1). SMR is the ratio between observed mortality in the population and expected mortality by mortality prediction based on severity of the case expressed by MSI. To permit calculation of SMR for all centers, a value of 0.1 was attributed, when no death was observed or there was no expected death due to the small sample size and/or low complexity of cases in that center.

In the original model, the categorization of performance was based on cut-off points selected assuming the normal distribution into five classes of care and the understanding that SMR < 0.5, i.e. the occurrence of half or less than the expected number of deaths could correspond to excellent care. Thus, the five categories of performance were defined as very high, high, intermediate, very low and low. [18]

In this analysis, SMR was calculated from the mean MSI for each of the 27 study centers. Due to the relatively small number of centers and to make analyses more consistent as an exercise to evaluate large systems, the original classification was modified, and groups were relocated to two new categories. Categories “very high”, “high” and “intermediate,” including SMR < 0.5 to 1.24, were reclassified as “adequate” care. Categories “low” and “very low,” with SMR of 1.25 to > 2, were recoded as “non-adequate.” Thus, this performance was analyzed as a dependent variable. Using both groups of adequacy of care, variables related to structure, process, management and delays were correlated as independent variables.

Furthermore, patient outcomes, their respective indicators and main causes of complication were evaluated for both groups of level of performance. Finally, Poisson multiple regression analysis was performed, using the level of performance as a dependent variable, estimating the Prevalence Ratio and its respective 95% CI to identify variables independently associated with performance. A 5% statistical significance level was used. All measures of effect in the study design and their respective p-values were calculated after adjusting for cluster effect.

Results

In Table 1, the mean MSI, number of observed deaths, sample size (potentially life-threatening and near miss conditions), expected number of deaths, SMR, and finally, the recategorized level of performance of care are presented for each of the 27 centers, 17 being classified as having "adequate" and 10 as "non-adequate" performance. Generally, the overall performance of Network was adequate, since there were only two more maternal deaths than expected due to severity of cases (SMR=1.02).

Table 2 shows the distribution of outcomes of severity and of main causes of morbidity, according to the level of performance of the centers. Although differences were not significant, there was proportionally almost twice the number of deaths among centers classified as "non-adequate" care. Maternal health indicators also show that the occurrence of maternal near miss was similar between performance groups, but there was an almost twofold increase in the maternal mortality ratio (MMR) in the group with non-adequate care.

Structure indicators according to level of performance are shown in Table 3. Centers with "adequate" performance were located with an almost 2.5 higher prevalence in the southeast and south of the country, but this difference was not significant. When process and management indicators (Table 4) were analyzed, there was twofold increase in ICU admissions in adequate care centers, but this difference was also not significant.

Correlation between delay in care and the level of performance is shown in Table 5. Generally, both detection of any type of delay and some specific categories of delays, particularly those concerning the third delay (related to quality of care) were significantly more common in the non-adequate performance group. Considering all the predictive

variables included in the multiple regression analysis (Table 6), the use of magnesium sulfate and location of the health center in the south or southeast were the main variables independently associated with adequate performance of care.

Discussion

With the use of the MSI and SMR, it was possible to assess the performance of centers from the Brazilian Network for Surveillance of Severe Maternal Morbidity. This was a first initiative to use the near miss concept as a tool for assessment of case-mix and adequacy of care provided in Obstetrics.

In the classification of performance, sample size per center corresponds to the number of cases with potentially life-threatening conditions and threatening life conditions (near miss and maternal death) and not the total number of live births, because only women presenting with some severity indicators were included in the study. Although calculation of SMR for all centers was possible after attributing a value of 0.1 to those that did not present any observed or expected death, these estimates had low accuracy. Therefore, the MSI seems limited and less precise for use in populations with a small number of cases, with lower clinical severity (low MSI) and those with no observed death. The lower accuracy of estimates in these cases should increase attention and care for interpreting the performance of these health services.

Centers participating in this Brazilian Network were selected considering their availability to participate in the study, the total number of annual deliveries and geographic location. Thus, the estimated sample size could be achieved, ensuring a broad distribution in national territory. Nevertheless, most of these hospitals were linked to large university institutions or had teaching activities, what implies they are mostly referral for healthcare of severe pregnancy complications, with evidence-based protocols and similar standards of care. The relative homogeneity of these facilities may have contributed to the lack of significant differences between levels of performance of care and most variables related to the profile of severity of illness, cause of morbidity and structure and management indicators, in addition to the limited number of centers participating in the study.

The greater proportion of infectious causes among centers with adequate performance may be perceived as better adequacy to international protocols for the

management of sepsis, [19] already widely known among academic medical services. Referral of these cases to hospitals equipped with a high complexity arsenal is a determining factor for the survival of these patients.

As observed, there was a twofold increase in number of deaths in centers with non-adequate performance. However, the prevalence of maternal near miss was practically the same in both groups of performance. This is in agreement with recent knowledge that severe pregnancy complications occur practically in the same frequency in all countries and regions, regardless of the level of development and availability of resources. In fact, the varying factor is mortality, which is always higher in contexts of lower development and scarce resources, how currently demonstrated. [20]

In this study, information on potential delays in obtaining care among women suffering severe complications was collected. In addition to objective information from medical charts, local researchers made a subjective assessment and searched for the three types of delay in obtaining care.[21]

The presence of any delay in care was significantly related to a worse performance of service. These results are in agreement with the concept that the main preventive factors in decreasing maternal mortality are delays in the care process, from symptom identification by the patient to the provision of adequate treatment by healthcare professionals. [21] Globally there was a greater delay in providing services in non-adequate care centers, mainly due to the absence of blood products and difficulty in establishing communication between services and/or regulatory centers.

These findings seem to follow a presumptive logic. Subjects living in geographic regions with difficult access have the greatest difficulty in seeking medical care, including antenatal follow-up. Healthcare facilities close to these homes are also probably on the outskirts of large cities and high-complexity hospitals are usually in the center of these cities. In general, this peripheral healthcare equipment does not have an adequate structure to provide immediate care and monitor complications. There is also difficulty in regulating complex cases to large referral centers. Finally, successive delays in providing care are related to a higher number of severe outcomes and deaths.

This hypothesis may corroborate information that health system strengthening may actually have the greatest impact on improvement of clinical care.[10] For instance, prompt

action of the whole health system for hierarchization of care, according to demand of severity, could ensure a reduction in deaths by improving adequacy of care. These strategies would go beyond the sole responsibility of the healthcare managers. Most probably, social development actions, civil and transport infrastructure are necessary to correct determining factors for the health of these more vulnerable populations.

The MSI for mortality prediction follows the same indications and limitations of similar models, such as the APACHE and MPM. Use for individual evaluation is limited, since the greatest outcome predictor is individual response to therapy administered.[2] In addition, waiting to provide specific measures only when certain markers of severity emerge is not recommended. Individual clinical care is dynamic and the use of severity scores for decision-making may delay healthcare, with poor provision of adequate resources. Most existing scores consider the clinical parameters obtained in the first 24 hours after ICU admission and do not assess time, care or alterations present before it. [2] MSI was developed using data from the pre-hospital phase until discharge, using several sources distributed all over the country, which may increase the accuracy of its prediction.

The SMR may be perceived as the evaluation of performance of a system rather than of a health service alone. In this study, SMR was re-categorized as "adequate" and "non-adequate", the cutoff point being the limit between intermediate and low care from the original classification. [18] Thus a group of centers that actually had SMR above 1 was classified as providing "adequate" care. Centers that could not prevent any expected death, and in some cases had a slight increase in the number of deaths in relation to the expected due to severity of their cases, were categorized as having adequate performance. Although this methodological option may have reduced the identification of variables related to actual excellent care (SMR between 0 and 0.8), it was a strategy adopted as a form of simplifying data analysis and prioritizing identification of centers with non-adequate performance. In the future, with a larger number of participating hospitals and subjects, it is likely that analysis with three categories (e.g. high, intermediate and low performance) may be a valuable strategy for evaluating all the components of performance individually.

Conclusions

In the Brazilian Network for Surveillance of Severe Maternal Morbidity, the near miss approach was used to simulate analysis of an obstetric health system. After applying the MSI and SMR, analysis of the performance of services was possible and its associated factors were assessed. Problems arising from the health system organization were identified as significant, especially those related to accessibility to health services and quality of medical care provided.

The use of this specific tool for mortality prediction may contribute to the analysis of Obstetric health systems and identification of weaknesses. Furthermore, it may to strengthen these systems, with an effective reduction in deaths. Nevertheless, new studies in different populations should be conducted for external calibration of tools developed in the Brazilian Network.

What was already known about the topic concerned

The concepts of severe maternal morbidity and maternal near miss applied to practice are currently recognized as an efficient way of understanding and dealing with maternal deaths. Maternal near miss and maternal death share exactly the same causes and determinants, differing only by the outcome due to the good care woman received or to luck. The WHO near-miss approach for maternal health has already been recommended as a tool for evaluating the quality of care for severe pregnancy complications.

What new knowledge the manuscript contributes

Using the maternal near miss approach, it is possible to estimate the severity of complications determined by the occurrence of a set of standardized organ dysfunction's criteria and also to predict mortality based on this severity. The current proposal shows by the first time an example on how to use the near miss concept as a benchmarking tool. By stratifying the severity of cases from each facility, the number of expected deaths can be compared to those observed in a population, with a further evaluation of the specific care provided to each group. This is a way thus available to measure the quality of obstetrical care and would allow appropriate technical and administrative procedures to overcome constraints and delays on provision of heath care.

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Table 1. Analyses of MSI, SMR and level of performance for each center of the Brazilian Network for Surveillance of Severe Maternal Morbidity

Center	MSI (%)	Observed Number of deaths	Sample Size	Expected Deaths	SMR	(95% CI)	Performance
1	0.44%	5	566	2	2.01	(0.65 - 4.69)	Non A
2	3.54%	4	96	3	1.18	(0.32 - 3.01)	A
3	0.57%	0	253	1	0.00	(0.00 - 2.56)	A
4	7.74%	6	112	9	0.69	(0.25 - 1.51)	A
5	1.92%	2	210	4	0.50	(0.06 - 1.79)	A
6	1.93%	17	1086	21	0.81	(0.47 - 1.30)	A
7	1.81%	3	172	3	0.96	(0.20 - 2.82)	A
8	0.25%	1	1050	3	0.38	(0.01 - 2.12)	A
9	1.40%	4	155	2	1.84	(0.50 - 4.72)	Non A
10	3.84%	30	609	23	1.28	(0.87 - 1.83)	Non A
11	0.68%	3	186	1	2.37	(0.49 - 6.93)	Non A
12	7.91%	8	98	8	1.03	(0.45 - 2.03)	A
13	4.55%	3	154	7	0.43	(0.09 - 1.25)	A
14	0.59%	0	841	5	0.00	(0.00 - 0.74)	A
15	3.24%	9	369	12	0.75	(0.34 - 1.43)	A
16	1.04%	11	945	10	1.12	(0.56 - 2.00)	A
17	1.15%	5	294	3	1.48	(0.48 - 3.45)	Non A
18	1.39%	1	66	1	1.09	(0.03 - 6.08)	A
19	0.69%	8	920	6	1.26	(0.54 - 2.48)	Non A
20	4.05%	8	118	5	1.67	(0.72 - 3.30)	Non A
21	0.53%	0	48	0	0.00	(0.0 - 14.52)	A
22	3.25%	5	74	2	2.08	(0.68 - 4.85)	Non A
23	0.47%	3	465	2	1.37	(0.28 - 4.01)	Non A
24	0.49%	1	263	1	0.78	(0.02 - 4.32)	A
25	1.66%	3	65	1	2.78	(0.57 - 8.12)	Non A
26	0.05%	0	59	0	0.00	(0.0 - 122.9)	A
27	0.11%	0	281	0	0.00	(0.0 - 11.93)	A
Overall	1.44%	140	9555	138	1.02	(0.86 - 1.20)	A

A: adequate; Non A: non-adequate

Figure 1: SMR Calculator

SMR Calculator

Instruction:

Enter the required information in the green boxes.

Enter the mean MSI (%):

Enter the observed number of deaths:

Enter the population size:

Expected number of deaths: 0

Performance assessment

SMR: N.A.

Performance Grade: N.A.

Precision of the assessment: N.A.

Parameters used in the assessment

Grades of Performance	SMR
Very High	<0.50
High	0.50-0.80
Intermediate	0.81-1.24
Low	1.25-2.00
Very low	>2.00

Precision	Number of performance grades included in the range of SMR 95% CI
High	One
Moderate	Two
Low	Three or more

Table 2. Distribution of cases of severe maternal morbidity according to the group of severity, main causes of morbidity and level of performance of care

	Level of performance of care				
	Adequate		Non-adequate		p[1]
Outcome of severity [&]	n	(%)	n	(%)	
PLTC	5,543	(90.8)	3,102	(89.9)	0.398
MNM	494	(8.1)	276	(8.0)	
MD	66	(1.1)	74	(2.1)	
Total	6,103	(100.0)	3,452	(100.0)	
Main causes					
Hemorrhage	1,438	(23.6)	840	(24.3)	0.924
Hypertension	4,323	(70.8)	2,383	(69.0)	0.833
Infection	83	(1.4)	17	(0.5)	**0.036**
Clinical-surgical	614	(10.1)	409	(11.8)	0.499
Total	6,103		3,452		
Maternal health indicators					
MNMR	10.02/1000LB		8.4/1000LB		
MMR	133.9/100.000LB		225.1/100.000LB		
SMOR	11.36/1000LB		10.65/1000LB		
LB	49.275		32.869		

LB: live births; MD: maternal death; MMR: maternal mortality ratio; MNM: maternal near miss; PLTC: potentially life-threatening condition; SMOR: severe maternal outcome ratio
& Comparisons: PLTC x (NM+MD): p=0.721; (PLTC+NM) x MD: p=0.123
[1] p-value adjusted for cluster effect

Table 3. Distribution of study centers according to structure indicators and level of performance of care

Structure indicator @	Level of performance		p[1]
	Adequate	Non-adequate	
Type of ICU			*
Obstetric	5 (29)	2 (20)	0.678 #
Only general ICU	9 (53)	5 (50)	>0.999 #
None	3 (18)	3 (30)	0.638 #
Level of complexity			>0.999 #
Secondary	3 (18)	2 (20)	
Tertiary	14 (82)	8 (80)	
Geographic region			0.057 #
North, Northeast and Center-West	5 (29)	7 (70)	
Southeast and South	12 (71)	3 (30)	
Level of government			*
Municipal	2 (12)	2 (20)	0.613 #
State	5 (29)	4 (40)	0.683 #
Federal	7 (41)	3 (30)	0.692 #
Non-public	3 (18)	1 (10)	>0.999 #
Total	**17 (100)**	**10 (100)**	

@ The following indicators were not taken into account: teaching hospital; blood bank; neonatal ICU and round the clock anesthetic available, due to the fact that almost all centers had these indicators

* Chi-square test not applicable for general comparison

Fisher Exact Test

[1] p-value adjusted for cluster effect

Table 4. Distribution of cases of severe maternal morbidity according to process and management indicators and level of performance of care

	Level of performance				p[1]
	Adequate		Non-adequate		
Process indicators	**n**	**(%)**	**n**	**(%)**	
Way of access (spontaneous)	3.227	(54.2)	1.082	(35.7)	0.056
Total (a)	5.958	(100.0)	3.033	(100.0)	
Way pregnancy is terminated (Cesarean)	3.748	(61.7)	2.406	(69.9)	0.211
Total (b)	6.074	(100.0)	3.441	(100.0)	
Admission to ICU	1.652	(27.1)	463	(13.4)	0.245
Long hospital stay (>7 days)	1.751	(28.7)	1.117	(32.4)	0.644
Referred to another place	46	(0.8)	32	(0.9)	0.681
Total	6.103	(100.0)	3.452	(100.0)	
Any *near miss* criteria on admission	196	(35.0)	95	(27.1)	0.281
Total	560	(100.0)	350	(100.0)	
Management indicators					
Use of magnesium sulphate	2.932	(48.0)	1.685	(48.8)	0.960
Blood product transfusion	855	(14.0)	711	(20.6)	0.129
Central venous access	261	(4.3)	102	(3.0)	0.447
Intubation unrelated to anesthesia	190	(3.1)	106	(3.1)	0.975
Hysterectomy due to infection or hemorrhage	116	(1.9)	55	(1.6)	0.691
Total	6.103	(100.0)	3.452	(100.0)	

Missing information for: (a) 564 cases; (b) 40 cases

[1] p value adjusted for cluster effect

Table 5. Distribution of cases of severe maternal morbidity according to occurrence of delays in obtaining obstetric care and level of performance of care

	Level of performance				
	Adequate		Non-adequate		p[1]
Type of delay, related to:	**n**	**(%)**	**n**	**(%)**	
1. User factors	567	(10.0)	286	(10.5)	0.886
Delay in seeking health services	303	(5.4)	139	(5.1)	0.924
Refusal of treatment	276	(4.9)	150	(5.5)	0.664
Unsafe abortion	48	(0.9)	3	(0.1)	**<0.001**
Total	5.645		2.735		
2. Health service accessibility	1.945	(34.4)	961	(35.0)	0.928
Total	5.647		2.744		
Difficulty accessing antenatal care	68	(1.1)	58	(2.1)	0.418
Difficulties with transportation city/hospital	54	(0.9)	63	(2.2)	0.058
Total	6.029		2.819		
Absent/ inadequate antenatal care	1.909	(33.8)	783	(28.6)	0.188
Geographic difficulty in accessing health service	22	(0.4)	176	(6.4)	**<0.001**
Total	5.645		2.735		
3. Quality of medical care	1.046	(17.3)	1.263	(42.6)	**0.012**
Total	6.039		2.962		
Absence of blood products	20	(0.3)	37	(1.3)	**0.013**
Lack of medication	67	(1.1)	50	(1.8)	0.380
Difficulty in communication between hospital and regulatory center	250	(4.1)	529	(18,8)	**0.004**
Lack of trained staff	127	(2.1)	144	(5.1)	0.095
Difficulty in monitoring	180	(3.0)	229	(8.1)	0.177
Total	6.029		2.819		
Delay in referral/transfer of the case	143	(2.4)	149	(5.2)	0.073
Delay in diagnosis	327	(5.4)	160	(5.6)	0.964
Delay in starting treatment	416	(6.9)	186	(6.5)	0.926
Improper management of the case	589	(9.7)	629	(21.8)	0.135
Total	6.052		2.879		
Any delay	2.750	(48.3)	1.937	(64.2)	**0.039**
Total	5.698		3.018		

[1] p-value adjusted for cluster effect

Table 6. Variables independently associated with adequate performance (Poisson multiple analysis [1] n = 9555)

Variable	PR	95%CI PR	p[1]
Use of magnesium sulfate	1.44	1.04–1.98	0.029
Geographic Region (SE,S)	2.21	1.05–4.65	0.038

[1] p-value adjusted for cluster effect; PR prevalence ratio; SE: Southeast; S: South

4. DISCUSSÃO GERAL

A amostra obtida no estudo da Rede Nacional de Vigilância de Morbidade Materna Grave mostrou-se heterogênea, com coeficientes de correlação intraclasse baixos, e possibilitou o desenvolvimento de um instrumento de predição de mortalidade baseado nos critérios de *near miss* da Organização Mundial de Saúde (OMS), o *Maternal Severity Index* (MSI). A partir dessa ferramenta, a análise de desempenho dos centros da Rede pode ser realizada, como um exercício da avaliação do cuidado obstétrico prestado em serviços e sistemas de saúde.

O estudo da Rede foi uma iniciativa científica com objetivo de criar um sistema de informação em saúde para identificação de casos de morbidade materna grave, utilizando como parâmetro diagnóstico os novos critérios de near mis e condições potencialmente ameaçadores à vida, definidos pela OMS (Cecatti et al., 2009). Além deste corte transversal contido na fase inicial de implementação (Haddad et al., 2011), o projeto teórico global da Rede contempla a avaliação das repercussões do evento morbidade materna grave a longo prazo, em um segundo momento próximo.

Todo o processo de elaboração do projeto e construção do estudo foi possível devido ao financiamento de agências nacionais governamentais de fomento à pesquisa, sem o qual essa iniciativa se tornaria inviável. Também, a disponibilidade das instituições de saúde participantes e o comprometimento de seus pesquisadores locais foram fundamentais para o cumprimento das normas técnicas estabelecidas e garantia da qualidade da informação obtida.

A vigilância com coleta prospectiva dos dados foi realizada por um período de doze meses e diversas medidas de verificação de consistência dos dados foram adotadas durante este período. Foram realizadas visitas técnicas aos centros da Rede, para consultoria sobre dos processos de trabalho e recoleta de dados de prontuários selecionados aleatoriamente.

Além desta avaliação local, procedimentos eletrônicos de verificação de consistência foram realizados em tempo real, durante a inclusão dos dados no sistema, com auditoria de dados conflitantes e repasse de dúvidas aos pesquisadores, para resolução de inconsistências e/ou complementação de informações faltantes.

Após o término da inclusão dos sujeitos em junho de 2010, durante oito meses os dados foram novamente avaliados a partir de um processo organizado de checagem e correção automáticas do banco de dados. Todos esses procedimentos foram adotados com alto rigor, levando em consideração que a coleta dos dados estaria sendo realizada por diversos pesquisadores, em múltiplos locais e à distância do centro coordenador da Rede em Campinas. O

principal objetivo dessa verificação criteriosa foi evitar que erros sistemáticos fossem enviados ao banco de dados, o que poderia compromenter as análises e a confiabilidade das estimativas advindas do estudo.

Com relação à variância dos dados entre os centros da Rede, os valores dos coeficientes de correlação intraclasse (ICC) encontrados no estudo podem ser considerados pequenos, próximos à zero (mediana 0,035), para a maioria das variáveis. Isso demonstra que a amostra incluída na rede possui dados heterogêneos, ou seja, as variáveis estão mais provavelmente distribuídas de forma aleatória entre os centros, conglomerados ou *clusters*.

Esta constatação aumenta a confiança das estimativas advindas do estudo, já que altos valores de ICC em estudos com desenho por conglomerados denotam homogeneidade intraclasse, ou seja, demonstram que a variância dos dados é decorrente somente da variação entre os clusters e não da distribuição dos eventos entre os indivíduos como um todo (Kish, 1965; Campbell et al., 2004; McGraw et al., 1996).

O Design Effect (Deff) ou efeito do desenho mede quanto a variância de um parâmetro é resultado do desenho por conglomerado em comparação com o que seria obtido em um estudo por amostragem aleatória simples (AAS) (Shackman et al., 2001). Em estudos por AAS, o tamanho amostral necessário para atingir poder estatístico suficiente geralmente é menor do que nos estudos por conglomerado (Campbel et al., 2004).

No estudo da Rede, o Deff mediano para as variáveis de resultado foi de 6,24, o que representa que a variância desses parâmetros foi seis vezes maior neste estudo do que seria observado em um estudo por amostragem aleatória simples. No entanto, o efeito do desenho foi utilizado para ajuste de todas as estimativas de todas as análises da Rede, corrigindo este efeito da variância dos conglomerados e equiparando a significância estatística àquela que seria obtida se o estudo fosse por AAS.

Ambas as medidas de variância, ICC e Deff, são adjuntos no cálculo do tamanho amostral em estudos com desenho por conglomerados e são utilizados como fatores de correção para evitar subestimativas. Os valores utilizados para esse cálculo devem ser aqueles relacionados com o principal desfecho de interesse no estudo.

No momento da elaboração do projeto da Rede não havia estudos com valores de ICC e Deff disponíveis para *near miss* e óbito materno. Desta forma, o cálculo do tamanho amostral na época levou em consideração apenas as prevalências obtidas para *near miss* e óbito materno em estudos anteriores. Como forma de verificar a adequação do tamanho amostral obtido na Rede, levando em consideração o desenho do estudo por *cluster*, os valores de ICC e Deff para *near miss* e óbito foram utilizados como fatores de correção e um novo cálculo de tamanho amostral foi realizado, segundo fórmula proposta por Piaggio et al. (2001).

O resultado obtido foi que uma amostra de 7.072 sujeitos seria necessária para atingir poder estatístico suficiente, o que representa aproximadamente 74% da amostra final obtida nesse estudo. O fato de o estudo não ter sido interrompido com a completude do tamanho amostral estimado de 75.000 partos vigiados e ter continuado até o término do cronograma de vigilância de doze meses permitou que 82.388 partos fossem observados e 9.555 sujeitos fossem incluídos no estudo, agregando um número amostral adequado inclusive para as correções do efeito da amostragem por conglomerados.

Valores de ICC para algumas variáveis relacionadas à morbimortalidade materna e perinatal foram publicados recentemente e esses valores foram comparativamente menores do que os encontrados na Rede (Taljaard et al., 2008). O coeficiente de correlação intraclasse é diretamente proporcional ao tamanho do cluster e à prevalência da condição (Adams et al., 2004).

O estudo de Taljaard et al. foi desenvolvido a partir da população obstétrica geral, onde a prevalência de condições mórbidas é inferior àquela encontrada em estudos de base hospitalar, como a Rede de Vigilância de Morbidade Materna Grave. Desta forma, os valores de ICC e Deff obtidos na Rede podem ser bons parâmetros de correção do tamanho amostral de novos estudos de base hospitalar, onde a prevalência de condições potencialmente ameaçadoras à vida e *near miss* é significativamente maior.

A partir da demonstração de adequação do tamanho amostral e da heterogeneidade intraclasse das variáveis do estudo, as análises para

validação dos critérios de *near miss* da OMS foram iniciadas. Todos os casos de óbito foram identificados como tendo pelo menos um dos critérios de condições ameaçadoras à vida (verdadeiro-positivos), com sensibilidade de 100%. Os falso-positivos dessa análise puderam ser classificados como casos de *near miss* materno, validando os critérios de *near miss* como de alta acurácia.

O número de critérios de gravidade (Maternal Severity Score) e todas as variáveis distais do estudo foram testados para avaliar a correlação com o desfecho óbito e o modelo de predição de mortalidade, Maternal Severity Index (MSI), foi desenvolvido com aquelas que mostraram correlação significativa, ou seja, câncer, pré-eclâmpsia, a chegada já com algum critério de *near miss* na admissão no centro, o número de critérios de gravidade (MSS) e os critérios de *near miss*.

Apresentaram efeito "protetor" as variáveis histerectomia e pré-eclâmpsia. A possível explicação para esse achado é que, em se tratando de estudo conduzido em hospitais de referência no cuidado obstétrico, a maioria vinculado a grandes instituições de ensino, provavelmente a adequação de protocolos de assistência à hemorragia, com realização oportuna da histerectomia, possibilitou a quebra no processo de disfunção orgânica nessas mulheres, evitando mais mortes.

Com relação à pré-eclâmpsia, a mesma explicação da adequação de protocolos de conduta pode ser utilizada. Alia-se, ainda, o fato de a pré-eclâmpsia ser uma

doença específica da gestação, com curso auto-limitado, excelente recuperação pós-parto e boa resposta à terapia quando instituída adequadamente. Desta forma, essas variáveis podem ter tido correlação negativa com mortalidade devido às características dos centros da Rede, restando o questionamente se de fato esse efeito seria reproduzido em diferentes cenários.

Todos os critérios de *near miss* foram incluídos no MSI. No entanto, seus respectivos coeficientes β não foram utilizados de forma independente para estimar a mortalidade, com exceção de histerectomia. Os critérios de *near miss* foram subdivididos entre aqueles relacionados com disfunção grave ou com falência orgânica, segundo a classificação do escore SOFA (*Sequential Organ Failure Assessment*) (Vincent et al., 1998).

Os critérios que correspondem à falência cardiovascular e falência respiratória foram os mais correlacionados com mortalidade e, para tornar o modelo mais simples e de fácil utilização clínica, a presença de qualquer um dos critérios dessas duas categorias foi utilizada como um coeficiente independente de falência cardiovascular e falência respiratória.

Para os demais sistemas (renal, hematológico, hepático e neurológico), a contribuição dos seus critérios específicos somente foi considerada para o *Maternal Severity Score*, que é a correlação entre o número de critérios de mortalidade. Com isso, apesar de haver simplificação da utilização clínica do modelo, essa transformação dos critérios falência cardiovascular e respiratória

em variáveis dicotômicas pode levar à superestimação de mortalidade entre os casos.

Como exemplo desta possibilidade de superestimação de mortalidade, uma mulher que apresentar lactato acima de 5 e choque (variáveis de disfunção grave) e pH menor que 7,1 (variável de falência orgânica) terá a mesma predição de mortalidade que aquela que apresentar uso de droga vasoativa contínua, parada cardíaca e reanimação cardiopulmonar, todas variáveis de falência orgânica.

O *Maternal Severity Index* apresentou boa calibração e discrimimação através dos testes como Hosmer-Lemeshow goodness-of-fit, Nagelkerke R square e área sob a curva ROC (receiver operating characteristic) de 95,5%. No entanto, possivelmente novas atualizações do modelo poderão ser necessárias após validação externa em populações diferentes da amostra da Rede, na qual o modelo foi desenvolvido e testado.

Ainda com relação à tendência de superestimar mortalidade, o MSI foi desenvolvido a partir de uma população de mulheres que apresentava pelo menos um dos critérios de condições potencialmente ameaçadoras à vida. Dentro desta subpopulação, o risco de morte por agravamento do quadro de base é mais presente quando comparado com a população geral de baixo risco. Essa observação também é comum aos demais escores de prognóstico e disfunção como APACHE, SAPS e MPM (Strand & Flaatten, 2008) e, também para o MSI, a interpretação dos resultados obtidos com a aplicação desses

preditores de mortalidade em nível individual ou entre populações de baixo risco deve ser cautelosa.

Com isso, a melhor utilização dos preditores de mortalidade se faz como ferramenta de *benchmark* e para avaliação de *case-mix, o* que representa a estratificação de gravidade de grupos de indivíduos, entre locais e/ou através do tempo. Esta aplicação garante a avaliação de adequação do cuidado de acordo com categorias de gravidade comparáveis e, também, a comparação de desempenho entre diferentes intervenções, entre serviços de saúde ou em momentos diferentes de uma mesma população.

O exercício da avaliação de adequação de cuidado em serviços de saúde obstétricos foi realizado com a aplicação do MSI entre os centros da Rede Nacional de Vigilância de Morbidade Materna Grave. A partir do cálculo do MSI médio de cada centro, o *Standardized Mortality Ratio* (SMR) de cada um foi estabelecido. O SMR representa a razão entre as mortes observadas de fato e aquelas esperadas de acordo com a gravidade dos casos nesta população.

O SMR leva em consideração o tamanho do *cluster,* o MSI e o número de mortes observadas. Para que todos os centros pudessem ter os SMR calculados, foi atribuído arbitrariamente o valor de 0,1 sempre que não houve nenhuma morte esperada. Nestes casos e naqueles com pequenas populações e MSI baixos (menor gravidade), a estimativa do SMR apresentou pouca precisão, com intervalos de confiança largos, o que pode representar uma limitação para a análise nesses locais.

O principal objetivo desta análise de desempenho foi avaliar os fatores que estavam mais frequentemente associados a um baixa desempenho. Com isso, os SMR foram recategorizados em duas classes de desempenho, “não adequado” e “adequado”, esta última sendo composta por centros com SMR entre 0 e 1,25. O SMR acima de 1 indica que nenhuma morte esperada foi evitada e que, eventualmente, alguma morte ocorreu além do esperado, o que indica um cuidado de saúde “intermediário baixo”.

Esta opção metodológica possibilitou a separação e identificação dos fatores realmente relacionados com um desempenho baixo ou muito baixo dos centros, o que geralmente é o principal foco de estratégias de ações em saúde. Porém, a utilização futura das cinco categorias originais do SMR ou, pelo menos, a divisão em três categorias (adequado, intermediário e não adequado) pode permitir a identificação específica dos fatores correspondentes a cada uma das qualidades de serviços de saúde.

Os resultados da avaliação de desempenho dos centros da Rede se mostraram em concordância com a evidência existente (WHO, 2009; WHO, 2011). O fortalecimento dos sistemas de saúde, desde a melhoria do acesso aos equipamentos de saúde, na comunicação entre serviços e no transporte para transferências até a capacitação dos recursos humanos para manejo adequado das condições de gravidade, são estratégias que parecem ser essenciais para melhora da prestação de cuidado obstétrico e redução da mortalidade materna.

5. CONCLUSÕES

1. A Rede Nacional de Vigilância de Morbidade Materna Grave foi um estudo de corte transversal multicêntrico que utilizou de forma pioneira os critérios de *near miss* da OMS para identificação de casos graves em obstetrícia. Os valores dos coeficientes de correlação intraclasse encontrados no estudo são considerados pequenos (mediana 0,035). A heterogeneidade amostral encontrada aumenta a confiabilidade das estimativas do estudo. Esses valores poderão ser utilizados para o planejamento de novos estudos por cluster em saúde materna e perinatal, principalmente aqueles referentes à morbidade materna grave / *near miss*, auxiliando um adequado cálculo de tamanho amostral.

2. A identificação dos casos de *near miss* materno utilizando os critérios de condições ameaçadoras à vida da OMS é válida, uma vez que estas condições estão associadas de forma acurada com as mortes maternas. O modelo MSI descreve adequadamente a relação entre os marcadores de gravidade e a mortalidade materna e pode ser usado como uma

ferramenta para a avaliação da gravidade em populações e análise de *case-mix*. O uso do modelo do MSI na abordagem do *near miss* materno tem o potencial de contribuir para a avaliação e melhoria do cuidado de saúde materno, principalmente aquele requerido por mulheres que apresentam morbidade materna grave. São necessários novos estudos de validação externa deste modelo, para análise do seu desempenho em outras populações obstétricas.

3. Na população de estudo da Rede, a abordagem do *near miss* foi utilizada para simular a análise de um sistema de saúde obstétrico. Após a aplicação do *Maternal Severity Index* e do *Standardized Mortality Ratio*, a análise do desempenho dos serviços foi realizada e os fatores correlacionados com a adequação do cuidado foram analisados. Problemas decorrentes da organização do sistema de saúde foram identificados como significativos, especialmente aqueles relacionados à acessibilidade aos serviços de saúde e à qualidade dos cuidados médicos prestados. A utilização desta ferramenta específica para a predição de mortalidade em obstetrícia pode contribuir para a análise de sistemas de saúde obstétricos e identificação de pontos fracos. Além disso, esta medida pode tentar fortalecer esses sistemas, com uma redução efetiva no número de mortes.

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7. ANEXOS

7.1. Anexo 1. Carta de aprovação do projeto pelo CEP

FACULDADE DE CIÊNCIAS MÉDICAS
COMITÊ DE ÉTICA EM PESQUISA

www.fcm.unicamp.br/pesquisa/etica/index.html

CEP, 05/03/09.
(Grupo II)

PARECER CEP: N° 097/2009 (Este nº deve ser citado nas correspondências referente a este projeto)
CAAE: 0071.1.146.000-09

I - IDENTIFICAÇÃO:

PROJETO: **"REDE NACIONAL DE VIGILÂNCIA DA MORBIDADE MATERNA GRAVE: A GRAVIDEZ NA ADOLESCÊNCIAE O ABORTO COMO FATORES DE AGRAVO À SAÚDE".**
PESQUISADOR RESPONSÁVEL: José Guilherme Cecatti.
INSTITUIÇÃO: CAISM/UNICAMP
APRESENTAÇÃO AO CEP: 06/02/2009
APRESENTAR RELATÓRIO EM: 05/03/10 (O formulário encontra-se no *site* acima)

II - OBJETIVOS

Desenvolver uma rede nacional de cooperação científica para vigilância da morbidade materna grave, com ênfase na adolescência e aborto.

III - SUMÁRIO

Estudo de corte transversal multicêntrico, a ser implementado com 25 unidades obstétricas de referência nas diversas regiões geográficas do Brasil. Durante um período de doze meses, os pesquisadores principais e os pesquisadores locais deverão realizar vigilância prospectiva de todas as mulheres internadas nessas unidades, para a identificação dos casos de near miss materno e morbidade materna grave não-near miss. Foi realizado cálculo do tamanho amostral, estimando-se que será necessária a vigilância de um total aproximado de 75.000 partos. Os dados serão coletados em ficha específica e enviados ao banco de dados central através de formulário eletrônico disponível no website do projeto. Análise de dados: A análise dos dados será feita por sub-grupos de acordo com a época da ocorrência do near miss ou morbidade materna grave (na adolescência e em outros momentos de sua vida reprodutiva) e causa determinante (aborto e outras causas), estimando-se as respectivas taxas, razões e riscos relativos para os respectivos preditores.

IV - COMENTÁRIOS DOS RELATORES

Após respostas às pendências, o projeto encontra-se adequadamente redigido e de acordo com a Resolução CNS/MS 196/96 e suas complementares, bem como a dispensa do Termo de Consentimento Livre e Esclarecido.

V - PARECER DO CEP

Comitê de Ética em Pesquisa - UNICAMP
Rua: Tessália Vieira de Camargo, 126
Caixa Postal 6111
13083-887 Campinas – SP

FONE (019) 3521-8936
FAX (019) 3521-7187
cep@fcm.unicamp.br

O Comitê de Ética em Pesquisa da Faculdade de Ciências Médicas da UNICAMP, após acatar os pareceres dos membros-relatores previamente designados para o presente caso e atendendo todos os dispositivos das Resoluções 196/96 e complementares, resolve aprovar sem restrições o Protocolo de Pesquisa, bem como ter aprovado a dispensa do Termo do Consentimento Livre e Esclarecido, assim como todos os anexos incluídos na Pesquisa supracitada.

O conteúdo e as conclusões aqui apresentados são de responsabilidade exclusiva do CEP/FCM/UNICAMP e não representam a opinião da Universidade Estadual de Campinas nem a comprometem.

VI - INFORMAÇÕES COMPLEMENTARES

O sujeito da pesquisa tem a liberdade de recusar-se a participar ou de retirar seu consentimento em qualquer fase da pesquisa, sem penalização alguma e sem prejuízo ao seu cuidado (Res. CNS 196/96 – Item IV.1.f) e deve receber uma cópia do Termo de Consentimento Livre e Esclarecido, na íntegra, por ele assinado (Item IV.2.d).

Pesquisador deve desenvolver a pesquisa conforme delineada no protocolo aprovado e descontinuar o estudo somente após análise das razões da descontinuidade pelo CEP que o aprovou (Res. CNS Item III.1.z), exceto quando perceber risco ou dano não previsto ao sujeito participante ou quando constatar a superioridade do regime oferecido a um dos grupos de pesquisa (Item V.3.).

O CEP deve ser informado de todos os efeitos adversos ou fatos relevantes que alterem o curso normal do estudo (Res. CNS Item V.4.). É papel do pesquisador assegurar medidas imediatas adequadas frente a evento adverso grave ocorrido (mesmo que tenha sido em outro centro) e enviar notificação ao CEP e à Agência Nacional de Vigilância Sanitária – ANVISA – junto com seu posicionamento.

Eventuais modificações ou emendas ao protocolo devem ser apresentadas ao CEP de forma clara e sucinta, identificando a parte do protocolo a ser modificada e suas justificativas. Em caso de projeto do Grupo I ou II apresentados anteriormente à ANVISA, o pesquisador ou patrocinador deve enviá-las também à mesma junto com o parecer aprovatório do CEP, para serem juntadas ao protocolo inicial (Res. 251/97, Item III.2.e)

Relatórios parciais e final devem ser apresentados ao CEP, de acordo com os prazos estabelecidos na Resolução CNS-MS 196/96.

VII- DATA DA REUNIÃO

Homologado na II Reunião Ordinária do CEP/FCM, em 17 de fevereiro de 2009.

Profa. Dra. Carmen Silvia Bertuzzo
PRESIDENTE DO COMITÊ DE ÉTICA EM PESQUISA
FCM/UNICAMP

Comitê de Ética em Pesquisa - UNICAMP
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7.2. Anexo 2. Ficha identificadora de casos

Rede Nacional de Vigilância de Morbidade Materna Grave

Nome:_____ HC:_____Data da alta:_____

- Anexar este formulário aos prontuários de todas as pacientes obstétricas (gestantes ou puérperas) internadas no serviço.
- Identificar durante a internação ou na alta hospitalar se houve o diagnóstico de alguma das condições abaixo descritas.
- Para as que apresentarem qualquer uma das condições abaixo ("SIM"), o prontuário será separado para revisão antes do seu arquivamento.
- Para as que NÃO tiverem nenhum das condições, esta ficha deverá ser arquivada em pasta específica e o prontuário pode ser liberado para arquivamento pelo SAME

Complicações hemorrágicas	**Sim**	**Não**
Descolamento prematuro de placenta		
Placenta prévia / acreta/increta/percreta		
Prenhez ectópica		
Rotura uterina		
Hemorragia grave por aborto		
Hemorragia pós-parto		
a) atonia		
b) retenção placentária		
c) lacerações de trajeto		
d) coagulopatia		
e) inversão uterina		
Complicações hipertensivas	**Sim**	**Não**
Pré-eclampsia grave		
Eclâmpsia		
Hipertensão grave		
HELLP síndrome		
Fígado Gorduroso		
Outras complicações	**Sim**	**Não**
Edema pulmonar		
Convulsões		
Sepse grave		
Trombocitopenia < 100 mil		
Crise tireotóxica		
Choque		
Insuficiência respiratória aguda		
Acidose		
Cardiopatia		
AVC		
Distúrbios de coagulação		
Tromboembolismo		
Cetoacidose diabética		
Icterícia / disfunção hepática		
Meningite		
Insuficiência Renal Aguda		
Indicadores de manejo de gravidade	**Sim**	**Não**
Transfusão de hemoderivados		
Acesso venoso central		
Admissão em UTI		
Hospitalização prolongada (>7dias)		
Intubação não relacionada à anestesia		
Retorno à sala cirúrgica		
Intervenção cirúrgica maior (histerectomia, laparotomia)		
Uso de sulfato de magnésio		

RESUMO ☐ SIM ☐ NÃO

Resp. pelo preenchimento: _____

7.3. Anexo 3. Ficha para coleta manual de dados

Rede Nacional de Vigilância de Morbidade Materna Grave - FORMULÁRIO DE COLETA MANUAL

IDENTIFICAÇÃO

1. Centro do Estudo*: ☐☐
2. Subject ID*: _____
3. Person ID*: _____

Data de nascimento*: ☐☐ ☐☐ ☐☐

DADOS PESSOAIS

4. Idade em anos completos*: ☐☐
5. Cor: [ ] 1 negra [ ] 2 branca [ ] 3 indígena [ ] 4 amarela [ ] 5 outro [ ] 8 não consta
6. Escolaridade: [ ] 1 analfabeta [ ] 2 Fundamental incompleto [ ] 3 Fundamental [ ] 4 Médio incompleto [ ] 5 Médio [ ] 6 Superior incompleto [ ] 7 Superior [ ] 8 não consta
7. Estado civil: [ ] 1 casada/amasiada [ ] 2 solteira [ ] 3 separada/divorciada [ ] 4 viúva [ ] 8 não consta
8. Peso em kg: _____
9. Altura em m: _____
10. Data da internação no centro*: ☐☐ ☐☐ ☐☐
11. A paciente fazia pré-natal no serviço?* [ ] 1 sim [ ] 2 não [ ] 3 sem pré-natal [ ] 8 não consta
12. Como foi o acesso da mulher ao centro?* [ ] 1 procura espontânea [ ] 6 encaminhamento da própria instituição [ ] 2 transferência por serviço de resgate/emergência [ ] 8 não consta [ ] 3 transferência inter hospitalar programada [ ] 4 transferência inter hospitalar não programada [ ] 5 encaminhamento de outro serviço
13. Qual cobertura financeira majoritária do pré-natal? [ ] 1 público [ ] 2 privado [ ] 3 seguro saúde/convênio [ ] 4 sem pré-natal [ ] 8 não consta
14. Qual cobertura financeira majoritária da internação?* [ ] 1 público [ ] 2 privado [ ] 3 seguro saúde/convênio [ ] 8 não consta

DADOS OBSTÉTRICOS

15. Número de gestações*: ☐☐
16. Número de partos*: ☐☐
17. Número de abortos*: ☐☐
18. Número de cesáreas prévias*: ☐☐
19. Número de nascidos vivos*: ☐☐
20. Anos desde o último parto: ☐☐
21. A mulher possui cirurgia uterina prévia? (excluindo cesárea seg. transv) [ ] 1 sim [ ] 2 não [ ] 8 não consta
22. Número de consultas de pré-natal*: ☐☐
23. A mulher estava grávida quando foi admitida?* [ ] 1 sim [ ] 2 não [ ] 8 não consta
24. Idade gestacional na internação*: ☐☐
25. Forma de início do trabalho de parto*: [ ] 1 espontâneo [ ] 2 induzido [ ] 3 sem trabalho de parto [ ] 4 aborto [ ] 5 continua grávida [ ] 8 não consta
26. Data da resolução da gestação: ☐☐ ☐☐ ☐☐
27. Idade gestacional na resolução*: ☐☐
28. Como foi ultimada a gestação? [ ] 1 parto vaginal [ ] 5 aborto [ ] 2 parto vaginal operatório [ ] 6 prenhez ectópica [ ] 3 parto cesárea antes do início do trabalho de parto [ ] 7 continua grávida [ ] 4 parto cesárea após o início do trabalho de parto [ ] 8 não consta

ABORTO

29. Como se iniciou o aborto? [ ] 1 espontâneo [ ] 2 induzido [ ] 8 não consta
30. O aborto foi mais provavelmente seguro ou inseguro? [ ] 1 seguro [ ] 2 inseguro [ ] 8 não consta
31. Quais procedimentos foram realizados? [ ] 1 dilatação e/ou curetagem [ ] 2 ocitocina [ ] 3 vácuo aspiração [ ] 4 prostaglandinas [ ] 5 outros [ ] 6 nenhum [ ] 8 não consta
32. Se outro procedimento, especifique: _____

DADOS DO RN

33. Número total de nascidos: ☐☐
34. Qual era a apresentação fetal ao nascimento? [ ] 1 cefálico [ ] 2 pélvico [ ] 3 outro [ ] 8 não consta
35. Sexo: [ ] 1 feminino [ ] 2 masculino [ ] 3 indeterminado [ ] 8 não consta
36. Condição do nascimento: [ ] 1 vivo [ ] 3 natimorto anteparto [ ] 2 natimorto intra-parto [ ] 8 não consta
37. Qual foi o Apgar de 1º. Minuto? ☐☐
38. Qual foi o Apgar de 5º. Minuto? ☐☐
39. Peso em gramas: ☐☐☐☐
40. Desfecho neonatal: [ ] 1 alta [ ] 2 internado [ ] 3 óbito neonatal precoce (<7dias) [ ] 4 óbito neonatal tardio (8-28 dias) [ ] 5 transferido [ ] 8 não consta
41. Se gemelar, informe os dados dos outros RN: _____ _____

CONDIÇÕES MATERNAS PRÉ-EXISTENTES

42. A mulher apresentava alguma condição patológica/ de risco prévios à gestação?* [ ] 1 sim [ ] 2 não [ ] 8 não consta
43. Quais condições estavam presentes?
[ ] 1 hipertensão arterial crônica [ ] 9 anemia falciforme-talassemia
[ ] 2 obesidade [ ] 10 HIV/AIDS
[ ] 3 baixo peso [ ] 11 tireoidopatias
[ ] 4 diabetes mellitus [ ] 12 doenças neurológicas / epilepsia
[ ] 5 tabagismo [ ] 13 colagenoses
[ ] 6 doenças cardíacas [ ] 14 neoplasias
[ ] 7 doenças respiratórias [ ] 15 outro
[ ] 8 doenças renais [ ] 16 drogadição
44. Se outra condição patológica, especifique: _____

CONDIÇÕES POTENCIALMENTE AMEAÇADORAS DA VIDA

45. Houve alguma complicação hemorrágica?* [ ] 1 sim [ ] 2 não [ ] 8 não consta
46. Qual complicação hemorrágica ocorreu no período?*
[ ] 1 descolamento prematuro de placenta [ ] 5 hemorragia grave por aborto
[ ] 2 placenta prévia/acreta/increta/percreta [ ] 6 hemorragia pós parto
[ ] 3 prenhez ectópica complicada [ ] 7 outra hemorragia grave
[ ] 4 rotura uterina [ ] 8 não houve/não consta
47. Se HEMORRAGIA PÓS- PARTO, especifique: [ ] 1 atonia [ ] 2 retenção placentária [ ] 3 lacerações de trajeto [ ] 4 coagulopatia [ ] 5 inversão uterina [ ] 6 outra causa obstétrica

48. Houve alguma complicação hipertensiva?*[ ] 1 sim [ ] 2 não [ ] 8 não consta

49. Qual complicação hipertensiva ocorreu no período?*

[ ] 1 pré-eclâmpsia grave [ ] 2 eclâmpsia [ ] 3 hipertensão grave

[ ] 4 HELLP síndrome [ ] 5 fígado gorduroso [ ] 8 não houve / não consta

50. Houve alguma outra complicação?*[ ] 1 sim [ ] 2 não [ ] 8 não consta

51. Quais complicações?*

[ ] 1 edema pulmonar [ ] 2 convulsões [ ] 3 trombocitopenia < 100 mil

[ ] 4 crise tireotoxica [ ] 5 choque [ ] 6 insuf. respiratória aguda

[ ] 7 acidose [ ] 8 cardiopatia [ ] 9 AVC

[ ] 10 dist. de coagulação [ ] 11 CIVD [ ] 12 tromboembolismo

[ ] 13 cetoacidose diabética [ ] 14 icterícia/disf hepática [ ] 15 meningite

[ ] 16 sepse grave [ ] 17 IRA [ ] 88 não houve / não consta

[ ] 18 complicação associada à suspeita ou confirmação de Influenza A (H1N1)

52. Se SEPSE GRAVE, especifique o foco:

[ ] 1 endometrite pós-parto [ ] 2 endometrite pós aborto [ ] 3 foco pulmonar

[ ] 4 foco urinário [ ] 5 outro [ ] 8 não consta [ ] 9 ignorado

53. Se outro foco, especifique:_____

54. A mulher apresentou alguma das condições de manejo de gravidade?*

[ ] 1 sim [ ] 2 não [ ] 8 não consta

55. Quais condições estavam presentes?*

[ ] 1 transfusão de hemoderivados [ ] 6 retorno à sala cirúrgica

[ ] 2 acesso venoso central [ ] 7 histerectomia/laparotomia

[ ] 3 admissão em UTI [ ] 8 uso de sulfato de magnésio

[ ] 4 hospitalização prolongada (>7 dias) [ ] 9 outro proc. cirúrgico maior

[ ] 5 intubação não relacionada à anestesia [ ] 88 não houve/não consta

CRITÉRIOS DE NEAR MISS MATERNO

56. A mulher apresentou algum dos critérios clínicos de near miss?*

[ ] 1 sim [ ] 2 não [ ] 8 não consta

57. Se SIM, indique quais*:

[ ] 1 cianose [ ] 9 acidente vascular cerebral

[ ] 2 gasping [ ] 10 convulsão não controlada – paralisia total

[ ] 3 FR > 40 ou < 6 [ ] 11 icterícia na presença de pré-eclâmpsia

[ ] 4 choque [ ] 88 não houve / não consta

[ ] 5 oligúria não responsiva a fluidos ou diuréticos

[ ] 6 distúrbios de coagulação

[ ] 7 perda da consciência durante 12 h ou mais

[ ] 8 ausência de consciência E ausência de pulso-batimento cardíaco

58. A mulher apresentou algum dos critérios laboratoriais de near miss?*

[ ] 1 sim [ ] 2 não [ ] 8 não consta

59. Se SIM, indique quais*:

[ ] 1 saturação de O_2 < 90% por > 60 min.

[ ] 2 PaO_2/FiO_2 < 200

[ ] 3 creatinina ≥300mmol/l ou ≥ 3,5 mg/dl

[ ] 4 bilirrubina ≥ 100 mmol/l ou ≥ 6 mg/dl

[ ] 5 pH < 7,1

[ ] 6 lactato > 5

[ ] 7 plaquetas < 50 mil

[ ] 8 ausência de consciência e presença de glicose e cetoácidos na urina

[ ] 88 não houve / não consta

60. A mulher apresentou algum dos critérios de manejo?*

[ ] 1 sim [ ] 2 não [ ] 8 não consta

61. Se SIM, indique quais*:

[ ] 1 uso de droga vasoativa contínua [ ] 6 R. Cardiopulm. (RCP)

[ ] 2 histerectomia por infecção ou hemorragia [ ] 88 não houve / não consta

[ ] 3 transfusão de ≥ 5 U de hemácias

[ ] 4 intubação e ventilação por ≥ 60 minutos não relacionada com anestesia

[ ] 5 diálise para insuficiência renal aguda

62. Alguma dessas condições já estava presente na admissão do sujeito?

[ ] 1 sim [ ] 2 não [ ] 3 não se aplica [ ] 8 não consta

DESFECHO MATERNO

63. Data da alta, transferência ou óbito*: [ ][ ] [ ][ ] [ ][ ]

64. Qual foi a condição de alta da mulher?*

[ ] 1 alta médica [ ] 2 alta a pedido [ ] 3 transferência [ ] 4 óbito [ ] 5 evasão

65. Comentários ou observações referentes a dados incluídos e dados relativos à transferência do sujeito: _____

_____

PESQUISA DE DEMORAS NO ATENDIMENTO

66. Durante o atendimento do caso, houve alguma demora relacionada ao serviço e/ou sistema de saúde?* [ ] 1 sim [ ] 2 não [ ] 9 ignorado

Se houve demora, especifique: (se NÃO houve, deixe em branco)

1 nível primário 2 nível secundário 3 nível terciário

67. Falta de medicação (sulfato, ATB, DVA, uterotônicos): [ ]

68. Dificuldade ou problemas com transporte municipal / hospitalar): [ ]

69. Dificuldade na comunicação (hospitalar/central reguladora): [ ]

70. Ausência de hemoderivados: [ ]

71. Dificuldade para monitorização (unidade de cuidados intensivos): [ ]

72. Falta de pessoal treinado: [ ]

73. Dificuldade de acesso ao pré-natal: [ ]

74. Houve alguma demora relacionada ao paciente e/ou seus familiares?*

[ ] 1 sim [ ] 2 não [ ] 9 ignorado

75. Se resposta SIM, especifique quais:

[ ] 1 demora na procura ao Serv. Saúde

[ ] 2 dificuldade geográfica ao acesso ao Serv. Saúde

[ ] 3 recusa ao tratamento

[ ] 4 Pré-natal ausente ou inadequado

[ ] 5 Aborto inseguro

76. Houve alguma demora na assistência relacionada aos profissionais de saúde?* [ ] 1 sim [ ] 2 não [ ] 9 ignorado

Se houve demora, especifique: (se NÃO houve, deixe em branco)

1 nível primário 2 nível secundário 3 nível terciário

77. Demora no diagnóstico: [ ]

78. Demora no início do tratamento: [ ]

79. Manejo inadequado do caso: [ ]

80. Demora na referência ou transferência do caso: [ ]

7.4. Anexo 4. Artigo referente ao projeto da Rede

Reproductive Health

BioMed Central

Study protocol

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Brazilian network for the surveillance of maternal potentially life threatening morbidity and maternal near-miss and a multidimensional evaluation of their long term consequences

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Abstract

Background: It has been suggested that the study of women who survive life-threatening complications related to pregnancy (maternal near-miss cases) may represent a practical alternative to surveillance of maternal morbidity/mortality since the number of cases is higher and the woman herself is able to provide information on the difficulties she faced and the long-term repercussions of the event. These repercussions, which may include sexual dysfunction, postpartum depression and posttraumatic stress disorder, may persist for prolonged periods of time, affecting women's quality of life and resulting in adverse effects to them and their babies.

Objective: The aims of the present study are to create a nationwide network of scientific cooperation to carry out surveillance and estimate the frequency of maternal near-miss cases, to perform a multicenter investigation into the quality of care for women with severe complications of pregnancy, and to carry out a multidimensional evaluation of these women up to six months.

Methods/Design: This project has two components: a multicenter, cross-sectional study to be implemented in 27 referral obstetric units in different geographical regions of Brazil, and a concurrent cohort study of multidimensional analysis. Over 12 months, investigators will perform

prospective surveillance to identify all maternal complications. The population of the cross-sectional component will consist of all women surviving potentially life-threatening conditions (severe maternal complications) or life-threatening conditions (the maternal near miss criteria) and maternal deaths according to the new WHO definition and criteria. Data analysis will be performed in case subgroups according to the moment of occurrence and determining cause. Frequencies of near-miss and other severe maternal morbidity and the association between organ dysfunction and maternal death will be estimated. A proportion of cases identified in the cross-sectional study will comprise the cohort of women for the multidimensional analysis. Various aspects of the lives of women surviving severe maternal complications will be evaluated 3 and 6 months after the event and compared to a group of women who suffered no severe complications in pregnancy. Previously validated questionnaires will be used in the interviews to assess reproductive function, posttraumatic stress, functional capacity, quality of life, sexual function, postpartum depression and infant development.

Background

Currently, more than half a million maternal deaths occur annually worldwide. Although an extremely rare event in developed countries, maternal mortality is higher in less developed countries. Better social conditions, better medical care in cases of severe complication and family planning are factors that contribute to reducing maternal mortality [1].

Nevertheless, quantifying maternal mortality in Brazil is a complex task. The Ministry of Health estimates the maternal death ratio at 75 maternal deaths per 100,000 live-born infants [2]. Reflecting the complexity of this estimate, other agencies, using different methods, have calculated maternal death ratios twice or even four times higher than the official figures [3,4].

Notwithstanding, the recorded cases of maternal deaths constitute a tiny proportion of the whole problem. Around the world, millions of women present severe maternal complications every year and the precise size of this specific population currently remains unknown. For this reason, women who have survived severe complications of pregnancy have in recent years sparked the attention of investigators and healthcare administrators. The World Health Organization (WHO) developed the maternal near-miss approach, a tool to uniformly identify near-miss cases and evaluate quality of care provided to women presenting severe complications. WHO defines a maternal near miss case as a woman who nearly died but survived a complication that occurred during pregnancy, childbirth or within 42 days of termination of pregnancy [5].

Therefore, the study of maternal near-miss cases has been suggested as a practical alternative to the surveillance of maternal morbidity and mortality, mainly in view of the larger number of cases and because the woman herself is able to provide information on the event and on the difficulties she had to face. It is believed that auditing near-miss cases would enable even smaller services to evaluate how the determinants of severe maternal morbidity (and consequently the determinants of maternal death) affect their users and services [6,7].

In addition, little is known on the long-term repercussions of severe, life-threatening complications related to pregnancy. An acute stress disorder associated with the occurrence of severe maternal complications has been suggested, but further research is needed. [8]. The repercussions of these events may lead to adverse effects in the women and their children, may negatively affect their quality of life and may persist for extended periods of time after the event [9-12].

Among the possible repercussions, studies have been carried out to evaluate the psychological impact and occurrence of posttraumatic stress disorder (PTSD), postpartum depression and changes in sexual health following delivery [10,13-17]. Considering that other factors such as mode of delivery, medical interventions and obstetrical complications [9,18,19] negatively affect women's quality of life, it is probable that in dramatic situations such as near-misses such repercussions would be even more evident. According to some authors, evaluation of the state of health, quality of life and sexual function of patients who suffered severe complications is poorer in the immediate postpartum period [15,20-23].

Nevertheless, doubts remain with respect to the long-term health status of women who suffer severe acute maternal morbidity and near-miss. Investigation of various aspects related to mental health and quality of life may offer a valuable perspective on the effect of maternal morbidity on the life of these women.

Studying the occurrence of severe complications in pregnancy and the factors associated with this event will result in a greater understanding of the process that occurs in

these women taking them from a state of health to one of sickness. Further knowledge on this issue may collaborate towards improving public policies and the healthcare provided to women who develop severe acute maternal morbidity.

Therefore, the objective of the present project is to evaluate this issue using clear goals to differentiate it from previous studies. These goals include estimating the frequency of the occurrence of maternal near-miss using a uniform set of criteria, carrying out a multicenter investigation into the quality of care provided to women with severe complications of pregnancy and performing a longitudinal evaluation of the quality of life of these women following the event.

Objectives and Hypothesis

The overall objective is to develop a nationwide network of scientific cooperation for the surveillance of severe maternal complications and maternal near-miss and their consequences.

Specific objectives

- To determine the frequency of maternal near-miss in healthcare facilities of different levels of complexity situated in different regions of Brazil, using the World Health Organization (WHO)'s new set of criteria for near-miss [5];
- To determine the frequency of non-near-miss severe maternal morbidity in these facilities using specifically defined potentially life threatening conditions;
- To evaluate the association between the indicators of organ dysfunction used to define maternal near-miss and the risk of maternal death;
- To determine the frequency of near-miss and non-near-miss severe maternal morbidity according to age-group and specific causes;
- To examine the occurrence of avoidable factors and other factors associated with maternal near-miss;
- To investigate the repercussions of severe maternal morbidity and near-miss on the quality of life of survivors up to six months after the event;
- To investigate the presence of sexual dysfunction, posttraumatic stress disorder and postpartum depression, as well as women's perception of their functional status in routine activities in the six months following an occurrence of severe maternal morbidity.
- To investigate the immediate perinatal outcome and subsequent neuromotor and weight-height development in children born from pregnancies associated with severe maternal morbidity.

Main hypotheses

In survivors of severe acute maternal morbidity:

- health and quality of life would be poorer;
- posttraumatic stress would be more common;
- postpartum depression would be more common;
- sexual function would have deteriorated and the woman's return to sexual activity would take longer;
- functional status in routine activities would be evaluated as poorer.

In the children born from a pregnancy associated with severe maternal morbidity:

- immediate perinatal outcome would be poorer;
- the occurrence of impaired neuromotor and weight-height development would be significantly higher.

Methods/Design

This study has two components: a multicenter cross-sectional study and a concurrent cohort study.

The cross-sectional study will be implemented in 27 referral obstetric units in different geographical regions of Brazil, which have already joined the initiative for building a national network for studies on maternal and reproductive health. Over a 12-month period, the principal and local investigators will carry out prospective surveillance and will collect data for the identification of maternal near-miss and non-near-miss cases, severe maternal morbidity (potentially life threatening conditions) and maternal deaths. To determine the number of collaborating centers to be included in the present study, calculation of sample size took into consideration the number of deliveries that would have to be monitored to identify cases of near-miss and maternal deaths. Previous studies have estimated a maternal near miss incidence of approximately 8 cases per 1000 deliveries [24] and a Brazilian maternal mortality ratio of 140 per 100,000 LB. Therefore, a total of approximately 75,000 deliveries would have to be monitored in order to identify around 100 maternal deaths and 600 maternal near miss cases. These numbers are believed to be sufficient to evaluate the use of the new criteria for near-miss established by the World Health Organization

in 2009 [5] and to perform analysis allowing for level of complexity of health facility, age group and specific cause.

The study population will consist of all the women admitted to the participating hospitals during the study period in whom organ dysfunction is registered (maternal near-miss, Appendix 1), in whom one of the diagnoses defined as non-near-miss severe maternal morbidity is present (Appendix 2), and those who died or were transferred to another healthcare service because of their bad health condition.

For the multidimensional analysis of the repercussions of severe maternal morbidity, a concurrent cohort, specific population study will be carried out with an externally selected comparison group. The main exposure factor will be the occurrence of severe maternal morbidity (both maternal potentially life threatening or near miss conditions). During the second half of the cross-sectional study, a sample of women identified as having severe maternal morbidity will be selected and invited to participate in the longitudinal evaluation. There will be a comparison group composed of women who did not suffer severe maternal morbidity. These women will be randomly selected externally in a proportion of 1:1 from postpartum women in the rooming-in wards of the same maternity hospitals as the cases. Controls will be selected at random and balanced according to mode of delivery, maternal age and gestational age at the time of delivery.

Main outcomes

Maternal near-miss

A woman who fulfills one of the clinical, laboratory or management criteria representing severity as defined by WHO [5] and who survives a complication occurring during pregnancy, childbirth or within 42 days postpartum.

Maternal potentially life threatening condition

A condition of severe morbidity found in women during pregnancy, childbirth or in the puerperium, classified as potentially life threatening conditions [5], including hemorrhagic or hypertensive disorders, other systemic disorders, and indicators of severe management (Appendix 2).

Main cause of complication/death

classification of the determinant main cause of the complication identified among cases and/or the main cause of death.

Maternal death

Death of a woman during pregnancy or within a 42-day period following the end of pregnancy irrespective of the duration or localization of the pregnancy, resulting from any cause related to or aggravated by the pregnancy or by measures taken with respect to it; however, not from accidental or incidental causes.

Conditions at birth

Vital status of the newborn infant as recorded on the medical chart, dichotomized into live or intrauterine death.

Vitality of the newborn infant

Evaluation of the newborn infant according to 1st and 5th minute Apgar scores as shown on the medical chart, classified from 0 to 10.

Neonatal outcome

Condition of the newborn infant at the time of data collection, identified from a review of the medical charts and classified as: discharged from hospital together with the mother, early neonatal death (<7 days) or late neonatal death (7-28 days).

Quality of life

The woman's perception of her position in life within the cultural context and value system in which she lives and in relation to her goals, expectations, health, standards and concerns (WHO); identified by the investigators using a standard SF-36 form.

Posttraumatic stress

Symptoms of intrusion, avoidance and hyperarousal following the occurrence of a pregnancy with severe complications; identified by the investigator using a standard questionnaire (PTSD - Checklist CV).

Ideal number of children

Number of children that the woman considered ideal prior to and following the index pregnancy.

Return to sexual activity

Time taken by the woman to recommence sexual activity after delivery and reason given for not recommencing sexual activity.

Sexual function

Sexual function and response; identified by the investigator using a standard questionnaire (*Female Sexual Function Index - FSFI*).

Postpartum depression

Depressive symptoms following the occurrence of a pregnancy with severe complications; identified by the investigator using a standard questionnaire (Edinburgh Postnatal Depression Scale - EPDS).

Functional status

Perception of the woman with respect to her functional status in six items related to her routine activities (understanding and communicating, getting around, self-care, getting along with people, life activities in the home/at work and participation in society), classified from 0 to 100 (from best to worst) [25].

Neuromotor development in the child born from the index pregnancy
Process of changes in motor behavior that involve both maturation of the central nervous system and interaction with the environment and stimuli given during the child's development; identified by the investigator using the Denver II - Revised Denver Developmental Screening Test [26].

Weight-height development of the child born from the index pregnancy
Process of weight and height increment during the child's development, weight measured in grams and height in centimeters, using scales and anthropometer, classified as adequate or inadequate for age, according to the standards of the World Health Organization [27].

Control variables
maternal age, marital status, place of residence, number of previous pregnancies, parity, previous abortions, previous Cesarean sections, number of children, mode of delivery, gestational age, birthweight, gender of neonate, condition of neonate at discharge, condition of mother at discharge.

Data Collection and Procedures

Cross-sectional component
Research assistants, referred to as local coordinators, will review the charts of hospitalized patients on a daily basis in search of cases with one of the conditions identifying severity (Appendix 2). In cases found with these diagnoses, the relevant hospital records will be reviewed for data collection following the women's hospital discharge, death or transfer to another healthcare facility. Data unavailable on the chart but of interest to the study will be obtained from the attending medical team. For each case included, data will be collected on the demographic and obstetric characteristics of the patient, the primary determinant of maternal near-miss (the first complication to occur in the chain of events leading to severe maternal morbidity), the duration of hospitalization (prior to delivery, following delivery and total time), the occurrence of indicators of maternal near-miss at any time during hospitalization, indicators of perinatal outcome and conditions of the woman at discharge from hospital.

These data will be collected on a previously coded form developed specifically for this purpose. A central database will be constructed and the data will be included by the local investigators themselves using electronic forms. The manually completed forms will be filed and made available at technical visits for the purpose of quality control.

For the electronic inclusion of data, each center will have its own restricted area on the study website where password-protected access will be granted only to cases included at that center. An overview of all the cases included in the network will be provided in the form of monthly graphs and tables containing the number of cases included by each center. In addition, the reported diagnoses will be provided by the coordinating center on the main page of the website.

In cases of near-miss, data will be collected on avoidable factors responsible for their occurrence (delays). These factors will be classified into those related to infrastructure, the patient or the healthcare professionals. Avoidable factors related to infrastructure include cases in which difficulties in obtaining supplies or medication, transportation, communication, blood components or monitoring and treatment may have led to less than ideal care. Factors related to the patient include those generated by the patient herself or her family, either by delaying seeking professional care or by refusing treatment. Factors related to the healthcare team include delays in defining the correct diagnosis and/or inappropriate management.

The degree of complexity at each hospital will be evaluated using an adapted version of the hospital complexity index developed for the WHO Global Survey project [28]. Participating institutions will provide information on a monthly basis via the website on the total number of deliveries, live births and maternal deaths that occurred the previous month. These data will be confirmed by the principal local investigator after data collection is finished.

To minimize the number of uncertainties that research assistants may face during data collection, a manual of operation was produced containing all the necessary information on how to use the internet, how to complete the written and electronic forms and how to access the database of each individual center, as well as information regarding the standardization of diagnostic definitions.

A meeting will be held with the investigators and local coordinators of each center (two individuals from each center) at the study coordinating center immediately preceding initiation of data collection in order to provide adequate training and clarify any queries regarding the data collection process and use of the website. Sometime after the initiation of data collection, a meeting of the study's Steering Committee will also be held. A second meeting will take place involving only the local investigators after data collection has finished to discuss facts related to the previous process, disclosure of partial results, scheduling of the preliminary and final analyses, agreement on papers to be written on the results and assignment of responsibility regarding execution of each item in this process.

Longitudinal component

As in the cross-sectional component, women with one of the conditions indicative of severity will be selected as potential subjects for longitudinal evaluation. Once identified, research assistants who are not involved in the cross-sectional portion of the study will invite eligible women to participate in the longitudinal evaluation of the study. Women who agree to take part will be asked to sign an informed consent form and two CATI (computer assisted telephone interview) will be scheduled for 3 and 6 months postpartum plus a medical visit with the woman and the newborn infant six months following delivery.

For the control group, all women admitted to the hospital for obstetric care in the same facility on the same day on which a case has been identified and who have none of the conditions indicating severity will be eligible. Following a process of randomized selection balanced according to mode of delivery, maternal age and gestational age at the time of delivery, women in the control group will be invited to participate in the study by the research assistants in the same way as candidates to the study group. Three months after delivery, the study call center will contact the women to carry out the first step in data collection. At the time of this contact, the interviewers will again go over the objectives of the study and will apply standard questionnaires designed to investigate quality of life and postpartum depression. This interview is estimated to last around 20 minutes.

At six months postpartum, the study call center will contact the women again to carry out the second step in data collection. At this contact, the interviewers will go over the study objectives once again and apply the same standard questionnaires on quality of life and postpartum depression, lasting no more than 20 minutes. In the case of women who do not have a telephone, a reminder letter will be sent asking them to phone the study call center at the sixth month postpartum to enable the interview to take place.

At the end of the 6-month telephone interview, the interviewer will confirm the date, time and place of the visit that was previously scheduled when the women were still in hospital. The women will be reminded that they should bring the baby to the visit. Even if they do not authorize the participation of their infants in the study, the women will be invited to return to the hospital and answer the questionnaires. The interview will be carried out by a trained female interviewer, who will apply standard questionnaires to evaluate posttraumatic stress disorder, sexual function and the woman's perception of her functional status in routine activities, taking no more than 35 minutes for each woman. After the mothers have answered the questionnaires, the weight, height and neuro-psychomotor development of the infants will be evaluated by a specially trained pediatrician, taking around 20 minutes. Finally, the women will receive a token cash payment as a contribution towards their transportation and food costs while attending this visit.

The following instruments will be used for data collection:

Posttraumatic Stress Disorder (PTSD) Checklist - Civilian Version (PCL-C)

This questionnaire has been validated in Brazil to screen for the diagnosis of posttraumatic stress disorder. It contains 17 items in which women will indicate to what extent she has been disturbed by symptoms over the past month on a scale of 1-5 (ranging from not at all to a lot). A score ≥ 3 (a medium score) for any one of the items is considered indicative of a clinically significant symptom.

Medical Outcomes Study 36-Item Short-Form Health Survey (SF36)

This is a generic questionnaire for evaluating quality of life that has been validated for use in Brazil. It is multidimensional with 36 items in 8 scales: physical functioning, role-physical, body pain, general health, vitality, social functioning, role-emotional and mental health. Final scores vary from 0 to 100 (poorest to best).

Female Sexual Function Index

A multidimensional questionnaire used to evaluate female sexual function consisting of 19 questions in 6 domains: desire, arousal, lubrication, orgasm, satisfaction and pain. Final scores vary from 2 to 36, a cut-off point < 26 having been proposed as determinant of sexual dysfunction. This questionnaire has been culturally adapted for use in Brazil.

Edinburgh Postnatal Depression Scale (EPDS)

A questionnaire used to screen for symptoms of depression and anxiety in the postpartum period, containing 10 questions that may be self-administered. A final score ≥ 10 has been defined as the cut-off point of greatest sensitivity in screening. The tool has been validated for use in Brazil.

The World Health Organization Disability Assessment Schedule II (WHODAS II)

A 36-item questionnaire used to evaluate the individual's perception of herself and her functional status, consisting of six activity domains related to the woman's routine activities (understanding and communicating, getting around, self-care, getting along with people, life activities in the home/at work and participation in society), on a 6-level scale varying from (1) no difficulty to (6) extreme difficulty/cannot do. Final score varies from 0 to 100 (from best to worst) [25].

Neuro-psychomotor development of the child

The Denver Developmental Screening Test II consists of 125 tasks or items organized in the form of tests of 4 general functions: personal-social, fine motor-adaptive, language and gross motor. At the end, a behavior test is applied that helps the examiner subjectively observe the overall behavior of the child and obtain an impression on how the child uses his/her skills.

Quality control

Quality control procedures will be adopted and include techniques such as reviewing completed forms, checking data entry, repeating data collection for selected medical charts and the use of a detailed manual of operation. Initial quality control of data collection will be performed by the local investigator prior to and during electronic data entry of the forms in order to identify any possible inconsistencies in the data.

A second quality control procedure will be carried out by one of the principal investigators, who will visit the participating centers. At this visit, consistency will be verified between the manual records on file and the data contained in the electronic forms. In addition, a random evaluation will be made of hospital records.

For the quality control of the longitudinal component, 10% of the records at each participating center will be randomly selected at the end of individual data collection and contact will once again be made with the patient in order to verify the data obtained at the first interview. The local investigators will maintain a record of any problems occurring during the study and any queries will be raised with the country coordinator of the project.

Data analysis

Data analysis will be performed in sub-groups according to the time of occurrence of the near-miss or severe maternal morbidity (in adolescence, older ages or at another time in the woman's reproductive life) and determining cause (hypertension, hemorrhage, abortion or other causes). The rates of maternal near-miss will be calculated for each collaborating center using the WHO maternal near miss approach [5], and frequencies of non-near-miss severe maternal morbidity will be calculated using specific defined diagnoses. General estimates will be calculated together with their respective 95% confidence intervals. The association between organ dysfunction and maternal death will be estimated using odds ratios, likelihood ratio test and their respective 95% confidence intervals. In addition, relative risks will be calculated for sexual dysfunction, postpartum depression, posttraumatic stress disorder, deterioration in quality of life, deterioration in the woman's perception of her own functional status in routine activities, risk of adverse perinatal outcome and risk of impaired neuromotor and weight-height development in the children born from the pregnancy associated with severe maternal morbidity.

Results obtained from the preliminary project

Initially, a meeting was held during the Brazilian national congress of Gynecology and Obstetrics in November, 2007, and attended by representatives of 35 healthcare facilities in Brazil. At this meeting, the main points featured in the initial concept of the project were presented and an invitation was made to institutions interested in participating in a Brazilian network on the topic. Those who were interested in participating filled out a registration form with the addresses and characteristics of their respective healthcare institutions. In December 2007, an electronic form was sent to them to be completed with specific information. In accordance with the data received, 27 of these candidate healthcare institutions were selected to participate in the network, taking regional characteristics, geographic distribution, level of complexity and the number of deliveries performed into consideration.

In August 2008, a meeting with representatives from all the centers was held at the coordinating center in Campinas. At this meeting, the proposal was presented and discussed in detail, and suggestions were incorporated into the final version of the protocol. Participating center representatives were identified, the operational issues involved in implementing the study and the theoretical concepts were discussed, and the final version of the research project was defined. Concurrently, a signed commitment was undertaken by each representative to participate in the Brazilian Network for the Surveillance of Severe Maternal Morbidity: the Brazilian Network of Studies in Reproductive and Perinatal Health was created. A Steering Committee was also designated for the study.

Ethical aspects

The coordinating center has already obtained the approval of the local Institutional Review Board and of the National Council for Ethics in Research (CONEP) of the Brazilian Ministry of Health for both components of the project. The participation of the collaborating centers in this study will only be confirmed after the project has been approved by their respective Institutional Review Boards. Individual signed informed consent will not be requested from the women involved in the cross-sectional analysis, since this study does not involve any type of intervention that could adversely affect their treatment; the data of interest will be obtained retrospectively from the patient's charts and without identifying the woman. Therefore, a waiver of the requirement for signed informed consent was obtained. It is understood that there is no other way of obtaining concrete, reliable information on cases of severe maternal morbidity or death,

since these patients are unable to give their consent. However, informed consent will be obtained from the women involved in the longitudinal component of the study. All the principles regulating research in human beings will be respected.

Based on the questionnaires applied, women diagnosed with some type of pathological condition, who are not receiving medical care, will be referred to healthcare facilities equipped to provide them with follow-up care. Women who have already received a diagnosis of a pathological condition but are not being followed up by a physician will also be referred to an appropriate healthcare service.

Technical and scientific contributions expected from the project

Brazil is a country with very high proportion of births taking place in health facilities (around 97%). The results of the present study will permit a prospective evaluation of severe maternal morbidity and deaths nationwide through the participation of healthcare facilities with different regional characteristics. No multicenter collaborative studies of this dimension are currently being carried out in healthcare institutions in Brazil in the field of Reproductive Health, and no data thus obtained are currently available. In addition to the specific study of maternal health hazards, the organizational structure required by this project will guarantee continuity of the investigation into various conditions of interest to public health beyond the period in which this study will be conducted. The implementation of a collaborative network is essential for expanding the production of substantive research in the field of maternal and perinatal health in Brazil.

Certainly, the availability of resources for the implementation and development of the Brazilian Network for the Surveillance of Severe Maternal Morbidity will lead to new scientific findings relevant to Brazil and other countries. Concomitantly, this will permit the construction of an innovative technological base from which health data may be obtained on a continuous basis, providing the evidence required to institute a real and effective improvement in the quality of life and health of the population. This network is committed to participating in future collaborative studies in the areas of perinatal and women's healthcare. The implementation of a series of multicenter studies is anticipated in this area in a way never before achieved in this country. This fact gives greater power to the results, which will therefore be more representative of the country, a particularly interesting achievement bearing in mind the wide ethnic, cultural and social diversity of the Brazilian population.

We hope that this initiative contributes to the improvement of health care and for the reduction of maternal and perinatal morbidity and mortality.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

The idea for the study arose in a group discussion with all authors. The first version of the protocol was drafted by JPS and JGC, then complemented with the suggestions of the others. RCP and RSC were responsible for including the initial proposal for a multidimensional evaluation of consequences. SMH was responsible for the final, complete version of the protocol. JGC supervised the whole process. All authors contributed to the development of the study protocol and approved the final version of the manuscript.

Appendix 1: Criteria defining Near-Miss (WHO)*

A woman who fulfills one of the following criteria and survives a complication during pregnancy, childbirth or in the 42 days postpartum should be considered a near-miss.

Clinical Criteria

Acute cyanosis

Breathing rate > 40 or < 6

Oliguria unresponsive to fluids or diuretics

Loss of consciousness for ≥ 12 hours

Unconscious, no pulse/heartbeat

Jaundice concomitantly with preeclampsia

Gasping

Shock

Coagulation disorders

Cerebrovascular accident

Total paralysis

Laboratory Criteria

Oxygen saturation <90% for > 60 minutes

Acute thrombocytopenia (<50,000 platelets)

Creatinine ≥ 300 μmol/l or ≥ 3.5 mg/dL

Bilirubin >100 μmol/l or > 6.0 mg/dL

Unconscious, presence of glucose and ketoacidosis in urine.

Lactate > 5PaO2/FiO2 < 200

pH < 7.1

Management Criteria
Use of continuous vasoactive drug

Dialysis for treatment of acute kidney failure

Puerperal hysterectomy due to infection or hemorrhage

Cardiopulmonary resuscitation (CPR)

Transfusion ≥ 5 units of red blood cell concentrate

Intubation and ventilation for a period ≥ 60 minutes, unrelated to anesthesia*

Modified from [5]

Appendix 2: Indicators of non-near-miss severe maternal morbidity (potentially life-threatening conditions) *

Hemorrhagic disorders
Abruptio placentae

Placenta accreta/increta/percreta

Ectopic pregnancy

Antepartum hemorrhage

Postpartum hemorrhage

Ruptured uterus

Abortion with severe hemorrhage

Hypertensive disorders
Severe Preeclampsia

Eclampsia

Severe hypertension

Hypertensive encephalopathy

HELLP syndrome

Other systemic disorders
Endometritis

Pulmonary edema

Respiratory failure

Seizures

Sepsis

Thrombocytopenia <100,000

Thyroid crisis

Management indicators of severity
Blood transfusion

Central venous access

Hysterectomy

ICU admission

Prolonged hospital stay (>7 postpartum days)

Intubation not related to anaesthetic procedure

Return to operating room

Major surgical intervention

*Modified from [5]

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7.5. Anexo 5. Artigo referente à implantação da estrutura operacional da Rede

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From planning to practice: building the national network for the surveillance of severe maternal morbidity

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Abstract

Background: Improving maternal health is one of the Millennium Development Goals for 2015. Recently some progress has been achieved in reducing mortality. On the other hand, in developed regions, maternal death is a relatively rare event compared to the number of cases of morbidity; hence studying maternal morbidity has become more relevant. Electronic surveillance systems may improve research by facilitating complete data reporting and reducing the time required for data collection and analysis. Therefore the purpose of this study was to describe the methods used in elaborating and implementing the National Network for the Surveillance of Severe Maternal Morbidity in Brazil.

Methods: The project consisted of a multicenter, cross-sectional study for the surveillance of severe maternal morbidity including near-miss, in Brazil.

Results: Following the development of a conceptual framework, centers were selected for inclusion in the network, consensus meetings were held among the centers, an electronic data collection system was identified, specific software and hardware tools were developed, research material was prepared, and the implementation process was initiated and analyzed.

Conclusion: The conceptual framework developed for this network was based on the experience acquired in various studies carried out in the area over recent years and encompasses maternal and perinatal health. It is innovative especially in the context of a developing country. The implementation of the project represents the first step towards this planned management. The system online elaborated for this surveillance network may be used in further studies in reproductive and perinatal health.

Keywords: surveillance network severe maternal morbidity, near-miss, multicenter cross-sectional study

Background

The reduction of maternal mortality is one of the targets of the Millennium Development Goals for 2015 [1]. In some countries, some progress has been achieved, but there is very little progress in the most of high mortality countries [2-4].

The high mortality ratios result mainly from difficulties in accessing healthcare services, the inadequate management of obstetrical complications and failure to provide effective interventions in poorly developed areas [5]. On the other hand, the occurrence of maternal death in developed settings is a relatively rare event compared to the total number of women who survive such complications [3]. The study of severe maternal morbidity has been suggested as a useful approach to investigating quality of health care systems in order to improve women's healthcare and effectively reduce

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maternal morbidity [5]. Nevertheless, differences also exist in the definitions and procedures used to identify cases of morbidity, which need also progressive transformation and development [6,7]. Hospital-based and population-based studies have shown that lack of standardization of the criteria used to define severe maternal morbidity, difficulty in identifying and reporting these conditions both with official records and by the women themselves, and the limitations of retrospectively conducted studies [8-14].

Electronic surveillance systems may introduce improvements in the process by facilitating complete data reporting and reducing the time required for data collection and analysis [15-18]. With the objective of providing support for healthcare programs, epidemiological surveillance systems may be defined as "the ongoing and systematic collection, analysis and interpretation of health data in the process of describing and monitoring a health event" [19]. In improving healthcare, greater benefits are obtained when an integrated system of data technology is available and if this systematic electronic data capture system is associated with a program to identify risks and propose clinical management based on evidence [20]. Few countries and institutions have well-structured systems of health data technology in which data are used in real-time for adjusting healthcare and performing surveillance [21-25].

Even in places where the health surveillance system is adequately structured such as in Canada, severe maternal morbidity is not yet fully studied due to various factors: the need to standardize the concepts, the range of the area in which surveillance has to be carried out and the prospective individual evaluation of each identified case, with effective feedback conveyed to the healthcare providers [25].

In Brazil, the distribution of maternal death is associated with disparities in socioeconomic development. Brazil's large territorial extension is also associated with cultural differences and socioeconomic inequalities, resulting in heterogeneity with respect to the incidence of complications and in the ways of dealing with them [26]. Health-related data systems are almost exclusively used for epidemiological evaluation and global management, and are not integrated into a specific prospective evaluation of care.

Only a few initiatives for the surveillance of maternal mortality and severe maternal morbidity have been carried out prospectively [23,24]. As recently defined by the WHO, maternal near-miss refers to a situation in which a woman almost dies but survives a life-threatening complication of pregnancy, childbirth or in the first 42 days following delivery [5]. In order to facilitate the practical use of this concept, potentially life-threatening conditions were listed that, together with specific criteria defining maternal near-miss, would operationally characterize the broader concept of severe maternal morbidity.

As a result, the surveillance and proposal of strategies to reduce maternal deaths worldwide may be founded on a single conceptual basis. Therefore, the objective of the present manuscript was to describe the methods and procedures adopted for the creation and implementation of the National Network for Surveillance of Severe Maternal Morbidity in Brazil [27], covering all the regions of the country and using the new standardized criteria for maternal near miss recently defined by the WHO [5].

Methods

Protocol design

In 2002, research was initiated at the University of Campinas, Brazil, focusing on severe maternal morbidity. The transition from studying death to studying maternal morbidity followed a worldwide trend, considering the absolute number of deaths is relatively small compared to the number of cases of morbidity. Data on maternal morbidity are more accessible and reliable for the evaluation of quality in obstetrical care. Within this scope, a study was conducted to evaluate the applicability of different concepts of severe maternal morbidity and of a severity score to identify cases of maternal morbidity [9].

Elaborating further on the concept that routine health data would be useful for systematically identifying the occurrence of complications associated with pregnancy, the National Health Service's Hospital Information System was evaluated. Data routinely collected from medical records of women with conditions suggestive of severe maternal morbidity were selected, and the diagnoses and procedures used in such cases were described in order to identify factors associated with the occurrence of maternal death [15]. Next, further evaluations on maternal morbidity were performed using data from demographic health surveys. The importance of the use of validated questionnaires for obtaining information on morbidity and the regional differences in the prevalence of morbidity were also highlighted [11].

Considering that the early identification of cases of maternal morbidity would allow a more appropriate way of monitoring, managing and preventing deaths [28], the proposal to establish the National Network for Surveillance of Severe Maternal Morbidity was developed as a research proposal [27].

Organization of the project

The project is a multicenter, cross-sectional study to be implemented in referral obstetrical units in all geographical regions of Brazil. Over a 12-month period,

prospective surveillance and data collection was planned to be performed to identify cases of maternal near-miss and potentially life-threatening conditions in accordance with the new criteria defined by WHO [5].

To determine the number of collaborating centers to be included in the study, sample size was calculated according to the number of deliveries that would have to be covered to identify cases of near-miss. Based on a previously reported incidence of 8 cases for 1000 deliveries [9], approximately 70,000 deliveries would have to be monitored. This number was believed to be sufficient to validate the new criteria issued by WHO [5]. The study population is composed of all the women admitted to the participating hospitals during the study period who suffer organ dysfunction (that will be a near-miss case or a maternal death, Table 1) or presenting potentially life-threatening conditions (Table 2), who die or are transferred to other healthcare services because they require more specialized services or procedures.

During the data collection period, at each participating hospital, local coordinators perform a daily review of all admitted women, looking for cases with any of the conditions indicative of severity (Table 2). The lists of patients with these diagnoses are sent for review and data collection following the patient's discharge from hospital, death or transfer to another hospital. Data unavailable from the record is obtained from the attending team. Data are collected on demographic and obstetrical characteristics, primary determinant of severe morbidity (the first complication in the chain of events that led to severe maternal morbidity), length of hospitalization, occurrence of any criteria of maternal near-miss, perinatal outcome and condition of the woman at discharge from hospital. The data are collected on a pre-coded form and are then sent electronically to the database. The manually completed forms are filed in such a way as to be easily accessible for inspection during technical quality control visits.

Table 1 Potentially life-threatening maternal conditions

HEMORRHAGIC COMPLICATIONS	
Abruptio placentae	Postpartum hemorrhage
Placenta previa/accreta/increta/percreta	Atony
Ectopic pregnancy	Retained placenta
Ruptured uterus	Perineal lacerations
Severe hemorrhage due to abortion	Coagulopathy
	Uterine inversion
HYPERTENSIVE DISORDERS	
Severe preeclampsia	Severe hypertension
Eclampsia	HELLP syndrome
Hypertensive encephalopathy	Acute fatty liver of pregnancy
OTHER COMPLICATIONS	
Pulmonary edema	Acute respiratory failure
Seizures	Acidosis
Sepsis	Cardiopathy
Postpartum endometritis	Cerebrovascular accident
Post abortion endometritis	Coagulation disorders
Urinary infection	Thromboembolism
Chest infection	Diabetic ketoacidosis
Thrombocytopenia < 100 000 platelets	Jaundice/hepatic dysfunction
	Meningitis
Thyroid crisis	Acute renal failure
Shock	
MANAGEMENT INDICATORS OF SEVERITY	
Transfusion of blood derivatives	Intubation unrelated to anaesthesia
	Return to operating theater
Central venous access	Major surgical intervention (hysterectomy, laparotomy)
ICU admission	
Prolonged hospital stay (> 7 days)	Use of magnesium sulfate

Table 2 WHO criteria for maternal near miss[5]

CLINICAL CRITERIA	
Acute cyanosis	Loss of consciousness for ≥ 12 h
Gasping	Unconscious, no pulse/heartbeat
Breathing rate > 40 or < 6 per minute	Cerebrovascular accident
	Uncontrolled convulsions/total paralysis
Shock	
Oliguria unresponsive to fluids or diuretics	Jaundice concomitantly with preeclampsia
Coagulation disorders/clotting failure	
LABORATORY CRITERIA	
Oxygen saturation < 90% for > 60 minutes	pH < 7,1
	Lactate > 5
PaO2/FiO2 < 200 mmHg	Acute thrombocytopenia (< 50 000 platelets)
Creatinine ≥ 300 mmol/l or ≥ 3,5 mg/dL	
	Unconscious, presence of glucose and ketoacidosis in urine
Bilirubin > 100 mmol/l or ≥ 6,0 mg/dL	
MANAGEMENT CRITERIA	
Use of continuous vasoactive drug	Intubation and ventilation for a period ≥ 60 minutes, unrelated to anesthesia
Postpartum or post abortion hysterectomy due to infection or hemorrhage	Dialysis for treatment of acute renal failure
Blood transfusion ≥ 5 units of red cell	Cardiopulmonary resuscitation (CPR)

Selection of the centers to constitute the network

After the general proposal was ready, a meeting was held during a national congress of the Brazilian Federation of Societies of Gynecology and Obstetrics in November 2007 where representatives of several healthcare institutions from around the country were present. The proposal to establish a National Network for Surveillance of Severe Maternal Morbidity was presented and those interested in participating applied for that.

Before the project could be implemented, the proposal was submitted for public funding and, following approval, an invitation letter was sent to all interested institutions, together with a summary of the planned objectives and methods. In addition, a form designed to obtain information on the characteristics of the collaborating center was also sent to the local investigator.

Basically, it had information on identification and location of the institution, nature and complexity level of the hospital, population covered, number of beds in the maternity department, availability of resources for more specialized care (blood bank, obstetrical and neonatal intensive care units, specialist care for high risk pregnancies, availability of other medical or surgical specialities, ultrasonography, laboratory, anesthetists available round the clock, resources for the parenteral administration of antibiotics, oxytocin and magnesium sulphate, resources for general anesthesia, mechanical ventilation, cardiorespiratory resuscitation of adults and newborn infants, hysterectomy), number of deliveries performed annually (minimum number required above 1,000 deliveries/year), availability of broadband internet connection, data on the prevalence of some obstetrical interventions based on scientific evidence performed during delivery, and availability of written protocols of procedures in the service.

Additionally telephone contacts occurred between the principal investigator and the person responsible for the institution. As a result of these different approaches, 35 institutions from all over Brazil applied for participating in the study. Evaluation of their characteristics and geographical distribution led to the selection of 27 institutions that fulfilled all the inclusion criteria.

Review of the criteria for severe maternal morbidity and data collection forms

Following selection of the centers, a meeting was held in August 2008 with the principal investigators from each center at the project headquarters in Campinas. At this time, a term of agreement was signed by all attendants to compose a Brazilian Network for Studies in Reproductive and Perinatal Health. The objective of this alliance was to proceed to develop further studies in the future in the matter, using the same multicenter strategy of achieving regional diversity in a developing country with continental extensions. The meeting lasted for two days when the research proposal was reviewed and discussed, the concepts of near miss and severe maternal morbidity were presented, the data collection forms were structured and the concept of developing an electronic data collection system was introduced. A copy of the proposal was provided to each center, to be evaluated and approved locally. The coordinating center had the research protocol approved by the local institutional review board (Committee of Ethics in Research from the School of Medical Sciences, University of Campinas - Approval letter CEP 097/2009), and then by the national IRB.

Selection of the electronic research system

The viability of the entire project depended on approval of the request for funding submitted to the National Research Council (CNPq)/Department of Science and Technology (DECIT). Initially, the plan was to develop software and a customized data management system control system for the study. Nevertheless, due to some practical constraints, it was decided to use a system that had already been developed and that would be cheaper to maintain. Therefore, a free, open source, online data entry system was selected (OpenClinica®) [29], which is available for use in clinical trials, was selected. This internet-based system consists of an electronic platform for data entry and management of data and is designed to support all types of clinical studies in a variety of locations [29]. The system permits autonomy in creating forms, in analyzing and storing data and in stratifying the right of access to be granted to users working in the same study (Figure 1).

Results

Development of specific software and hardware tools

Following selection of an electronic data entry system for the network and registration of the study in the OpenClinica®, an internet server was created in the host institution to safely store the data. The electronic address of the server was hosted in the institution's homepage with an individual safety certificate https://openclinica.caism.unicamp.br:8443/OpenClinica/MainMenu that allowed encrypted data to be sent to the central database (Figure 1). A detailed training was then carried out for the development of an electronic environment to serve the network. For this purpose, usernames and passwords were created for all research team, allowing individual access to their respective centers. Investigators, coordinators, supervisors, data managers at central and local levels were granted different levels of accessibility and privileges for the inclusion and evaluation of data. The electronic data collection form was developed in accordance with the standardized pattern offered by the system, with the inclusion of different sections containing all the variables pertinent to the study. Several versions had to be created and evaluated internally before the final version was reached.

Development of material

In order to identify potential research subjects during hospitalization, an identification form was developed listing all the potentially life-threatening conditions. This form was produced and provided to the centers as a suggestion for use in selecting subjects at the moment of their discharge from hospital, mainly for hospitals with a large number of admissions. The manual data collection form was developed with exactly the same structure as the electronic version.

The manual of operations was designed to contain all the information required by the investigators and to provide well-structured material that could be easily and rapidly accessed. It contains the main concepts of the

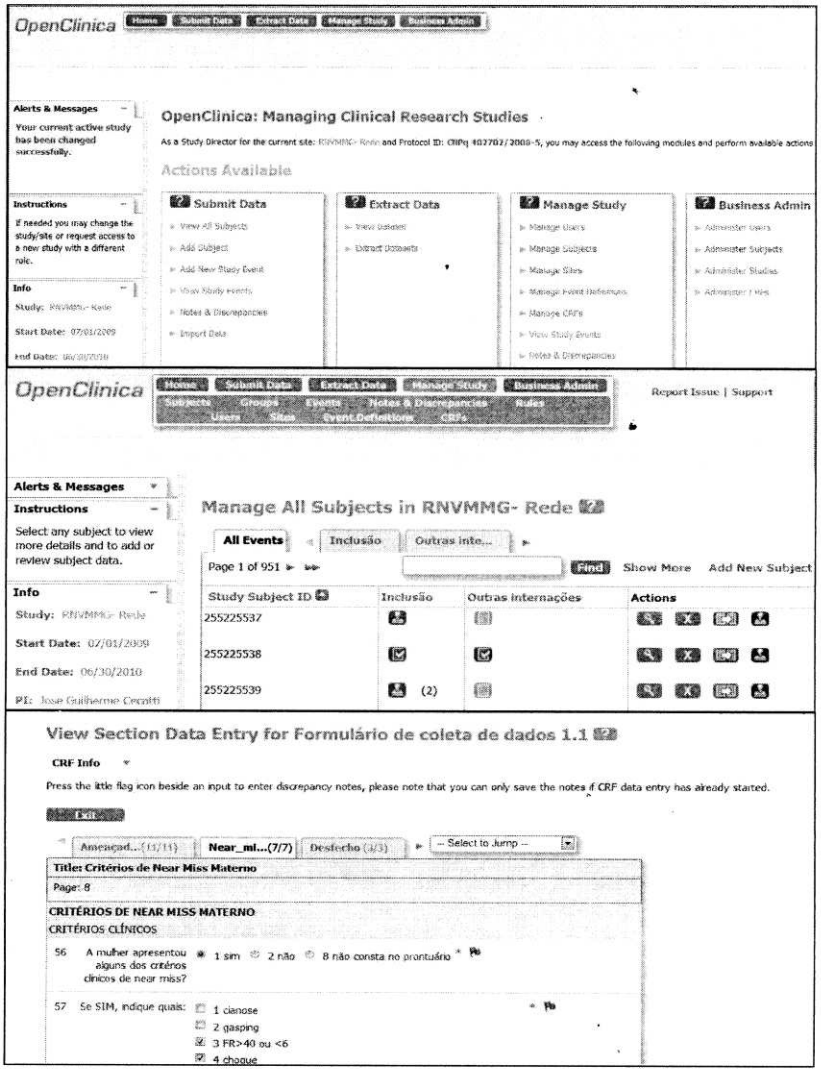

Figure 1 Sample screens from the online data entry and management system: A. Cover sheet for the study in OpenClinica; B. Form for the management of all subjects; C. Form for data entry on criteria for maternal near-miss.

study, information on the participating centers and investigators, a detailed description of the basic steps involved in electronic data input and management and standardized definitions of the variables used in the study.

Implementation process

With electronic data system and preliminary materials ready, a meeting was held in Campinas in April 2009 to present the system to all research teams and train them to use the the network. To assure the minimal material infrastructure required for the study, a computer was supplied to each center and training was provided using these same computers in an appropriate environment with internet support. The study documents and procedures were presented at the meeting and distributed to all the participants, who then discussed them and the

electronic data system, making suggestions for changes in accordance with their individual experience at each site. The material was tested and personnel trained in its use through the presentation of clinical cases of maternal morbidity and mortality in order to recreate situations as close as possible to the actual routine expected for the study.

The meeting lasted three days and, in addition to practical training in the system, operational procedures were discussed to ensure that the study would function homogenously in the different sites of the network. It provided the opportunity to deal with a variety of aspects including defining concepts, routine procedures and the way the centers would operate. These debates resulted in changes that improved the instruments and standardized network operations.

Data collection was planned to start simultaneously in all centers, which happened at the beginning of July, 2009. The forms and manual of operations were provided to the investigators on a password-protected virtual disk, which is also hosted at the website, and contains the latest versions of all the documents used in the network.

Analysis of the implementation process

After data collection was initiated, the process of data consistency checks and technical visits to the participating centers also started. Communication between all centers and the coordinating center was generally conducted by e-mail and telephone contact was seldom required. To verify the consistency of cases included in the system, a schedule was developed to be carried out at each individual center. During this procedure, all included cases are checked for inconsistencies by a team of trained research assistants in the coordinating center following a pretested protocol of general and specific consistencies between variables. Any errors or queries identified for any specific case are transmitted electronically to the local investigator and coordinator on a structured table. After evaluation and resolution of any inconsistencies, the local investigators return this table to the principal investigators, who conclude the audit by retaining, modifying or excluding the case.

Another quality control procedure that has been developed consists of technical visits to the centers, when evaluation is made of the working conditions of the equipment supplied, the appropriateness of the filing system used to store the manual forms, the use of the manual of operations and the particular strategies used to locally identify cases. A random check of selected patient forms is also made and the consistency of the data previously collected by the local investigators is verified. A report is then prepared for the local and central team. If a problem/situation arising from this visit is considered to be of general interest for all centers, a note is prepared and circulated among all research staff.

As initially planned, the availability of the professionals involved was crucial in controlling the network. In addition to the local staff, the existence in the coordinating center of a principal investigator, general and deputy coordinators, research assistants, network manager, system analyst, statistician, accounts manager and other technical assistants has proved to be essential for the follow-up of surveillance on such a broad scale.

Discussion

The development of a prospective surveillance system for severe maternal morbidity in Brazil resulted in the National Network for the Surveillance of Severe Maternal Morbidity [27]. This is an innovative scientific initiative based on the experience acquired in the area by a research group on maternal morbidity and mortality at the coordinating center. In addition, this corresponds to the first time the new WHO criteria for maternal near miss will be prospectively used and validated. The full process was guaranteed by financial resources obtained from Brazilian funding agencies. These funds enabled the necessary infrastructure, including computers, the internet server, software, human resources to perform the surveillance and notification of data, the entire core organization of the study and the expenses involved in traveling to training meetings and technical visits. Nevertheless, these resources could be considered small taking into account the scale of the network structure, the complexity involved in controlling the quality of data collection and the duration of surveillance.

The decision to use an open data collection system specifically developed to support clinical studies rendered the implementation process less expensive and more practical. Although similar systems have already been used in developed countries to collect data on other subjects [16], to the best of our knowledge this is the first system developed for the prospective, widespread collection of data on severe maternal morbidity, thus permitting current epidemiological surveillance. More widespread analyses on the occurrence of severe maternal morbidity in Canada, for instance, were obtained using databases containing information routinely collected in healthcare services [25].

Meetings were of crucial importance for the development of a homogenous study. Situations differ greatly from one center to another as a result of their diverse geographical locations and resources available, although all of them were tertiary health facilities with neonatal intensive care units. Regarding their institutional capacity of providing appropriate care to obstetric complications, some of them are also provided with obstetrical ICU, some with general ICU and few have no ICU at

all. The training allowed to update electronic and support material, a fruitful debate and the investigators to share their individual experiences. Communication between the centers, including discussions on problems and suggestions, was conducted by e-mail, ensuring a quick and cheap solution.

Data collection was initiated before the system could be tested by the investigators themselves in their own work environment. This resulted in the need to modify the form and the manual of operations after the first month of data collection. This may be considered a limitation in the planning and implementation of this study, highlighting the importance of pilot studies once the system is already fully operational in order to solve any difficulties or inconsistencies detected early. Despite that, all the updates required could be considered minor, involving completion of the electronic form and the definition of a few variables. Following these adjustments, no other changes have been required.

The manual of operations incorporated around 90% of the queries raised by the investigators prior to review and this efficacy increased following the modifications. The entire data entry procedure is described in detail there, including illustrations taken from the system itself for guidance. Nevertheless, many of the investigators sought advice before consulting the manual. This shows that reading instructions prior to initiating surveillance is a mandatory step to ensure that the process flows as effectively as possible.

Another possible limitation of the study would be that this kind of surveillance would identify only cases delivering in hospitals or health care facilities. However, nowadays, fortunately this is no longer a limitation in Brazil, considering the vast majority of deliveries occur in hospitals. Anyway, the new WHO criteria for identifying maternal near miss cases has a set of criteria that could theoretically be applied to any setting, even for community deliveries.

Currently the network has already finished its data collection's activities, with more than nine thousand and five hundred of cases of potentially life threatening and maternal near miss condition s included in the database, a number much higher than what was initially expected. The initiation of data collection coincided with the H1N1 influenza epidemic [30], which may have led to an increase in the occurrence of severe cases. Indeed, one of the changes made to the system was to add this diagnosis to the form.

Taking into account this partial experience, a next special concern arises on how to guarantee sustainability for a routine surveillance in a national environment. Considering that the process has showed to be more efficient in places where the form for identifying any potentially life threatening conditions or maternal near miss was routinely implemented, this should probably be an important content of a package directed to a nationwide system for surveillance of severe maternal morbidity. The development of a national electronic database system could facilitate the interpretation and management in different settings, by different professionals, and allow adaptation to local reality. To be more effective and complete, probably the surveillance might be a governmental strategy with scientific support by researchers and/or universities with expertise in the field. The Ministry of Health could enhance hospitals participation through supporting such surveillance as a public health policy. It could be first piloted as an official process in some facilities that had already participated in the current initiative, before a broader national implementation. The government could also enable adaptation of health information systems in use nowadays to the maternal morbidity surveillance needs.

Finally, there is an interesting point that appeared when this network first went into operation that should be the subject of a more in-depth qualitative investigation in a near future. Although this current project consists of a cross-sectional, observational study for the surveillance and detection of the occurrence of episodes of severe maternal morbidity in the participating centers, there have been emphatic reports from the network participants at each center that implementation and participation in this system has generated interventions that were not routine at these centers, including the use of some evidence-based interventions that had not yet been adopted (such as the routine prophylactic use of uterotonics at all deliveries), the review of the criteria of severity in obstetrical cases for referral to intensive care units and earlier request for specialist services to help manage cases in which specific dysfunctions and organ failure are detected, among others.

Conclusions

The expectation generated following implementation of the National Network for Surveillance of Severe Maternal Morbidity is that it will lead to an increase in the production of knowledge on information technology and the surveillance of health events. The pioneering use of the criteria for near miss recently defined by the WHO [5] may permit validation of these criteria for later studies on a worldwide level. Hopefully other developing countries, and even developed countries, could implement similar surveillance systems and increase the consistency of data on maternal health. This increases the possibility of implementing actions that would indeed lead to a reduction in the unnecessary deaths of pregnant or postpartum women worldwide, as well as possibly also decreasing the burden of disease resulting from this condition for the many women who survive severe

maternal morbidity. Therefore this initiative could complement the global strategy to reduce maternal mortality.

Abbreviations

MDG: millennium development goal; WHO: World Health Organization

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Authors' contributions

The idea for the study arose in a group discussion among all the authors. The first version of the manuscript was drafted by SMH and JGC, and then complemented with the suggestions of the others. JGC supervised the entire process. All authors contributed to the development of the study protocol and approved the final version of the manuscript.

Competing interests

The authors declare that they have no competing interests.

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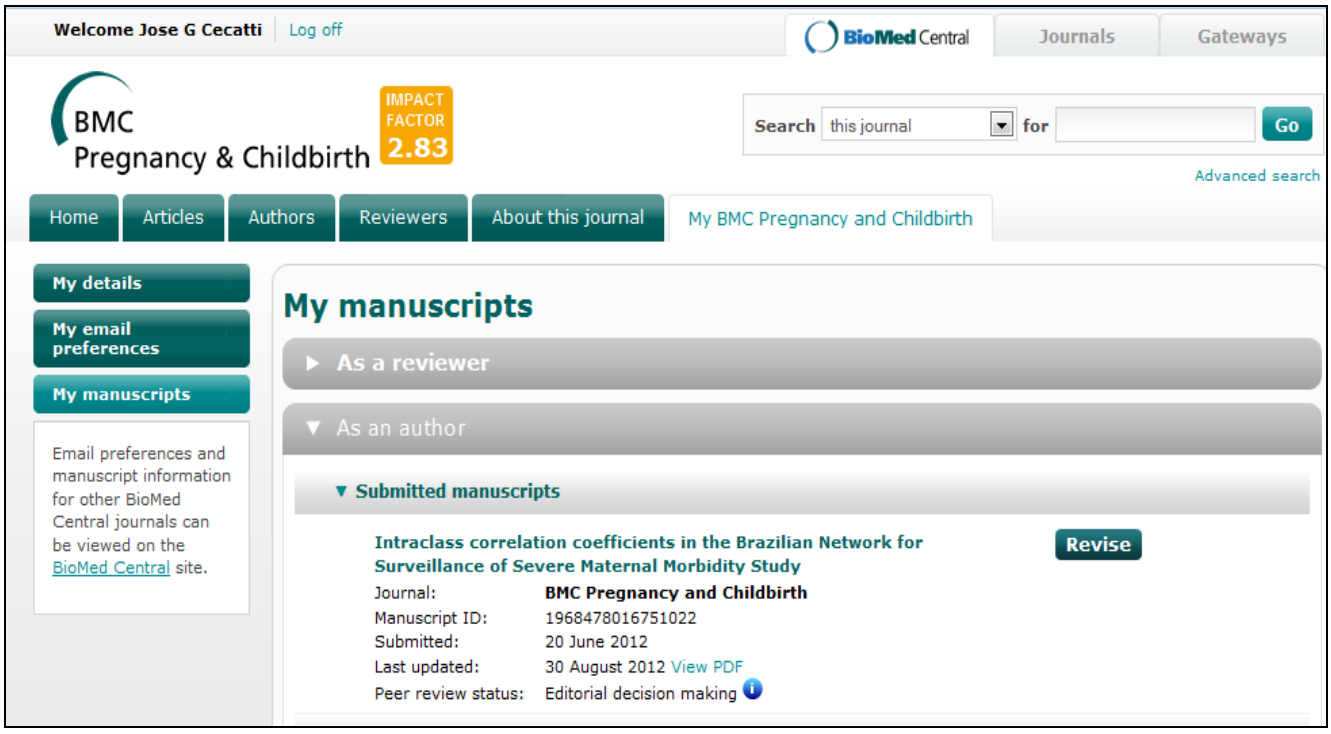
7.6. Anexo 6. Comprovante do envio do artigo para a revista *BMC Pregnancy Childbirth*



7.7. Anexo 7. Comprovante da publicação do artigo na revista *PlosONE*

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PLOS ONE

The WHO Maternal Near-Miss Approach and the Maternal Severity Index Model (MSI): Tools for Assessing the Management of Severe Maternal Morbidity

Joao Paulo Souza[1]*, Jose Guilherme Cecatti[2], Samira M. Haddad[2], Mary Angela Parpinelli[2], Maria Laura Costa[2], Leila Katz[3], Lale Say[1], on behalf of the Brazilian Network for Surveillance of Severe Maternal Morbidity Group[¶]

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Abstract

Objectives: To validate the WHO maternal near-miss criteria and develop a benchmark tool for severe maternal morbidity assessments.

Methods: In a multicenter cross-sectional study implemented in 27 referral maternity hospitals in Brazil, a one-year prospective surveillance on severe maternal morbidity and data collection was carried out. Diagnostic accuracy tests were used to assess the validity of the WHO maternal near-miss criteria. Binary logistic regression was used to model the death probability among women with severe maternal complications and benchmark the management of severe maternal morbidity.

Results: Of the 82,388 women having deliveries in the participating health facilities, 9,555 women presented pregnancy-related complications, including 140 maternal deaths and 770 maternal near misses. The WHO maternal near-miss criteria were found to be accurate and highly associated with maternal deaths (Positive likelihood ratio 106.8 (95% CI 99.56–114.6)). The maternal severity index (MSI) model was developed and found to able to describe the relationship between life-threatening conditions and mortality (Area under the ROC curve: 0.951 (95% CI 0.909–0.993)).

Conclusion: The identification of maternal near-miss cases using the WHO list of pregnancy-related life-threatening conditions was validated. The MSI model can be used as a tool for benchmarking the performance of health services managing women with severe maternal complications and provide case-mix adjustment.

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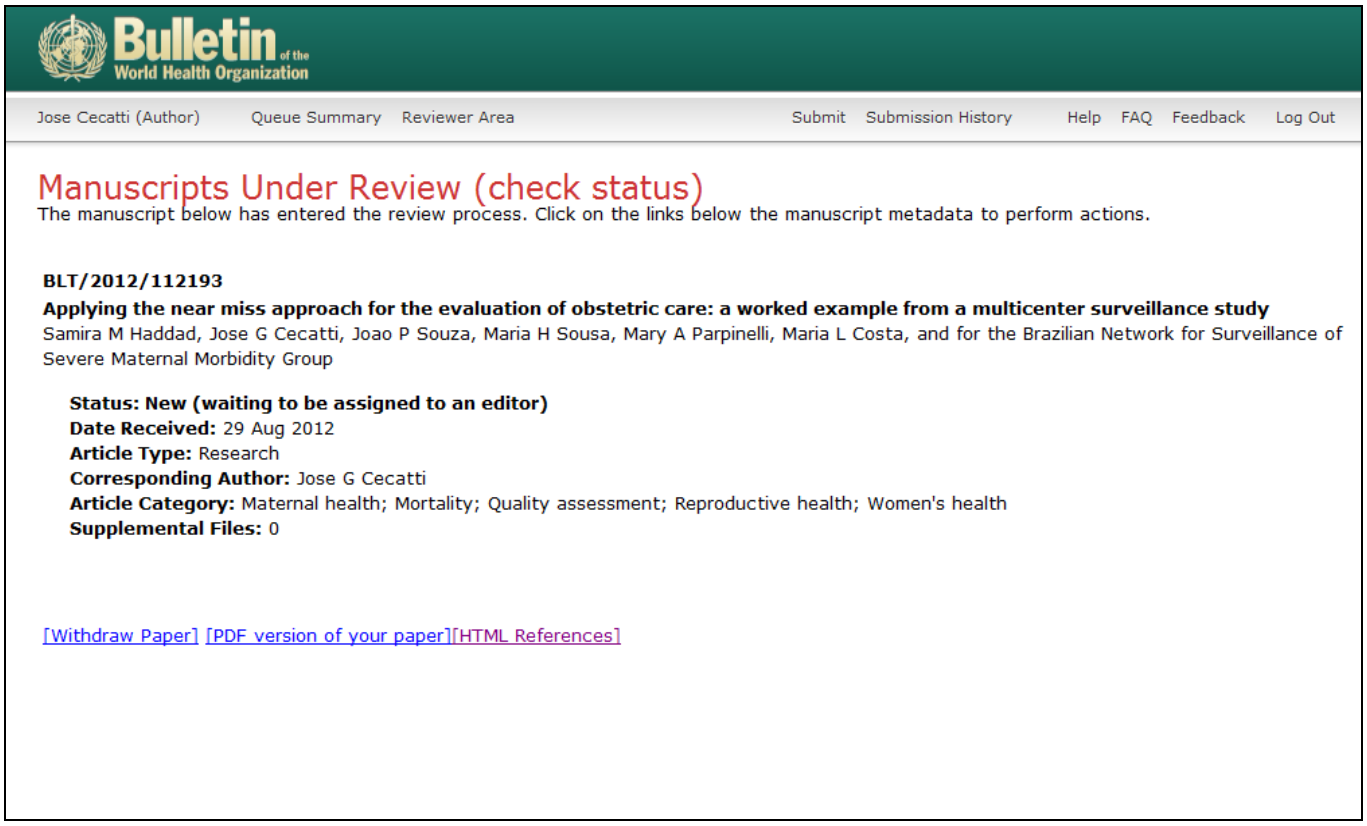
Introduction

An estimated 287 000 maternal deaths occurred in 2010 around the world. Despite the substantial reduction as compared to 1990, much has to be done for achieving the relevant target of the Millennium Development Goals [1]. Most of the burden of maternal deaths is carried by low-income countries, but maternal mortality is still a relevant public health problem among middle-income countries. In this context, strengthening health systems and services to provide optimal care for women during pregnancy and childbirth is crucial, particularly to those women experiencing acute pregnancy-related complications [2–5].

Confidential enquiries of maternal deaths have been used for many years to understand health systems and services failures in the provision of appropriate maternal health care. Based on these enquiries, lessons can be learned and used to strengthen health systems and improve quality of care [6]. Despite the positive contribution of this approach, it has limitations, particularly in low mortality settings or at the health service level, where the amount of maternal deaths is generally insufficient to provide useful information. In the last 20 years, the concept of maternal near miss has been explored in maternal health as an adjunct to maternal-death confidential enquiries. Women who nearly died but survived complications have been studied as surrogates of maternal deaths. Among other positive characteristics, maternal near-miss cases can directly inform on problems and obstacles that had to be overcome during the process of health care. Maternal

Anexo 8. Comprovante do envio do artigo para a revista *Bull World Health Organiz*



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Applying the near miss approach for the evaluation of obstetric care: a worked example from a multicenter surveillance study

Samira M Haddad, Jose G Cecatti, Joao P Souza, Maria H Sousa, Mary A Parpinelli, Maria L Costa, and for the Brazilian Network for Surveillance of Severe Maternal Morbidity Group

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