ORIGINAL ARTICLE / ARTIGO ORIGINAL

Classification of deaths in women with human immunodeficiency virus/acquired immunodeficiency syndrome in pregnancy and childbirth

Classificação de óbitos em mulheres com vírus da imunodeficiência humana/síndrome da imunodeficiência adquirida no ciclo gravídico-puerperal

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ABSTRACT: Objective: To reclassify deaths of women infected with the human immunodeficiency virus/acquired immunodeficiency syndrome in pregnancy and childbirth in the State of Pernambuco, Brazil, from 2000 to 2010. Methods: A descriptive exploratory study, developed from the following steps: translation to Portuguese of the item "HIV and aids" of the United Nations document "The WHO application of ICD-10 to deaths during pregnancy, childbirth and the puerperium: DCI MM 2012"; development of a classification algorithm of deaths of women living with the human immunodeficiency virus/acquired immunodeficiency syndrome in pregnancy and childbirth; and reclassification of deaths by a group of experts. Results: Among the 25 reclassified deaths, 12 were due to human immunodeficiency virus/acquired immunodeficiency syndrome, and pregnancy condition was coexisting; 9 were reclassified as indirect maternal death, with O98.7 code, proposed by the World Health Organization; 2 as direct/indirect maternal death; and 2 were considered indeterminate. Conclusion: The reclassification showed a possible pattern of change in maternal mortality, since most of the deaths were attributed to the virus and may lead to a reduction in deaths from maternal causes. The algorithm will subsidize the use of the new classification of maternal death and human immunodeficiency virus/acquired immunodeficiency syndrome.

Keywords: Women. Maternal mortality. HIV. Aids. International Classification of Diseases. Causes of death.

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RESUMO: Objetivo: Reclassificar os óbitos de mulheres portadoras do vírus da imunodeficiência humana/síndrome da imunodeficiência adquirida no ciclo gravídico-puerperal no Estado de Pernambuco, no período de 2000 a 2010. Métodos: Estudo descritivo exploratório, desenvolvido a partir das seguintes etapas: tradução para português do item "HIV and aids" do documento da Organização das Nações Unidas "The WHO application of ICD-10 to deaths during pregnancy, childbirth and the puerperium: ICD MM, 2012"; elaboração de um algoritmo de classificação dos óbitos de mulheres portadoras do vírus da imunodeficiência humana/síndrome da imunodeficiência adquirida no ciclo gravídico-puerperal; e reclassificação dos óbitos por um grupo de especialistas. Resultados: Dentre os 25 óbitos reclassificados, 12 foram devido ao vírus da imunodeficiência humana/síndrome da imunodeficiência adquirida e a condição gravídica era coexistente; 9 foram reclassificados como morte materna obstétrica indireta, com o código O98.7, proposto pela Organização Mundial de Saúde; 2 como morte materna obstétrica direta/indireta; e 2 foram considerados indeterminados. Conclusão: A reclassificação apontou uma possível mudança de padrão de mortalidade materna, visto que a maioria dos óbitos foi atribuído ao vírus, podendo levar a uma redução dos óbitos por causas maternas. O algoritmo subsidiará o uso da nova classificação sobre morte materna e do vírus da imunodeficiência humana/síndrome da imunodeficiência adquirida.

Palavras-chave: Mulheres. Mortalidade materna. HIV. Aids. Classificação Internacional de Doenças. Causas de morte.

INTRODUCTION

Maternal mortality is considered a severe violation of women's human rights, being preventable in more than 90% of the cases. The World Health Organization (WHO), the United Nation Children's Fund (UNICEF), the United Nations Population Fund (UNPFA) and the World Bank estimated that, in 2013, 289 thousand women all over the world died from complications related to pregnancy and childbirth, which corresponds to a maternal mortality ratio (MMR) of 210 per 100 thousand live births. Approximately 99% of them lived in developing countries, mostly in sub-Saharan Africa and Asia¹.

Infection by the human immunodeficiency virus (HIV) and the acquired immunodeficiency syndrome (aids), identified in 1981, represents a dynamic and global phenomenon. aids, among other emerging infectious diseases, stands out due to its magnitude and extended damage toward population². Many sub-Saharan countries have coexisting elevated maternal mortality and high HIV prevalence, among women in reproductive age, representing the two main causes of death among young women³⁻⁵.

Worldwide, it is estimated that 2.6% maternal deaths are related to HIV-aids¹. Therefore, there is a risk of death due to the progression of HIV as well as due to complication related to pregnancy^{3,6}.

In Pernambuco, notifications and investigations of these cases have shown deaths of women in pregnancy and childbirth, often difficult to be classified as deaths by aids or women's death by HIV-aids. According to the Ministry of Health (MoH), the

deaths of women with HIV during pregnancy and childbirth are part of a compulsory investigation of women's deaths in reproductive age and may, therefore, be classified as maternal deaths⁷. The rules for selecting the cause of death used in Brazil prioritized, until 2013, classifying aids as the underlying cause of death (B20-B24)⁸. However, many of these women may have died from aids (aids as the main underlying cause) or from HIV (the disease is a comorbidity). The absence of a protocol to guide the classification of deaths among women with HIV/aids, during the discussion and analysis of a death by the Technical Groups of the Committees, may overor underestimate the true cases resulting from aids⁹.

In an attempt to address all these difficulties, the WHO suggests the use of code O98.7 to classify indirect obstetric maternal deaths from $HIV/aids^{10}$.

Given that, it is necessary that strategies to guide the discussion on these female deaths are proposed. Thus, the objective of the present study was to reclassify deaths of women with HIV/aids occurred in pregnancy and childbirth, living in the state of Pernambuco, from 2000 to 2010, having WHO's CID 10 as a reference on maternal death.

METHODS

It is an exploratory, cross-sectional study, carried out in Pernambuco. The deaths of women living in Pernambuco were studies, from 2000 to 2010, whose underlying cause of death was HIV/aids, registered as maternal by the Mortality Information System (*Sistema de Informações sobre Mortalidade* – SIM) and discussed by the Municipal/Regional/State Technical Groups Committees of Maternal Mortality. According to the International Statistical Classification of Diseases and related Health Problems (ICD-10)⁸, by definition, such deaths are those occurred among women between 10 and 49 years of age in codes B20 to B24, in Parts I or II of the Death Certificate (DC), *i.e.*, both the underlying cause and associated causes of death. These last ones regarding diseases and their complications at the moment of death, informed in the death certificate¹¹.

The sources of data used were the SIM, the Notification of Injury Information System (Sistema de Informação de Agravos de Notificação – Sinan), the Laboratory Testing Control System (Sistema de Controle de Exames Laboratoriais – Siscel) of CD4/CD8 and Viral Load (Siscel), the investigation files and the final judgement of maternal deaths, discussed by the Municipal/Regional/State Technical Groups Committees of Maternal Death. As an additional step, a search through the Sinan of the IST/aids/HIV State Program of maternal deaths in the presence of HIV/aids were performed, in order to confirm diagnosis, notification and investigation of the case.

The development of the study was carried out in through the following steps:

 Translation into Portuguese of the item "HIV and aids" of the document of the World Health Organization (WHO) "The WHO Application of ICD-10 to deaths during pregnancy, childbirth and the puerperium- ICD MM, 2012" 10, still not translated and implemented in Brazil by the MoH, carried out by two professionals, one with experience in maternal mortality and another in HIV/aids, proficient in English. After translation, it was consolidated into a single document in Portuguese and retranslated into English by an English translator. The similarity of interpretation was observed (whether or not the interpretation of the language is similar to the original one, even there are different words)¹².

2. Elaboration of an algorithm to classify the deaths of women with HIV/aids during pregnancy and childbirth, using clinical, laboratory and care criteria: *Essentials*: onset of symptoms and/or worsening of the disease associated to pregnancy; presence of comorbidities; adherence to antiretroviral therapy (ART); information regarding viral load and CD4+ lymphocyte levels. *Complementary*: obstetric history; information on the newborn; necropsy reports.

This algorithm has been adjusted during the process of discussing the cases, with the aggregation of components which would become necessary in order to classify the deaths, such as alterations in values regarding T CD4+ lymphocytes for classification and inclusion of the "undetermined" category;

- 3. Reclassification of deaths, carried out through the appreciation of a group of specialists, during five meetings. This group consisted of a professional obstetrician with expertise in HIV/aids, an experienced professional in the State IST/aids/HIV Program, an experience professional in the Technical Area of Women's of the State, an experienced professional in Maternal Death Surveillance of the State and a professional with expertise in maternal mortality and member of the State Committee of Studies on Maternal Mortality (*Comitê Estadual de Estudos da Mortalidade Materna* CEEMM). The algorithm was used based on the classification proposed by the WHO, translated into Portuguese, which defined inclusion criteria as:
 - Death of woman in reproductive age by HIV/aids, with the coexisting condition of pregnancy;
 - Maternal death due to indirect obstetric causes, code O98.7;
 - Maternal death due to direct obstetric causes in Chapter XV of ICD-10;
 - Death by indeterminate cause.

Discarded cases both for maternal and HIV/aids deaths were excluded.

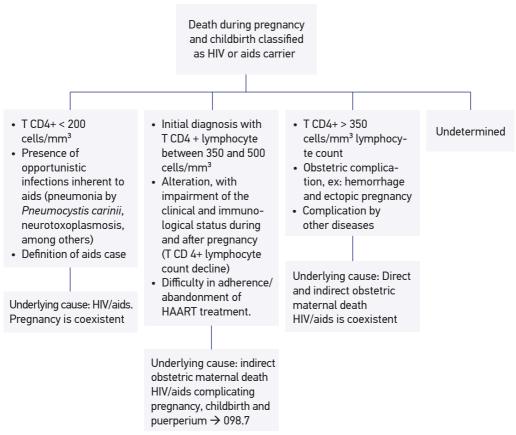
4. After reclassification, the results were represented as diagram, by using Microsoft Office's Word 2007.

The project was approved by the Research Ethics Committee of the Center of Health Sciences of the Federal University of Pernambuco, meeting the requirements established in Resolution No. 466, December 12th, 2012, of the MoH, and there were no conflicts of interests during the research.

RESULTS

Based on the variables needed for reclassification of the cases, and during the assessment of the group of specialists, the algorithm presented in Figure 1 was created. All clinical, laboratory and health care information were obtained from secondary data (investigation records and information systems related to maternal death and HIV/aids); of these, only 32% had records of T CD4+ lymphocyte count.

Of the 25 deaths, previously classified as maternal with code B20-24, 12 (48%) were considered by HIV/aids (B20-24) and the pregnancy condition was coexistent; only 9 (36%) kept the initial classification of indirect obstetric maternal death, with code O98.7 proposed by the WHO; 2 deaths (8%) were reclassified as direct/indirect obstetric maternal death (the direct one being post-cesarean hemorrhage and the indirect one, deep vein thrombosis); and 2 (8%) were considered indeterminate (Figure 2).



ART: antirretroviral therapy.

Figure 1. Algorithm to reclassify the deaths occurred in pregnancy and childbirth of women with HIV/aids, based on the proposal by the World Health Organization, 2012.

Among the 12 deaths reclassified as HIV/aids, 3 occurred during pregnancy, 9 in late childbirth and none in early childbirth. In the cases occurred during pregnancy, the woman already had signs of the diseases' development when pregnant and in late childbirth it was observed that the physiological alteration of pregnancy did not interfere in the progression of the disease. When it was possible to locate the results of T CD4+ lymphocytes, these were below 350 cells/mm³ (2 with values below 200 cells/mm³). Seven among the 12 women reclassified as HIV/aids did not start their ART or it was not mentioned in the beginning of the treatment. Among the comorbidities found, pulmonary tuberculosis, neurotoxoplasmosis and non-Hodgkin lymphoma can be mentioned. Of the deaths reclassified with code O98.7, 8 occurred in early childbirth and only 1 in late childbirth (60 days postpartum), this last one with several reports of visits due to fever and diarrhea after normal delivery. Six women already knew they had HIV before the pregnancy that led to death and three got their diagnosis during pregnancy/childbirth. It should be noted that 6 out of the 12 women (50%) had begun their ART. The presence of opportunistic infections, such as pulmonary tuberculosis and neurotoxoplasmosis, and 2 results of T CD4+ lymphocyte lower than 350 cells/mm³ were also detected, though they were related to the commitment of the clinical state during or after pregnancy.

As for the deaths reclassified as obstetric, the HIV/aids diagnosis did not interfere in the occurrence of death. They resulted from complications intrinsically related (direct) or aggravated (indirect) by pregnancy and childbirth, both late diagnosed with HIV.

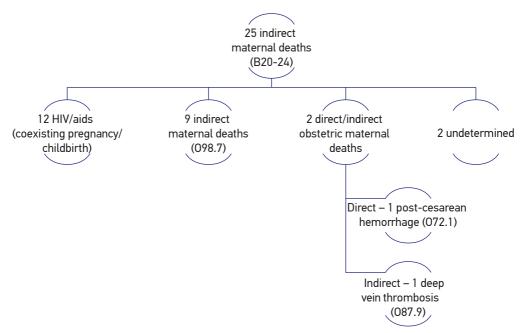


Figure 2. Representation of the reclassification of death of women with HIV/aids during pregnancy and childbirth.

The deaths for which it was not possible to establish a relation between HIV/aids and pregnancy and childbirth were reclassified as indeterminate. In one of the cases, an unspecified cerebral lesion was detected, with no histopathological result, making it impossible to identify if associated or not with aids. In the other one, occurred in 2000, insufficient data made it impossible to be reclassified, once there was no information on prenatal care, the beginning of ART and the moment of diagnosis of the disease.

DISCUSSION

The results showed that, from the 25 indirect obstetric maternal deaths previously classified by technical groups, only 9 remained with the same classification, taking over a new code, O98.7. Twelve were reclassified as deaths of women in reproductive age by HIV/aids, codes B20 to B24, with pregnancy coexisting with the moment of death. This difference in classification confirms the importance of an algorithm or a protocol to guide the use of the code.

Few studies examined the causes of maternal death distinguishing indirect deaths related to HIV from coincidental ones. A document from the WHO, 2012¹⁰, suggests the deaths of pregnant and postpartum women infected by HIV should be categorized as indirect obstetric deaths (they die from aggravating effects of HIV on pregnancy) and deaths related to HIV (they die from fatal complications of HIV or aids, which coincide with the pregnancy). However, as stated by Calvert and Ronsmans¹³ (2013), no guidance is made as for how this distinction should be done.

According to the MoH¹⁴, from 2013 on, diseases caused by HIV (B20 to B24 – Chapter I) are no longer an exclusion of Chapter XV of ICD-10 (pregnancy, childbirth and puerperium) and became a subcategory of Category O98. Therefore, the deaths of women with aids which, after investigation, have their deaths confirmed due to complications aggravated the physiological effects of pregnancy, were coded as O98.7 (HIV disease complicating pregnancy, childbirth and the puerperium).

Classifying the death of a woman in reproductive age in the presence of HIV/aids has always been a challenge for the technical group using more sensitive and less specific criteria, including the deaths coded in B20-B24 in the presence of pregnancy and childbirth. Therefore, the classification was conducted in the absence of a standardized guidance which would allow for better identifying the relation between disease and pregnancy, a difficulty which extends to other deaths due to indirect obstetric causes¹⁵. In addition to that is the fact that one of the main objectives of the surveillance of maternal death and of mortality committees is capturing undeclared deaths in order to reduce under-reporting information.

The difficulty to use this classification, at least at this moment of implementing a new code, remains, once it requires frequent consultation to MoH protocols and discussions with specialists of the area. The construction of this algorithm has the objective to guide the classification of deaths in women with HIV/aids in pregnancy and childbirth, proposed by the WHO 10 in 2012 and incorporated by the MoH 14 in 2013.

Algorithms for this kind of classification of maternal deaths are still not used in Brazil. This first exercise was proven important in order to support the technical groups, which do not count, necessarily, on the availability of specialists, and the investigations not always have all information regarding the process of illness and death of women.

Although algorithms are not mentioned, Moran and Moodley⁵, considering the rules of evaluation of the National Committee on Confidential Enquiries into Maternal Deaths (NCCEMD)¹⁶, already emphasized criteria for the attribution of aids as cause of death, which are similar to the ones included in the algorithm in this study, namely: women who had a positive HIV test and a differentiation cluster 4 (CD4) of < 200 cells/mm³ or an aids-defining condition in order to minimize the bias in relation to a diagnosis mistake as the cause of maternal death.

Considering this, it may be stated that this study is unprecedent in Brazil, since there are no reports in the national literature to classify women during pregnancy and childbirth in terms of "HIV status". Besides, this new orientation, with the use of the algorithm, may reveal a more realistic role of HIV/aids in maternal deaths, interfering, also, in the distribution of indirect obstetric deaths in the total maternal deaths.

The mechanism by which the presence of HIV/aids increases the risk of death among pregnant women may be related to immunosuppression during pregnancy associated with infection by HIV, which may accelerate the progression of the disease and increase the risk of obstetric complications¹⁷.

International publications, especially in African countries, bring a deeper look upon maternal health and HIV, due to the high prevalence of the virus and the increased MMR, often coexisting the status of the disease and the pregnant condition. These countries still do not use code O98.7, though they already discuss the relation between HIV/aids in pregnancy¹⁸⁻²⁰.

The nature of the interaction between HIV and pregnancy is what underlies the need to classify these deaths. The information about the state of health of the woman during pregnancy and the knowledge of the diagnosis of the infection by the virus were determining factors when using the new classification. Although authors indicate the increased mortality and morbidity is associated to the clinical progression of the disease, it is essential to know the degree of women's clinial and immunological involvement, evaluated by CD4 counting and viral loads¹⁷.

Recent evidences suggest pregnancy seem to have no discernible effect on the increased progression of the infection by HIV in asymptomatic infected women, however, symptomatic infected women are in higher risk of dying by infectious diseases than uninfected women ^{18,20}. Efforts in order to prevent, diagnose and treat these conditions before and during pregnancy may reduce morbidity and mortality among infected pregnant women ¹⁷.

In a study by Le Coeur et al.¹⁹ carried out in Congo, among women with HIV, pregnancy seemed to grant an apparent advantage, with a mortality ratio five times lower among pregnant than among non-pregnant women, demonstrating the impact HIV has on the population of women may vary according to their pregnancy status and likely by their access to ART and care services.

It was observed that 12 of the deaths studies were due to HIV, which was also observed in a recent systematic review¹³. For these authors, the excessive mortality attributed to HIV among pregnant and postpartum women have a great impact on mortality related to pregnancy, even when the prevalence of HIV is relatively low. Thus, part of the deaths which would be classified as indirect obstetric maternal ones acquire a new classification, allowing greater prominence to the infectious disease and lower prominence to maternal mortality.

The fact that 7 out of 12 women reclassified with HIV/aids did not begin ART could be a contributing factor to accelerating the disease. Calvert and Ronsmans¹³ further describe that this was the finding for most the studies reviewed by them, in which a significant number of HIV-infected women would have progressed to clinical stages of aids due to lack of therapy, with high mortality rates as an outcome.

In South Africa, according to NCCEMD¹⁶, it was found that 27.8% of maternal deaths, in which the underlying cause of death was classified as aids, mothers also had an obstetric condition which could be classified as the underlying cause of death, such as abortion and postpartum hemorrhage. Even if these deaths were classified as maternal ones due to indirect obstetric causes, 78.9% would still be attributed to HIV infection, similarly to the study carried out.

Data from a randomized study, carried out in Uganda, demonstrate that MMR of HIV-infected mothers was 1686.8/100 thousand live births in comparison to 309.8/100 thousand live birth of HIV-non-infected women²¹. Moodley et al. ¹⁷ also stated having no doubt the infection by HIV is the greatest threat to maternal mortality in South Africa.

Due to the lack of an international consensus about the relation HIV/aids and maternal death, and considering that Brazil has made progress in the prevention, diagnosis and treatment of infected or diseased pregnant women, there is no doubt the algorithm elaborated may collaborate with the initiatives of the WHO and MoH to classify indirect obstetric maternal deaths by HIV/aids in Pernambuco and in the country.

In order to assign a causal relation between HIV infection and pregnant and/or post-partum conditions, it was necessary to use information contained in the classification algorithm. In some cases, the medical chart was retrieved so that more detailed information on the hospitalization of the woman was collected, such as complaints and diagnosis at the moment of admission in healthcare services.

As the study used secondary data for the discussion with the group of specialists, information as for the state of health of the woman during pregnancy and postpartum and the use of ART were not always available, especially for those who spent long period without ambulatorial care or hospitalization. The interview with the family could ensure more reliability in describing the disease-pregnancy relation, however, only information recorded during domiciliary investigation conducted by surveillance were used, and a new interview with family members was not conducted.

For some women in the study, HIV testing occurred late. Carvalho²², when investigating the factors associated to unknown serostatus for HIV among pregnant women in the metropolitan region of Recife, Pernambuco, identified greater chance of unknown serostatus for HIV during the assistance in delivery of pregnant women who started a late prenatal

care. Therefore, it could interfere in the search for specialized health care, and in the management and use of ART. In one of the cases in the study, the diagnosis was performed during brain death tests.

The cases studies were classified twice. The first classification was performed by technical groups, in which all deaths were considered indirect obstetric maternal ones by consensus, with reference to ICD-10, in which all maternal deaths of women with HIV would be classified with codes B20-B24. And the second classification (reclassification), carried out by the group of specialists, obeyed the logic of the algorithm, also by consensus, with code O98.7 as reference.

CONCLUSION

When influencing the distribution of maternal deaths and female deaths by HIV, this new perspective may imply in changes in the organization and offer of care to those women, whether on reproductive health or on infectious diseases. The validation of reclassification used in this study will need a new reclassification with other participants in discussing cases and with the standardization of instruments for information collection.

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