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## CLINICAL ARTICLE

## H1N1 influenza pandemic and maternal mortality in Antioquia, Colombia

Jesús Velásquez, Gladis Vélez, John Zuleta, Francisco Franco, Joaquín Gómez\*

Department of Obstetrics and Gynecology, University of Antioquia School of Medicine, Center Nacer in Sexual and Reproductive Health, Medellín, Colombia

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## ABSTRACT

**Objective:** To evaluate the impact of the H1N1 influenza pandemic on maternal mortality in the province of Antioquia, Colombia, in 2009. **Methods:** The present study was a descriptive, retrospective, cross-sectional study of maternal deaths in Antioquia in 2009 caused by H1N1-related pneumonia. The study formed part of the epidemiologic surveillance process undertaken by the Health and Social Protection Directorate of Antioquia and the particular healthcare institutions involved in the cases. **Results:** In 2009, there were 42 maternal deaths in Antioquia, corresponding to a maternal mortality ratio of 46 per 100 000 live births. Ten deaths were due to pneumonia, 9 of which occurred after the H1N1 outbreak was first reported in early 2009. In 3 cases, the women were confirmed to have H1N1 virus infection, and the remainder fulfilled probable case criteria. The main factors contributing to the deaths were underestimation of H1N1 symptoms, and delays in administration of antiviral medication and in hospitalization. **Conclusion:** For the population subgroup of pregnant women in Antioquia, it is crucial to remain alert regarding H1N1 virus infection, guaranteeing patients adequate monitoring and/or timely administration of immunization, medication, and hospitalization. © 2011 International Federation of Gynecology and Obstetrics. Published by Elsevier Ireland Ltd. All rights reserved.

## 1. Introduction

The health authorities in the province of Antioquia, Colombia, have systematically been undertaking epidemiologic surveillance of maternal mortality for the past 15 years in order to identify the determinant causes and factors of maternal death and to implement strategies geared to its reduction. Because of their findings and interventions, Antioquia's epidemiologic profile has changed considerably. The maternal mortality ratio has decreased significantly—from 68.5 per 100 000 live births in 2004 to 45.9 per 100 000 live births in 2009 [1].

On June 11, 2009, the World Health Organization (WHO) officially declared the H1N1 influenza a pandemic, yet multiple learning and management experiences associated with H1N1 virus infection had been taking place worldwide since early 2009. The aim of the present study was to identify the main determinant healthcare factors influencing maternal deaths in Antioquia and to extract lessons, thus helping to prevent more maternal deaths due to H1N1 influenza/pneumonia.

## 2. Materials and methods

The present study was a retrospective, descriptive, cross-sectional investigation of maternal mortality cases due to H1N1-related pneumonia in Antioquia between January 1 and December 31, 2009.

\* Corresponding author at: University of Antioquia, PO Box 1226, Medellín, ANT 050010, Colombia. Tel.: +57 4 2195400; fax: +57 4 2191031.

E-mail address: joaquin.gomez@medicina.udea.edu.co (J. Gómez).

To assess the quality of medical care, the medical procedures set down in women's clinical histories were compared with the recommendations in the protocol issued by the Colombian Ministry of Social Protection (MPS) for the diagnosis and treatment of suspicious, probable, and confirmed cases of H1N1 infection [2].

In compliance with Resolution 8430 issued by the republic of Colombia in 1993, the present study was risk-free. It used retrospective research methods and techniques; no intervention, or modification, of the biologic, physiologic, psychologic, or social variables pertaining to the individuals included in the study was practiced. The study formed part of the epidemiologic surveillance process undertaken by the Health and Social Protection Directorate of Antioquia and the particular healthcare institutions involved in the cases. Owing to the fact that the study was not designed as an independent research project to begin with, it did not require Institutional Review Board approval. Confidentiality and anonymity have been respected.

Three sources of information were consulted: the national computerized public health epidemiologic surveillance system (SIVI-GILA), to which all maternal deaths must be reported by law; the death certificates of all women aged 10–54 years in Antioquia; and the oral accounts of maternal deaths reported by either the community or public health workers. Therefore, all probable or confirmed H1N1-related cases of maternal death in 2009 were included in the present study.

Full clinical records corresponding to all maternal deaths in Antioquia during the study period were examined, compiling the data available from all institutions involved in the healthcare process, and semi-structured interviews with relatives of the deceased were also conducted. Probable or confirmed H1N1-related cases were then selected.

A committee of experts with 7 years of experience in the analysis of maternal mortality causes examined the cases. The committee applied the *Guidelines for Maternal Mortality Epidemiological Surveillance*, which were issued by WHO and the Centers for Disease Control and Prevention (CDC) [3] and adopted by the Health and Social Protection Directorate of Antioquia. The committee analyzed every case, defining the basic and direct cause of death. It determined how these demises might have been avoided, and identified the factors contributing to them—vis-à-vis the women, their communities, and health services—such as patient delays in seeking medical care at a health service and delays in diagnosis, initiation of treatment, or transfer to tertiary healthcare facilities. Findings in each case were discussed with all healthcare actors involved.

According to the MPS-issued *Protocol for the Care and Handling of Cases of Pandemic AH1N1/09 Virus and their Contacts* [2], a suspected case is a person in any age group showing signs and symptoms of acute respiratory infection, with mild clinical manifestations, or presenting a disease similar to influenza, with a fever of 38 °C or higher, and cough or other upper respiratory tract symptoms of up to 7 days' duration.

A probable case is a person in any age group manifesting severe acute respiratory infection (SARI) that merits hospitalization, or SARI in the following situations: a person with unusual signs and symptoms of SARI—live or deceased—fulfilling or not fulfilling the epidemiologic criteria of exposure to sources of infection; and any death, of unknown etiology, due to SARI and associated with some kind of exposure to sources of infection.

A confirmed case involves the following situations: a person classified as a suspected or probable case—live or deceased—in whom the H1N1 influenza virus has been identified by means of rRT-PCR laboratory test, genetic sequencing, or viral culture; or a person who dies owing to SARI of unknown etiology, after having been in close contact with a confirmed case of H1N1, either at home or in a healthcare facility.

Severe illness was defined as a patient's need for mechanical ventilation assistance, and the time of demise was defined either by gestational age or by the number of days after childbirth that death took place. Quantitative variables included median and range, and qualitative variables included number of cases and proportion. The corresponding data were stored in a database (Access; Microsoft, Redmond, WA, USA), and the database of maternal deaths in Antioquia from 2004 to 2008 was also reviewed.

### 3. Results

In 2009, there were 42 maternal deaths in Antioquia, corresponding to a maternal mortality ratio of 46 per 100 000 live births. Ten deaths were due to pneumonia, and 9 occurred after the H1N1 outbreak

was reported in early 2009. Between 2004 and 2008, there were 7 maternal deaths from pneumonia in Antioquia, corresponding to 1–2 deaths per year.

Of the 9 deaths that occurred after the H1N1 outbreak was reported in 2009, 7 were of women in the third trimester of pregnancy and 2 occurred in the postpartum period. One of the 9 women, who had not sought medical care before, was pronounced dead upon arrival when she was finally taken to a health service. Four women had attended their healthcare facility for respiratory symptoms at least 3 times before being hospitalized. Four women fulfilled the suspected case criteria from the first time they sought care, and when they were hospitalized these women fulfilled the probable case criteria. The other 4 women who were alive on arrival were hospitalized, or left under observation in an emergency ward, at the time of their first consultation—fulfilling the probable case criteria.

The average time between the onset of symptoms and the first consultation was 2.5 days (range, 1–7 days) and the average time between onset of symptoms and decompensation forcing hospitalization was 4.8 days (range, 2–7 days). Four women had no associated medical or obstetric comorbidity; of the 5 patients with associated comorbidity or obstetric conditions, 3 experienced pre-eclampsia and 2 were expecting twins. To confirm the presence of H1N1 virus infection, a nasopharyngeal sample was taken from 6 of the 9 women. In the 3 confirmed cases, the sample was taken within the first 6 days following the onset of symptoms. In the 3 non-confirmed cases, the patients were on mechanical ventilation when the samples were taken; these samples were obtained 7 days after the onset of symptoms for 2 patients, and 14 days after onset for 1 patient. In 2 cases, the treating physician did not suspect H1N1 infection and, thus, did not order the tests necessary for diagnosis, and in the other case the woman was dead on arrival at the healthcare facility and no sample was obtained. Her autopsy yielded evidence of pus in the lungs but, despite this finding, H1N1 infection was never considered and the samples indicated were not obtained. The 6 women for whom it was not possible to confirm H1N1 infection fulfilled MPS criteria to be considered probable cases (Table 1).

The most common initial symptoms were cough (n=8 [88.9%]); fever (n=6 [66.7%]); myalgia and headache (n=5 [55.6%]); and shortness of breath (n=3 [33.3%]). None of the 9 women had been vaccinated against H1N1. Six of the 8 women who were alive on arrival were administered oseltamivir. On average, the women with confirmed H1N1 infection received medication 7 days (range, 4–14 days) after the onset of symptoms. The women for whom H1N1 infection was not confirmed were administered the same medication 7–14 days after symptoms appeared. The average time between onset of symptoms and death was 27.2 days (range, 2–41 days).

According to the Colombian MPS protocol [2], all women met the criteria to be considered suspected or probable cases from the time of

**Table 1**  
Clinical variables of suspected and confirmed maternal deaths due to H1N1 in Antioquia, 2009.

Case No.	State of H1N1 infection	H1N1 vaccination	Age, y	Delivery	Perinatal result	Gestational age at time of delivery, wk	Moment of complication	Associated medical conditions	Associated obstetric conditions
1	Confirmed	No	27	Cesarean	Live	31	Week 31	None	Twin pregnancy
2	Confirmed	No	39	Cesarean	Live	34	Week 34	Hypothyroidism	None
3	Confirmed	No	37	Cesarean	Live	33	Week 33	None	None
4 <sup>a</sup>	Probable	No	42	Cesarean	Live	37	2 Weeks post partum	Chronic arterial hypertension	Superimposed pre-eclampsia
5 <sup>b</sup>	Probable	No	22	Undelivered	Fetal death	34	Week 34	None	None
6 <sup>a</sup>	Probable	No	26	Vaginal	Live	38	2 days post partum	None	None
7 <sup>a</sup>	Probable	No	32	Cesarean	Live	27	Week 27	None	None
8 <sup>a</sup>	Probable	No	20	Cesarean	Live	36	Week 36	None	Moderate pre-eclampsia
9 <sup>a</sup>	Probable	No	22	Cesarean	Live	35	Week 35	None	Severe pre-eclampsia; twins

<sup>a</sup> Fulfilled criteria for severe acute respiratory infection, meriting hospitalization.

<sup>b</sup> Patient dead upon arrival at hospital.

**Table 2**  
Characteristics of care for maternal mortality cases due to pneumonia in Antioquia, 2009.

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9
Time between onset of symptoms and sample-taking, d	4	5	5	Not taken	Not taken	Not taken	9	15	8
Time between onset of symptoms and first consultation, d	1	2	2	7	Unknown	1	1	2	4
No. of consultations prior to hospitalization	3	4	2	1	0	1	5	2	3
Time between onset of symptoms and severe illness, d	4	4	2	7	Unknown	1	7	7	7
Administration of oseltamivir	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes
Time between onset of symptoms and administration of oseltamivir, d	4	4	6	Not applicable	Not applicable	Not applicable	7	14	7
Time between onset of symptoms and death, d	8	41	40	8	Unknown	2	34	44	41

their first consultation. H1N1 infection was not suspected from the onset, however, so no precautions were taken to place patients in isolation or to administer antiviral treatment in time.

The required precaution of isolating the women during hospitalization or ambulance transfer was not observed in any of the cases. Isolation was implemented only when H1N1 infection was finally suspected at more complex healthcare facilities. Only 1 of the clinical records evaluated indicated attempts to trace possibly infected contacts. The main clinical characteristics of the 9 cases are summarized in Table 1.

Among the determinant factors for maternal mortality due to the H1N1 pandemic, the most significant was the quality of healthcare (Table 2). In 7 cases, the factors influencing outcome were identified as follows: lack of familiarity with the healthcare protocol for H1N1 patients; not taking into account the number of times a woman sought medical care when symptoms persisted as a risk factor; and failure to identify symptoms of sepsis quickly enough. In 4 cases, there was a delay in referring women to tertiary healthcare facilities owing to deficiencies in the management of the healthcare network. The woman who had not attended a healthcare facility previously was the only one for whom the delay in seeking medical treatment was the critical factor.

#### 4. Discussion

According to WHO, 11 516 people worldwide were confirmed to have died by December 2009 because of H1N1 infection—a figure much lower than that reported for deaths caused by seasonal influenza, which is estimated to be 600 000 [4]. Pregnant women represent 1%–2% of the total number of people infected with H1N1 worldwide. However, they account for 10% of the hospitalizations due to this infection; up to 9% of the admissions to intensive-care units; and 6%–10% of H1N1 demises [5]. The 196 confirmed H1N1 demises that had occurred in Colombia as of December 28, 2009, included 23 (11.7%) pregnant women [6]. There are clear indications that pregnant women and very young people are the population subgroups most at risk of dying from the H1N1 influenza virus [6].

Among women fulfilling the criteria for suspected cases in Antioquia, the possible reasons for H1N1 infection not being confirmed were delays in taking samples after symptoms had fully set in and the fact that nasopharyngeal samples were taken from patients on mechanical ventilation. In one of the first reports about AH1N1 infection in China, it was found that the average time for a sample to turn positive using nasopharyngeal rRT-PCR was 6 days (range, 1–17 days) [7]. A study carried out in the USA [8] showed that 19% of viral RNA cases detected via bronchoscope had, at first, yielded negative results when the sample was aspirated via the nasopharynx [8].

If the clinical risk is high and mechanical ventilation is in use, it is recommended that samples from different sites in the respiratory tract be extracted—via endotracheal or intratracheal aspiration, or a bronchoscope—not via nasopharyngeal procedure [9].

In an article about H1N1 infection during pregnancy in the USA, the 6 patients who died had received treatment 8 days or more after the onset of symptoms [10]. An Australian report revealed that

the average time between onset of symptoms and treatment with oseltamivir among women who died was 6 days [11]. The average in Antioquia among the 6 patients who received H1N1 medication was 7 days after the onset of symptoms.

According to the reviewed literature, no publication analyzed maternal mortality H1N1 related using the methodology proposed by WHO and CDC, and no technical committee discussed the cases in order to establish the various determinant factors. In most cases, the delay in beginning treatment influenced the outcome. The main determinant causes and factors of the maternal mortalities that were referred to involved inadequate healthcare quality.

None of the women who died had been vaccinated against H1N1. The influenza vaccine currently in use protects against H1N1, which makes it desirable for the Colombian public health system to prescribe vaccination against influenza for all pregnant women in their second and third trimesters during the influenza season. At present, the vaccine is mandatory among children aged 6–60 months and for adults older than 65 years of age. For pregnant women, it is recommended optionally [12]. Enough evidence exists about the benefits, safety, and cost efficiency of this proposed measure—not only for mothers but also for newborns [13,14]. This measure can decrease the excess of morbidity and mortality due to influenza among pregnant women [15] and it should become part of the set of indispensable procedures performed at prenatal controls. Likewise, more effort should be made to adopt the H1N1 care protocol at the national level, and to monitor and follow-up compliance with this protocol.

It is important to recognize the shortcomings of the present investigation. It was a descriptive study and, therefore, it is not possible to draw inferences from it or to trace causal links with statistical criteria. Its findings may not be extrapolated to other populations. Owing to the fact that there was no information regarding the total number of pregnant women who actually contracted H1N1 infection within the same period, it is not possible to calculate the incidence or lethal nature of the infection.

The H1N1 influenza pandemic increased maternal mortality in Antioquia. Pregnant women, together with very young people, are the population subgroup at highest risk of suffering complications or dying from this infection. Underestimating H1N1 infection symptoms, and delays in administering medication and hospitalizing patients reflected a lack of familiarity with the corresponding healthcare guide on the part of healthcare providers. Together with the obstacles posed by insurance companies and the healthcare network in general, these were the chief determinant factors implicated in the maternal mortalities due to pneumonia in the province of Antioquia in 2009.

It is crucial to remain alert about H1N1 infection with regard to the population subgroup of pregnant women in Antioquia, guaranteeing them adequate monitoring and/or timely administration of medication and hospitalization.

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## Conflict of interest

The authors have no conflicts of interest.

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