

# Maternal Mortality Secondary to Acute Respiratory Failure in Colombia: A Population-Based Analysis

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## Abstract

**Purpose** To estimate the mortality rate and trends of respiratory failure in the pregnant and postpartum population of Colombia.

**Methods** A retrospective analysis of the national registry of mortality in Colombia was performed from 1998 to 2009. Maternal death was defined as death that occurred during pregnancy or up to 42 days postpartum. Two independent investigators reviewed maternal deaths to determine deaths caused by respiratory failure. Inter-rater agreement was assessed by kappa correlation coefficient. Causes of respiratory failure were identified according to the International Classification of Diseases (ICD-10).

**Results** During the study period, 8,637,486 live births were reported with 6,676 maternal deaths for an overall maternal mortality rate (MMR) of 82.9 per 100,000 live births. Of these, a total of 835 cases were related to respiratory failure, with a specific MMR of 9.69 per

100,000 live births. The main causes of maternal deaths due to respiratory failure included pulmonary sepsis (284 cases, or 3.58 per 100,000 live births), pulmonary embolism (119 cases or 1.50 per 100,000 live births), and preeclampsia-related pulmonary edema (112 cases or 1.41 per 100,000 live births). All-cause maternal mortality ratio decreased yearly from 1998 to 2009 by  $-3.76\%$  (95 % CI  $-4.83$  to  $-2.67$ ), while the trend of mortality secondary to respiratory failure remained stable over time ( $P = 0.449$ ). **Conclusions** Respiratory failure is an important cause of mortality in the obstetric population in Colombia, with pulmonary sepsis as the lead cause of respiratory failure among maternal deaths. While overall maternal mortality rates have decreased in the last decade, respiratory failure-related deaths have remained stable over time.

**Keywords** Respiratory insufficiency · Colombia · Maternal mortality · Pregnancy · Postpartum · Sepsis · Pulmonary embolism

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## Introduction

Acute respiratory failure (ARF) in pregnancy may be associated with high mortality, with some reports as high as 40 % [1, 2]. However, reports describing acute respiratory failure as a cause of maternal mortality are limited. The most recent report, performed in a single center over a decade ago in the US, suggests an incidence of respiratory failure in pregnancy of 15.9 per 100,000 live births [1]. There are no reports regarding the incidence or the main causes of respiratory failure in Latin America [3]. Causes of respiratory failure in pregnancy are similar to the non-pregnant population for the most part; however, some pregnancy specific disorders such as preeclampsia or

anaphylactoid syndrome of pregnancy may also lead to respiratory failure and death. In addition, certain infections or conditions that affect both the pregnant and non-pregnant populations may present different challenges in the pregnant population, leading to worse outcomes. The identification of the main causes of respiratory failure associated with maternal mortality may help target specific populations at risk, with a potential to identify public health interventions that can reduce maternal mortality.

Colombia is a middle-income country in South America with a historical maternal mortality of 70–105 maternal deaths per 100,000 live births. The objectives of this study were to (a) assess trends of maternal mortality rate secondary to respiratory failure in Colombia over the study period and (b) determine the main causes of this disorder.

## Methods

### Design and Setting

This is a retrospective, population-based study of pregnant and postpartum patients in Colombia. Data obtained from deaths certificates between January 1, 1998 and December 31, 2009 were gathered for our analyses. Reporting of this study is performed based on STROBE statement for cohort studies.

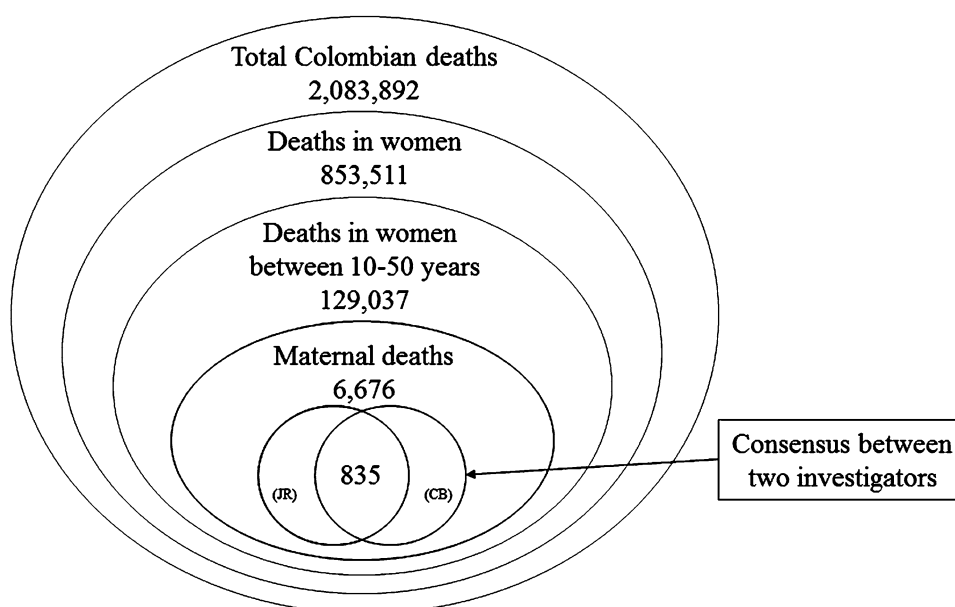
### Data Collection and Variable Definition

Maternal death reporting is mandatory in Colombia. Death certificates require recording of the main cause of

death as well as related causes using the International Classification of Diseases, tenth edition (ICD-10) [4]. Information regarding diagnoses and socioeconomic data (age, sex, insurance, education, and place of death) is maintained by the National Department of Statistics (DANE) [5].

In collaboration with the Department of Health in Colombia, the investigators accessed the national mortality database. A selection process was designed to examine and analyze maternal mortality from the national registry of deaths (see Fig. 1). According to this model, the first phase identifies deaths in men and women of all ages during the study period. The second and third phases identify deaths in women and then women of reproductive age (between 10 and 50 years). The fourth phase identifies maternal deaths according to the definition of the World Health Organization (WHO), i.e., death during pregnancy or during the first 6 weeks postpartum [6]. The fifth phase determines deaths related to acute respiratory failure. This phase is independently performed by two investigators (JAR and CB). Respiratory failure was identified as the cause of death if one of the following ICD-10 diagnoses were used: Acute respiratory failure (J960), adult respiratory distress syndrome (J80X), respiratory failure, unspecified (J969), lung disease complicating pregnancy, childbirth, and the puerperium (O995), and any related diagnoses according to ICD-10 nomenclature. Deaths deemed to be accidental, self-inflicted, or related to violence were excluded, as per the WHO criteria [6]. In cases of disagreements, the two investigators attempted to reach consensus. Cases were included only if a successful agreement was reached.

**Fig. 1** Phases of data collection from the national registry of deaths and analysis



Once the deaths secondary to respiratory failure were identified, we classified cases according to their etiology into eight main causes: pulmonary sepsis, pulmonary embolism, hypertensive disorders, indirect sepsis, obstetric sepsis, other respiratory causes, chronic pulmonary disease, hemorrhagic complications, amniotic fluid embolism, trophoblastic disease, and deaths not specified where the cause could not be ascertained.

### Data Analysis

Data were analyzed using Excel (Microsoft; Richmond, WA) and Stata 11 (StataCorp; College Station, TX, USA). Maternal mortality ratio was calculated using live births and expressed as deaths per 100,000 live births. Categorical variables were described as percentages and continuous data were expressed in median and interquartile range (IQR). To assess for trends of maternal mortality, a Poisson regression model was used for all-cause deaths and acute respiratory failure-related deaths. The Equation 100 ( $\exp\beta - 1$ ) was estimated and 95 % confidence intervals (95 % CI) were calculated for the model. A *P* value <0.05 was considered statistically significant.

### Results

There were 2,083,892 deaths in Colombia during the study period; 853,511 were female and 129,037 between the ages of 10 and 50 years. Of these, 6,676 occurred in pregnancy

or during the first 6 weeks postpartum. Respiratory failure was the cause of death in 835 women (11.9 %). Respiratory-related maternal mortality rate (MMR) was 6.69 deaths per 100,000 live births (Table 1).

Median age was 26 years (IQR 21–33). A total of 627 (75.0 %) women had data on educational level, with 56 % of women having only an elementary education.

### Causes of Respiratory Failure-Related Deaths

The main cause of acute respiratory failure-related deaths was pulmonary sepsis, occurring in 284 maternal deaths (34 %) (Table 2). Pulmonary embolism and hypertensive emergencies were other important causes of respiratory failure-related deaths and occurred in 119 (14.3 %) and 112 (13.4 %) of all maternal deaths, respectively. Other causes for respiratory failure leading to maternal mortality included chronic pulmonary diseases, analphylactoid syndrome of pregnancy, trophoblastic disease, and others. Kappa coefficient measurement of inter-observer agreement for the underlying causes of respiratory failure was 0.91 (95 % CI 0.88–0.92).

### Trends of Maternal Deaths

All-cause maternal mortality ratio decreased yearly from 1998 to 2009 by −3.76 % (95 % CI −4.83 to −2.67) (Fig. 2), while the trend of respiratory failure-related deaths remained stable over time (*P* = 0.449) (Table 2). Even after excluding 2009, an unusual year for respiratory

**Table 1** All-cause and respiratory-related maternal deaths in Colombia from 1998 to 2009

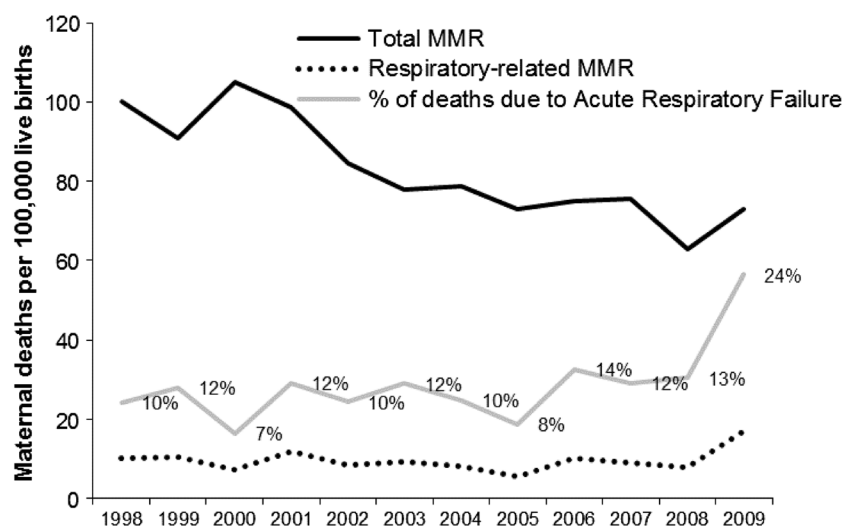
Year	All-cause maternal deaths	Respiratory failure-related deaths	Live births	All-cause MMR (per 100,000 live births)	Respiratory failure-related MMR (per 100,000 live births)	Percentage of deaths due to respiratory failure (%)
1998	722	73	720,984	100.1	10.1	10.1
1999	677	79	746,194	90.7	10.6	11.7
2000	790	54	752,834	104.9	7.2	6.8
2001	714	87	724,319	98.6	12.0	12.2
2002	591	60	700,455	84.4	8.6	10.2
2003	553	67	710,702	77.8	9.4	12.1
2004	569	59	723,099	78.7	8.2	10.4
2005	526	41	719,968	73.1	5.7	7.8
2006	536	73	714,450	75.0	10.2	13.6
2007	536	65	709,253	75.6	9.2	12.1
2008	449	57	715,453	62.8	8.0	12.7
2009	510	120	699,775	72.9	17.1	23.5
Overall results	7173	835	8,637,486	82.9	9.69	11.93

MMR maternal mortality ratio

**Table 2** Related causes within 835 deaths due to acute respiratory failure (ARF) in Colombian women

Associated diagnosis	1998–2000 <i>n</i> (%) <sup>a</sup>	2001–2003 <i>n</i> (%) <sup>a</sup>	2004–2006 <i>n</i> (%) <sup>a</sup>	2007–2009 <i>n</i> (%) <sup>a</sup>	Total <i>n</i> (%)
Pulmonary sepsis	68 (33)	69 (32.2)	62 (35.8)	85 (35.1)	284 (34)
Pulmonary embolism	36 (17.5)	28 (13.1)	33 (19.1)	22 (9.1)	119 (14.3)
Hypertensive disorders	21 (10.2)	32 (15)	28 (16.2)	31 (12.8)	112 (13.4)
Indirect sepsis	13 (6.3)	26 (12.1)	14 (8.1)	22 (9.1)	75 (9)
Obstetric sepsis	15 (7.3)	12 (5.6)	6 (3.5)	24 (9.9)	57 (6.8)
Other respiratory causes	11 (5.3)	7 (3.3)	9 (5.2)	23 (9.5)	50 (6)
Chronic pulmonary disease	10 (4.9)	7 (3.3)	7 (4)	8 (3.3)	32 (3.8)
Hemorrhagic complications	3 (1.5)	8 (3.7)	4 (2.3)	15 (6.2)	30 (3.6)
Anaphylactoid syndrome of pregnancy	8 (3.9)	6 (2.8)	7 (4)	2 (0.8)	23 (2.8)
Trophoblastic disease	4 (1.9)	4 (1.9)	1 (0.6)	3 (1.2)	12 (1.4)
Not specified	17 (8.3)	15 (7)	2 (1.2)	7 (2.9)	41 (4.9)
Total	206 (100)	214 (100)	173 (100)	242 (100)	835 (100)

<sup>a</sup> Percentage of deaths within the selected 3 years

**Fig. 2** Estimated all-cause and respiratory failure-related maternal mortality in Colombia (1998–2009)**Table 3** Negative binomial regression detailing the mortality trend of maternal deaths due to all-cause and respiratory-related mortality in Colombia

Percentage of yearly change	100 ( $\exp\beta - 1$ )	(95 % CI)	<i>P</i> value
From 1998 to 2009			
All-cause deaths	−3.76 %	−4.83 to −2.67 %	<0.001
Respiratory failure-related deaths	1.59 %	−2.48 to 5.84 %	0.449
From 1998 to 2008 <sup>a</sup>			
All-cause deaths	−4.22 %	−5.38 to −3.05 %	<0.001
Respiratory failure-related deaths	−2.02 %	−5.20 to 1.27 %	0.227

<sup>a</sup> Excluding 2009, year of the pandemic influenza virus H1N1

failure-related maternal deaths due to the H1N1 pandemic, the trend of respiratory failure-related deaths remained stable ( $P = 0.227$ ), and all-cause maternal deaths decreased yearly by  $-2.02\%$  (95 % CI  $-5.20$  to  $1.27$ ) (Table 3).

## Discussion

This is the first study describing maternal deaths due to acute respiratory failure in Latin America. Data from our study suggest that overall maternal mortality in Colombia is following a downward trend. However, respiratory failure-related deaths have not significantly changed during the study period. These results remained unchanged even after the year 2009 where 10 % of all confirmed deaths due

to H1N1 pandemic virus in the country occurred in pregnant and postpartum women was excluded. This finding will increase awareness among healthcare decision makers about the importance of respiratory failure in causing maternal deaths and provide a framework in which targeted interventions can lead to a greater reduction of MMR. For example, pulmonary sepsis was the leading cause of respiratory failure during pregnancy in our study. During the recent H1N1 epidemic, pregnant women contributed to 6.3 % of all hospitalizations, 5.9 % of ICU hospitalizations, and 5.7 % of total deaths, while making up only about 1 % of the total population [7]. These data suggest that pregnancy predisposes to severe complications of influenza infection and possibly other pulmonary infections [7–9]. Numerous studies show that the implementation of immunization reduces clinical disease by 54–89 % [10, 11], reduces biochemically confirmed disease by 70–90 % [12], and decreases the severity of respiratory symptoms [13]. The influenza vaccine has been proven safe for both mother and fetus [14, 15] without evidence of an increased risk of malformations or fetal death [14, 16] and provides protection against influenza for up to 6 months in the infant [17]. Hence, strategies and specific recommendations regarding seasonal influenza vaccination for all pregnant patients and the use of antivirals for patients with acute respiratory infection have been put forth by the Centers for Disease Control and Prevention (CDC), including offering—not just encouraging—vaccine administration during prenatal care [18]. In Colombia and many Latin American countries, this immunization is not universally implemented during pregnancy. In a prior study, we reported that none of the pregnant women who died from H1N1 during the 2009 epidemic had received the influenza vaccine [19], further highlighting the lack of universal implementation. New protocols should be developed to help with the implementation of vaccination in all pregnant women, regardless of trimester, as recommended by The Advisory Committee on Immunization Practices (ACIP) and the American College of Obstetricians and Gynecologists (ACOG) [18, 20].

Pulmonary embolism is the second leading cause of death from respiratory failure, with a rate that is more than three times higher than that of recent data from the United Kingdom [21]. Compared to non-pregnant controls, pregnant women have a seven- to ten-fold increase in the risk of venous thromboembolism [22]. Risk assessment of venous thromboembolism (VTE) also is not a part of routine prenatal care in Colombia. As such, thromboprophylaxis may be underutilized in our population. Thromboprophylaxis has been associated with a 70 % reduction in the number of thromboembolic events in adult patients undergoing major surgery [23]. The incidence of VTE as a cause of death has been reduced by half in the UK following national

implementation of thromboprophylactic strategies [24] between 2003 and 2005 [25], and 2006–2008 mortality reports. Many recent reviews and guidelines for the diagnostic management of pulmonary embolism and the use of thromboprophylaxis have been published to guide providers with risk assessment, diagnosis, and the implementation of thromboprophylaxis [23, 26–29]. Operative delivery increases the likelihood of death compared to vaginal delivery [30] and it is estimated that a large number of these deaths are related to thromboembolic events [31]. In addition to Cesarean deliveries being a potential culprit, population-based differences in the risk for VTE, such as prevalence of thrombophilia, cannot be excluded.

Hypertensive disorders resulting in pulmonary edema were found to be the third leading cause of respiratory failure and death in pregnancy. Pulmonary edema is one of the leading causes of mortality and intensive care unit (ICU) admission in hypertensive disorders [32]. Pulmonary edema is estimated to occur in up to 2.9 % of patients with preeclampsia, with up to 70 % taking place after delivery [33]. Pulmonary edema may be largely due to greater volume expansion used to treat the relative hypovolemia in these patients. Volume expansion in preeclampsia does not improve maternal or fetal outcomes [34] but increases the risk of pulmonary edema [35]. In fact, positive fluid balance greater than 5,500 cc are most associated with the development of pulmonary edema in patients with preeclampsia [35]. Hence, limiting volume expansion in this population will likely help reduce the occurrence of pulmonary edema and mortality from this disorder.

Strengths of this population-based study is that it included all maternal deaths from the official national database and the fact that categorization of cause of death was established by two independent investigators with an excellent inter-observer agreement. Limitations of this study are inherent to the type of data available (registry-based) and the lack of direct access to the primary records or autopsy registry.

In Colombia, though autopsy is not mandated, it is encouraged for clinical purposes in some cases for public health surveillance, and deaths in young, otherwise healthy women would qualify under these criteria. However, this information is not collected as part of the national mortality database and was not available for our review.

In conclusion, respiratory failure is a major cause of maternal mortality in Colombia, with the most common causes of respiratory failure being amenable to preventive strategies. Thus we suggest that universal influenza vaccination, adequate risk stratification for VTE in pregnant women, and judicious fluid resuscitation patients with preeclampsia are possible actions that may reduce maternal mortality due to respiratory failure. More studies are needed to validate these recommendations.



**Conflict of interest** All authors report that no potential conflicts of interest exist.

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