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ORIGINAL ARTICLE

Epidemiology of fetal death in Latin America

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Background. To identify risk factors associated with fetal death, and to measure the rate and the risk of fetal death in a large cohort of Latin American women.
Methods. We analyzed 837,232 singleton births recorded in the Perinatal Information System Database of the Latin American Center for Perinatology and Human Development (CLAP) between 1985 and 1997. The risk factors analyzed included fetal factors and maternal sociodemographic, obstetric, and clinical characteristics. Adjusted relative risks were obtained, after adjustment for potential confounding factors, through multiple logistic regression models based on the method of generalized estimating equations.
Results. There were 14,713 fetal deaths (rate=17.6 per 1000 births). The fetal death risk increased exponentially as pregnancy advanced. Thirty-seven percent of all fetal deaths occurred at term, and 64% were antepartum. The main risk factors associated with fetal death were lack of antenatal care (adjusted relative risk [aRR]=4.26; 95% confidence interval, 3.84–4.71) and small for gestational age (aRR=3.26; 95% CI, 3.13–3.40). In addition, the risk of death during the intrapartum period was almost tenfold higher for fetuses in noncephalic presentations. Other risk factors associated with stillbirth were: third trimester bleeding, eclampsia, chronic hypertension, preeclampsia, syphilis, gestational diabetes mellitus, Rh isoimmunization, interpregnancy interval<6 months, parity ≥4, maternal age ≥35 years, illiteracy, premature rupture of membranes, body mass index ≥29.0, maternal anemia, previous abortion, and previous adverse perinatal outcomes.
Conclusions. There are several preventable factors that should be dealt with in order to reduce the gap in fetal mortality between Latin America and developed countries.

Key words: epidemiology; fetal death; fetal death risk; risk factors

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It is estimated that worldwide there are annually more than 7.6 million perinatal deaths, of which 57% are fetal deaths (1). Ninety-eight percent of the perinatal deaths take place in the developing world. In these countries, the infant mortality has declined markedly during the period 1983–1995, although most of this improvement has occurred among older infants. However, the fetal mortality rate has fallen only slightly during that period (1, 2). In contrast, a significant decline in the fetal death rate in developed countries, mainly intrapartum deaths, has been reported by several authors (3–5). Despite the evident importance of fetal deaths as both a clinical and public health problem, relatively little attention has been focused on their epidemiology, specially in the developing world.

The Latin American and Caribbean Perinatal Information System database, which includes data on maternal sociodemographic characteristics and pregnancy outcomes, provides an excellent opportunity to study the epidemiology of fetal death in this region. We believe it important to know the relationship between several sociodemographic,

Abbreviations:
SIP: Perinatal Information System; CLAP: Latin American Center for Perinatology and Human Development; BMI: body mass index; RR: relative risk; aRR: adjusted relative risk; CI: confidence interval; GEE: generalized estimating equations.

medical, obstetric, and fetal risk factors and fetal death to determine possible preventive actions for reducing the rate of fetal death in our countries.

The objective of the present study was to identify maternal sociodemographic and clinical characteristics as well as fetal factors associated with fetal death, and to measure the rate and the risk of fetal death in a large cohort of Latin American women.

Materials and methods

This research is based on the Perinatal Information System (SIP) database, developed and managed by the Latin American Center for Perinatology and Human Development (CLAP) (Montevideo, Uruguay) since 1983. The SIP consists of a basic perinatal clinical record, complementary forms and charts, a perinatal card, and a software package for personal computers (6). In 1985, the SIP was adopted by many Latin American and Caribbean institutions. Since then, the SIP has prospectively recorded antenatal and perinatal care of women from the following countries: Uruguay (25.3%), Argentina (24.1%), Peru (9.4%), Colombia (8.6%), Honduras (8.2%), Paraguay (6.9%), El Salvador (4.2%), Chile (2.8%), Bolivia (2.3%), Costa Rica (2.2%), Panama (1.4%), Dominican Republic (1.3%), Nicaragua (1.2%), Brazil (0.8%), Ecuador (0.6%), Mexico (0.4%), Bahamas (0.2%), and Venezuela (0.1%). Currently, over 700 hospitals are using SIP.

Descriptions of the database have been reported elsewhere (7, 8). From the first antenatal visit until discharge of both mother and neonate, the attendant physicians or nurses collect data in the perinatal clinical record in check-box format which includes demographic information, reproductive history, maternal characteristics, antenatal care, labor management, maternal complications during pregnancy, delivery, and the puerperium, and neonatal outcomes. After hospital discharge of both mother and infant, data are entered in on site computer and quality control of them is done. Periodically, the institutions send their data banks to CLAP where a further data entry, quality control check, and validation is performed.

Between 1985 and 1997, a total of 1,008,954 births were recorded in the SIP database from 308 hospitals (tertiary: 74%; regional: 19%; community: 7%). The great majority of these hospitals were public in which either the medical care was given free or a direct payment was required. We restricted our analyses to women from Latin American countries (n=995,297) and excluded births in which the gestational age was less than 20 completed weeks (n=31,241) or was missing (n=49,585), multiple births (n=15,241), infants with congenital malformations (n=9,562), and pregnancies with missing information on adverse pregnancy outcomes (n=52,436). Thus, the final study population included 837,232 singleton births.

Dependent variable

Fetal death was defined as the birth of a fetus at 20 weeks' gestation or later which shows no sign of life after birth. Gestational age was calculated from the date of last menstrual period, possibly amended by means of early ultrasonography. In addition, gestational age estimated from physical and neurologic assessments of the newborn was also recorded. The time of fetal death was attributed to the week of birth of the stillborn infant. Primary cause of fetal death was not available in SIP database.

Independent variables

Maternal age was defined as completed years at time of delivery. It was stratified into three groups: less than 20 years, 20–34 years, and 35 or more years. Marital status was dichotomized between those who did and did not live with the infant's father. Mother's education was defined as number of completed years and was categorized into 0 (none), 1–11, and 12 or more years. Maternal height and prepregnancy weight were recorded at the woman's first antenatal visit in centimeters and kilograms, respectively. The body mass index (BMI), defined as pre-pregnancy weight in kilograms divided by height in meters squared, was categorized according to the National Academy of Sciences Institute of Medicine (9) as follows: underweight (BMI$<$19.8), normal weight (BMI=19.8$-$26.0), overweight (BMI=26.1$-$29.0), and obese (BMI$>$29.0). Information on cigarette smoking was also recorded at the first antenatal visit, and categorized into nonsmokers and smokers. Parity was defined as the number of previous births, including stillbirths. Interpregnancy interval was defined as the time elapsed between the woman's last delivery and the date of the last menstrual period for the index pregnancy. Intervals were computed in weeks and then converted to months. Interpregnancy intervals were categorized in months as follows: 5 or less, 6 to 23, and 24 or more.

Diseases during pregnancy or delivery were classified according to the English version of the International Classification of Diseases, tenth revision (ICD-10) (10). Chronic hypertension, preeclampsia, and eclampsia were coded as ICD-10 codes O10, O14 and O15, respectively. Third tri-

mester bleeding included placenta previa with hemorrhage (ICD-10 code O44.1) and abruptio placentae (ICD-10 code O45). Anemia, premature rupture of membranes, gestational diabetes mellitus, syphilis, Rh isoimmunization, and urinary tract infection were coded as ICD-10 codes O99.0, O42, O24.4, O98.1, O36.0, and O23, respectively. Small for gestational age was defined as a birth weight below the 10th percentile for the gestational age and gender, using Williams et al. (11) standards.

Statistical analysis

Plots of fetal death rate and fetal death risk were constructed using techniques previously described (12). Fetal death rates for the entire population were calculated by dividing the number of fetal deaths by the total births for each gestational age between 20 and 44 weeks. In addition, we determined the fetal death risk by means of methodological approach proposed by Yudkin et al. (13), in which the number of fetal deaths during each week of gestation is divided by the total number of fetuses unborn at the beginning of the gestational age considered. The denominator of this fraction represents the number of fetuses actually at risk of death during that gestational age.

Estimates of crude relative risk (RR) with 95% confidence interval (CI) were computed as measures of association between fetal death and independent variables considered. Adjusted odds ratios were derived through logistic regression models as estimates of adjusted relative risks (aRR). Those variables that were debated in the literature as important risks factors for fetal death or that produced a point estimate at a p-value <0.10 on the univariate analysis were entered into a multiple logistic regression model. Variables that were selected by regression procedures were included in the final model. In addition, geographic area (Andean region, Central America, and Southern cone), hospital type (tertiary, secondary, and primary hospitals), and year of delivery (1985 to 1989, 1990 to 1994, 1995 to 1997) were included for adjustments in all the analyses. Dummy variables for missing information were constructed for each of those variables with information missing on more on 10%.

In order to study the interactions and relative importance of the various risk factors for fetal death in Latin America, we also performed a Poisson regression modeling. The dependent variable in the Poisson model was fetal death. Data were stratified according to country (18 strata) and year (13 strata), which resulted in 234 strata. The independent variables included in the analysis were the same variables entered into the multiple logistic regression model.

Statistical analyses in the present study are based on data that span 13 years (1985 to 1997), thus allowing for the possibility of including several pregnancies for a woman. Because women who suffer fetal death are at increased risk for repeating this disorder in subsequent pregnancies, an analysis of more than one pregnancy to the same women violates the assumption of the usual methods of estimation and testing for multiple logistic regression model. To address this problem, we performed all statistical analysis using the generalized estimating equations (GEE) model (14) to incorporate the dependence among the variables from the same woman and to provide robust variance estimates of the regression coefficients.

Since information on both cigarette smoking during pregnancy, routinely recorded since 1990, and pre-pregnancy BMI was missing for 50% and 36% of the women, respectively, several models were performed to assess the effects of adjustment for these variables for each independent variable. In the several multivariate analyses performed, we found no evidence of confounding of the effect of independent variables on fetal death by cigarette smoking and pre-pregnancy BMI. The patterns were similar, although the widths of the confidence intervals varied slightly. In addition, the rates of fetal death were 17.4 per 1000 births among women for whom information about cigarette smoking was available and 17.8 per 1000 births among those for whom it was missing. The corresponding rates of fetal death for women with missing data about pre-pregnancy BMI and women with complete data about that variable were 18.4 and 17.1 per 1000 births, respectively.

Population attributable risk percent was defined as the proportion of fetal deaths in the study population that is attributable to a specific risk factor and thus could be prevented if that risk factor was eliminated. We estimated 95% confidence intervals for population attributable risks according to Daly's method (15).

All analyses were done using the SPSS 8.0 programme package (SPSS Inc., Chicago, IL).

Results

Among the 837,232 singleton births, 14,713 were recorded as fetal deaths (rate=17.6 per 1,000 total births). The highest rates (per 1,000 total births) were recorded in hospitals from Paraguay (52.1) and Bolivia (44.3) while the lowest values came from Chile (9.0), Uruguay (11.9), and Costa Rica (12.6). The fetal death rates for three time periods considered, 1985–1989, 1990–1994, and 1995–1997

were 19.9, 18.3, and 13.8 per 1,000 births, respectively. Sixty-four percent of the fetal deaths were antepartum, 12% were intrapartum, and the time of death could not be determined for the remaining 24%. Sixty-three percent of fetal deaths occurred before term (24% before 28 weeks' gestational age) and 37% occurred at term.

Fetal death rates throughout pregnancy for all births are presented in Fig. 1. Before 24 weeks, the majority of births were fetal deaths, and even as late as 28 weeks, 24% of all births were stillbirths. Thereafter, the rates gradually dropped reaching a minimum of 4.9 per 1,000 at 39 weeks, and rose to 7.7 per 1,000 at 41 weeks and after. Fig. 2 shows that fetal death risk was relatively low from 20 to 35 weeks' gestation, and increased exponentially as pregnancy advanced to a peak at 44 weeks. At this time, the risk was almost 12 times higher that at 39 weeks (RR, 11.72; 95% CI, 8.93 to 15.29). The risk of fetal death at 42 weeks was 50% higher than at 41 weeks (RR, 1.52; 95% CI, 1.31 to 1.77).

Table I provides information on the association between maternal sociodemographic characteristics and risk of fetal death. Absence of antenatal care was strongly associated with increased risk of fetal death. In effect, women with no antenatal visits had a fourfold higher risk for fetal death than those with 5 or more visits. Compared with women aged 20–34 years, women aged ≥35 years faced a 53% increased risk of fetal death while illiteracy was associated with a 36% increased risk when compared with high education (≥12 years). Obese women also had a slightly, but significant, increased risk for stillbirth. Marital status, gestational age at first antenatal visit, and cigarette smoking were not associated with the risk of fetal death in our study population.

Of all obstetric and fetal factors studied (Table II), third trimester bleeding was associated with the highest risk of stillbirth. Women with placenta previa or abruptio placentae had nearly a sixfold increase in the risk of fetal death. Small for ges-

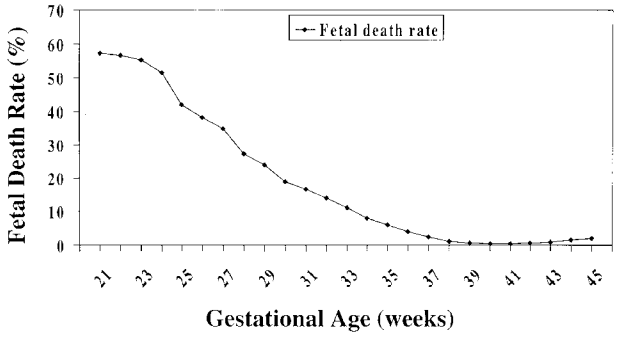

Fig. 1. Fetal death rates by gestational age in a cohort of 837,232 Latin American women delivering singleton infants, 1985–1997.

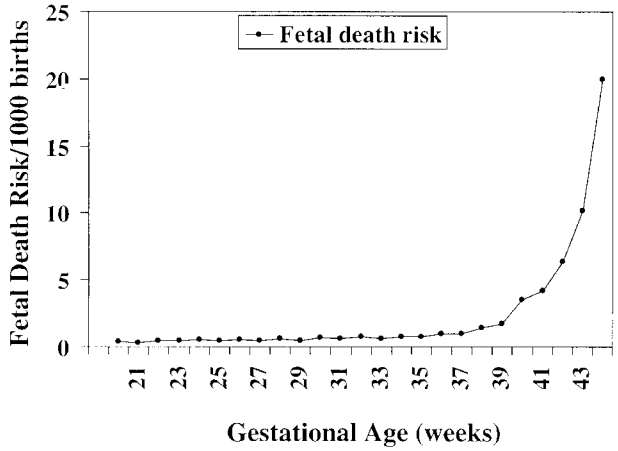

Fig. 2. Fetal death risks by gestational age in a cohort of 837,232 Latin American women delivering singleton infants, 1985–1997.

Table I. Maternal sociodemographic risk factors for fetal death

Characteristic	No. of births (n=837,232)	Fetal death: No. of cases (n=14,713)	Rate/ 1,000	Adjusted RR	(95% CI)
Maternal age (yr)					
10–19	170,780	2,638	15.4	1.02	(0.97–1.08)
20–34	579,389	9,400	16.2	1.00	Reference
≥35	87,063	2,675	30.7	1.53	(1.42–1.55)
Living with infant's father					
Yes	655,456	11,064	16.9	1.00	Reference
No	166,706	3,375	20.2	1.12	(1.00–1.25)
Missing	15,070	274	18.2		
Maternal education (yr)					
0	35,475	1,056	29.8	1.36	(1.18–1.55)
1–11	728,080	12,617	17.3	1.04	(0.91–1.17)
≥12	42,699	514	12.0	1.00	Reference
Missing	30,978	526	17.0		
Gestational age at first antenatal visit (wk)					
1–13	241,369	4,174	17.3	1.00	Reference
14–26	364,052	6,321	17.4	1.00	(0.95–1.05)
≥27	231,811	4,218	18.2	1.02	(0.95–1.09)
Number of antenal visit					
0	164,346	6,475	38.2	4.26	(3.84–4.71)
1–4	270,131	4,942	18.3	1.23	(0.95–1.52)
≥5	402,755	3,296	8.2	1.00	Reference
Prepregnancy body mass index (kg/m^2)					
<19.8	82,551	1,296	15.7	0.98	(0.88–1.08)
19.8–26.0	344,270	5,783	16.8	1.00	Reference
26.1–29.0	59,276	1,001	16.9	1.00	(0.90–1.11)
>29.0	49,745	1,087	21.9	1.19	(1.07–1.31)
Missing	301,390	5,546	18.4		
Cigarette smoking					
No	375,339	6,438	17.2	1.00	Reference
Yes	44,959	854	19.0	1.04	(0.90–1.18)
Missing	416,934	7,421	17.8		

RR=relative risk, CI=confidence interval.

Table II. Obstetric and fetal risk factors for fetal death

Risk factor	No. of births (n=837,232)	Fetal death: No. of cases (n=14,713)	Rate/ 1,000	Adjusted RR	(95% CI)
Parity					
0	307,162	5,099	16.6	1.00	Reference
1–3	417,496	6,345	15.2	0.97	(0.90–1.04)
≥4	112,574	3,269	29.0	1.52	(1.39–1.67)
Previous fetal death					
No	808,764	13,547	16.8	1.00	Reference
Yes	22,607	1,060	46.9	2.53	(2.27–2.80)
Missing	5,861	106	18.1		
Previous early neonatal death					
No	817,570	14,142	17.3	1.00	Reference
Yes	19,662	571	29.0	1.48	(1.30–1.68)
Previous low birthweight					
No	796,950	13,667	17.1	1.00	Reference
Yes	40,282	1,046	26.0	1.32	(1.18–1.47)
Previous abortion					
No	673,383	10,864	16.1	1.00	Reference
Yes	156,614	3,716	23.7	1.18	(1.08–1.28)
Missing	7,235	133	18.4		
Interpregnancy interval* (months)					
<6	11,960	580	48.5	2.09	(1.75–2.46)
6–23	199,680	3,560	17.8	1.00	(0.93–1.07)
≥24	265,961	4,700	17.7	1.00	Reference
Missing	52,469	774	14.8		
Third trimester bleeding					
No	828,646	13,565	16.4	1.00	Reference
Yes	8,586	1,148	133.7	5.82	(5.17–6.54)
Premature rupture of membranes					
No	773,927	13,027	16.8	1.00	Reference
Yes	63,305	1,686	26.6	1.49	(1.38–1.50)
Small for gestational age					
No	681,416	9,267	13.6	1.00	Reference
Yes	93,688	4,421	47.2	3.26	(3.13–3.40)
Missing	62,128	1,025	16.5		
Fetal sex					
Female	406,804	7,078	17.4	1.00	Reference
Male	430,428	7,635	17.7	1.00	(0.97–1.03)

*Only for parous women, RR=relative risk, CI=confidence interval.

tational age fetuses had a 3.3-fold higher risk for fetal death. Women with interpregnancy intervals shorter than 6 months were twice as likely to have a fetal death as compared with women with intervals of 24 or more months whereas women para 4 or more had a significantly higher risk of stillbirth than nulliparous ones. Previous fetal and early neonatal deaths, low birth weight infants, and abortion were factors independently associated with an increased risk of fetal death. Fetal mortality was 49% greater when premature rupture of membranes occurred. The risk of fetal death was unrelated to fetal sex. The risk of death during intrapartum period was almost tenfold higher for fetuses with either breech or shoulder presentations when compared with fetuses with cephalic presentation (aRR, 9.82; 95% CI, 8.91 to 10.83). When this analysis was performed according to gestational age (<28 weeks, 28 to 36, and ≥37 weeks), the results were similar. The prevalence of noncephalic fetal presentations was 4.8%.

Table III shows the relationship between maternal medical conditions and fetal death. Eclampsia was found to have the highest risk of stillbirth (aRR, 3.8). In addition, Rh isoimmunization, syphilis, chronic hypertension, gestational diabetes mellitus, preeclampsia, and maternal anemia were associated with a significant risk of fetal death. In contrast, urinary tract infection was not associated with stillbirth.

The Poisson and multiple logistic regression models yielded nearly identical relative risks estimates and confidence intervals in all situations.

Population attributable risks of significant risk factors for fetal death in the present study are shown in Table IV. No antenatal care, restriction in fetal growth, parity ≥4, and maternal age ≥35 years were the risk factors with the highest population attributable risks. Conversely, risk factors

Table III. Medical risk factors for fetal death

Characteristic	No. of births (n=837,232)	Fetal death: No. of cases (n=14,713)	Rate/ 1,000	Adjusted RR	(95% CI)
Chronic hypertension					
No	825,141	14,172	17.2	1.00	Reference
Yes	12,091	541	44.7	2.25	(1.97–2.55)
Gestational diabetes mellitus					
No	826,445	14,360	17.4	1.00	Reference
Yes	10,787	353	32.7	1.88	(1.53–2.14)
Preeclampsia					
No	795,622	13,590	17.1	1.00	Reference
Yes	41,610	1,123	27.0	1.62	(1.49–1.76)
Eclampsia					
No	835,171	14,579	17.5	1.00	Reference
Yes	2,061	134	65.0	3.80	(3.21–4.49)
Maternal anemia					
No	801,932	13,941	17.4	1.00	Reference
Yes	35,300	772	21.9	1.18	(1.06–1.31)
Syphilis					
No	656,385	10,882	16.6	1.00	Reference
Yes	11,491	464	40.4	2.41	(2.10–2.79)
Missing	169,356	3,367	19.9		
Rh Isoimmunization					
No	770,588	13,372	17.4	1.00	Reference
Yes	2,190	91	41.6	2.56	(2.04–3.21)
Missing	64,454	1,250	19.4		
Urinary tract infection					
No	802,928	14,109	17.6	1.00	Reference
Yes	34,304	604	17.6	1.00	(0.91–1.10)

RR=relative risk, CI=confidence interval.

Table IV. Population attributable risks of significant risk factors for fetal death

Risk factor	(%) Study population with risk factor	Adjusted relative risk	Population attributable risk (%)	(95% CI)
No antenatal care	19.6	4.26	30.3	(29.4–31.3)
Small for gestational age	12.1	3.26	23.0	(22.1–23.9)
Parity ≥4	13.4	1.52	10.1	(9.4–10.9)
Maternal age ≥35 years	10.4	1.53	8.7	(8.0–9.4)
Previous abortion	18.9	1.18	8.2	(7.3–9.1)
Third trimester bleeding	1.0	5.82	6.7	(6.3–7.1)
Previous fetal death	2.7	2.53	4.7	(4.2–5.1)
Interpregnancy interval <6 months	2.5	2.09	4.2	(3.7–4.7)
Premature rupture of membranes	7.6	1.49	4.2	(3.7–4.8)
Illiteracy	4.4	1.36	3.2	(2.7–3.7)
Body mass index ≥29.0 kg/m^2	9.3	1.19	2.8	(2.1–3.6)
Preeclampsia	5.0	1.62	2.8	(2.4–3.3)
Previous low birthweight	4.8	1.32	2.4	(2.0–2.8)
Syphilis	1.7	2.41	2.4	(2.0–2.8)
Chronic hypertension	1.4	2.25	2.2	(1.9–2.5)
Previous early neonatal death	2.3	1.48	1.6	(1.3–1.9)
Gestational diabetes mellitus	1.3	1.88	1.1	(0.9–1.4)
Maternal anemia	4.2	1.18	1.1	(0.7–1.5)
Eclampsia	0.2	3.80	0.7	(0.5–0.8)
Rh Isoimmunization	0.3	2.56	0.4	(0.3–0.5)

strongly associated to fetal death such as eclampsia, Rh isoimmunization, syphilis, chronic hypertension, and gestational diabetes mellitus had the lowest population attributable risks. When analyzing only intrapartum fetal deaths, the population attributable risk of noncephalic fetal presentations was 28%. The population attributable risks did not substantially change over time.

Discussion

Our study confirmed previous findings that several maternal sociodemographic characteristics and medical and obstetric conditions are risk factors for fetal death. In this population, the fetal death rate of 17.6 per 1000 births is similar to stillbirth rates reported in previous studies from Latin America (1, 16). During the period 1982–1986, Gadow et al. (16) collected information on 869,750 births in 102 hospitals belonging to 11 Latin American countries. In this study, the overall fetal death rate was 20.5 per 1,000 total births, the highest being in Bolivia (44.3) and Paraguay (34.5) and the lowest in Chilean hospitals (9.0). When compared with women in developed countries (5, 17), Latin American women have a three times higher stillbirth rate.

The large sample size that confers sufficient power to evaluate the relationship between the several risk factors considered and fetal death, the possibility to control for many confounding factors, and the relatively homogeneous population of women studied support the findings of our study. Moreover, the prospective data collection on exposures during pregnancy ensures that recall bias could not have influenced the results.

In the present study, fetal death risk was calculated for each week of gestation using as the denominator all fetuses *in utero* at the start of that period. By this method, the risk of stillbirth was found to increase exponentially with advancing gestational age, consistent with earlier reports from developed countries (12, 13, 18). However, the risks of preterm and term fetal death in our population are approximately two and three times higher, respectively, than the risks reported in those countries.

The present analysis shows the influence of several preventable risk factors on fetal death in Latin America. Lack of antenatal care, in particular, was strongly associated with a marked increase in stillbirth, in agreement with some prior studies (19, 20). Consistent with previous reports (21, 22), we have found that small for gestational age fetuses are at increased risk of fetal death regardless of the underlying determinants. This finding is, however, limited by the methodological difficulties in studying antepartum stillbirths as death could have occurred several weeks before birth with the subsequent overestimation of gestational age at death. In addition, loss in fetal weight from death *in utero* to birth may cause underestimation of fetal weight at death. Thereby, antepartum stillbirths, that constituted 64% of total fetal deaths, may falsely appear as small for gestational age.

In accordance with previous investigations (5,

16, 18, 23), we found that advanced maternal age, and prior abortion and adverse perinatal outcomes were associated with fetal death. Our finding that obese mothers are at increased risk of fetal death is consistent with a recent study by Cnattingius et al. (24), who reported an increased incidence of fetal death among obese women, compared with lean mothers. With regard to parity, some previous studies (16, 25) have found an increased incidence of stillbirths among multiparous women, while others have found no increase (5, 18, 26). Our study indicates that Latin American women with parity ≥ 4 have a higher risk for stillbirth than nulliparous ones.

Our findings that mothers with third trimester bleeding, premature rupture of membranes, and medical conditions such as hypertensive diseases of pregnancy, gestational diabetes mellitus, maternal anemia, syphilis, and Rh isoimmunization are at increased risk of fetal death, are consistent with previous reports from both developed and developing countries (26, 27). Nonetheless, the prevalence of these conditions are low in our study population and consequently were associated with a low proportion of all stillbirths.

Several studies have demonstrated the adverse effect of smoking during pregnancy on the risk of fetal death (5, 18, 26). This finding was not confirmed in the present study. However, earlier reports (18, 28, 29) have shown that the association between smoking and fetal death is eliminated when intrauterine growth restriction and placental complications are taken into account in the multivariate analyses. In the present study, we examined both of these conditions simultaneously. Another possibility is that smoking is not actually a risk factor for fetal death in our population in accordance with prior reports (23, 30). It is also possible that the lack of association between cigarette smoking and fetal death in our study is spurious due to the large number of missing values on smoking.

Several constraints and potential biases of this study must be considered. Firstly, underreporting and misclassification of births and deaths are common in sources of perinatal data. A review of studies on underreporting indicates that, while both live births and neonatal deaths may be underreported, fetal deaths are much more likely to go unreported (31, 32). Nonetheless, since perinatal mortality rates are usually higher in hospitals than in the community because hospitals handle a high percentage of complications or referrals, the net result of these biases is unknown but is unlikely to be large enough to alter the estimates of fetal mortality found in this study. Secondly, inaccuracy of gestational age calculated from the date of last menstrual period is a well-recognized problem in epidemiological research addressing perinatal mortality. However, when we replicated the entire analyses using gestational age estimated from physical and neurologic assessments of the newborn, the results were essentially unchanged (data not shown). Thirdly, a potential limitation of our analysis is the high proportion of data missing on pre-pregnancy BMI and cigarette smoking. Nevertheless, to investigate this potential source of bias, we performed multiple analyses of the effects of adjustment for these variables and found no evidence of confounding of the effect of significant risk factors on fetal death by pre-pregnancy BMI and cigarette smoking. Fourthly, our study is not population-based. Rather, it is based at several different hospitals in Latin America. In general, less than 2% of all Latin American births are represented by our database. However, almost 60% of all births in Uruguay are recorded in the SIP database. Fifthly, Uruguay and Argentina contributed with almost 50% of births registered at SIP database. Thus, our results may not be generalized to the whole of the Latin American population. Finally, even though we adjusted for several factors, there is still potential for confounding and bias by other unknown factors.

The decline in the fetal death rate, mainly that occurring at term, in the developed world has been attributed to an improvement in obstetric surveillance and management during labor, the introduction of electronic fetal monitoring, and to early delivery (3). Identification of women not attending antenatal care (19.6% of all women), and a comprehensive approach to their unmet needs, i.e. provision of care and alleviation of both economical and psychosocial constraints, could have a great impact on fetal mortality in our region. Moreover, implementation of adequate screening, diagnosis, and management programs for fetal growth restriction is likely to lead to a reduction in the number of fetal deaths. Special attention should be focused on adequate management of noncephalic fetal presentations to reduce the intrapartum fetal mortality. On the other hand, efforts to manage and treat maternal medical conditions would have a smaller impact on the reduction of fetal death in Latin America.

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