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Risk-factors for antepartum fetal deaths in the city of São Paulo, Brazil

Fatores de risco para mortes fetais anteparto no Município de São Paulo, Brasil

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ABSTRACT

OBJECTIVE: To assess risk factors for antepartum fetal deaths.

METHODS: A population-based case-control study was carried out in the city of São Paulo from August 2000 to January 2001. Subjects were selected from a birth cohort from a linked birth and death certificate database. Cases were 164 antepartum fetal deaths and controls were drawn from a random sample of 313 births surviving at least 28 days. Information was collected from birth and death certificates, hospital records and home interviews. A hierarchical conceptual framework guided the logistic regression analysis.

RESULTS: Statistically significant factors associated with antepartum fetal death were: mother without or recent marital union; mother's education under four years; mothers with previous low birth weight infant; mothers with hypertension, diabetes, bleeding during pregnancy; no or inadequate prenatal care; congenital malformation and intrauterine growth restriction. The highest population attributable fractions were for inadequacy of prenatal care (40%), hypertension (27%), intrauterine growth restriction (30%) and absence of a long-standing union (26%).

CONCLUSIONS: Proximal biological risk factors are most important in antepartum fetal deaths. However, distal factors – mother's low education and marital status – are also significant. Improving access to and quality of prenatal care could have a large impact on fetal mortality.

KEYWORDS: Antepartum fetal death. Prenatal care. Risk factors. Socioeconomic factors. Case-control study. Pregnancy.

RESUMO

OBJETIVO: Analisar os fatores de risco para óbitos fetais anteparto.

METODOS: Estudo de caso-controle de base populacional realizado no Município de São Paulo, SP, de agosto de 2000 a janeiro de 2001. Os indivíduos foram selecionados a partir de uma coorte de nascimentos, obtida por meio de vinculação de declarações de nascimento e óbito. Os casos foram 164 óbitos fetais anteparto e os controles, uma amostra aleatória de 313 de sobreviventes até 28 dias. Foram realizadas entrevistas domiciliares com as mães e aplicado protocolo hospitalar. Foi empregada regressão logística para análise dos dados, baseado em modelo conceitual hierárquico.

RESULTADOS: Os fatores estatisticamente significantes associados aos óbitos fetais anteparto foram: mães com união recente ou sem união; escolaridade da mãe

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inferior a quatro anos; nascimentos anteriores de baixo peso; mães com hipertensão, diabetes, e sangramento durante a gestação; ausência ou pré-natal inadequado presença de malformação congênita e presença de pequeno para idade gestacional. As maiores frações de risco atribuível na população foram inadequação do pré-natal (40%), hipertensão (27%), presença de pequeno para idade gestacional (30%), e ausência de união com mais de um ano (26%).

CONCLUSÕES: Os fatores de risco proximais são os mais importantes para a mortalidade fetal anteparto. Entretanto, fatores distais como mães de baixa escolaridade e união recente ou ausente também desempenham importante papel. Melhorar acesso e qualidade do pré-natal pode promover impacto positivo na mortalidade fetal.

DESCRITORES: Óbito fetal anteparto. Atenção pré-natal. Fatores de risco. Fatores socioeconômicos. Estudo de casos e controle. Gravidez.

INTRODUCTION

Fetal deaths are an increasingly important component of perinatal mortality with the continuing decrease in early neonatal mortality, occurring either before onset of labor (antepartum) or during labor and delivery (intrapartum).[1] Intrapartum fetal deaths mostly result from sub-optimal management of complications during labor or delivery and decreases as access to good quality obstetric care is improved.[11,18] Antepartum fetal deaths are the main component of fetal mortality in developed countries, whereas in the poorer developing countries intrapartum fetal deaths are still dominant.

Factors associated with antepartum fetal deaths include: socioeconomic and demographic conditions (social condition of head of household, social and psychological burden, no marital union, low maternal education);[4,11,18] characteristics of the mother before pregnancy (maternal age over 35, high parity, short inter-pregnancy interval, height <1.5 m, body mass index (BMI >29.0 kg/m^2);[4,7,11] previous unfavorable pregnancy outcomes;[7,19,24] conditions during pregnancy (syphilis or other infections, premature rupture of membranes, diabetes, hypertension, preeclampsia, bleeding, placental problems or smoking);[4,7] inadequate prenatal care;[4,7] fetal characteristics (intrauterine growth restriction, congenital malformations).[4,7,24] These factors show significant associations in almost all studies, but many of them did not adjust for potential confounders. Clinical conditions of mother and fetus are the dominant risk factors. A consistent proportion of fetal deaths are considered unexpected and unexplained.[11]

The cause of fetal deaths have been studied mostly in audit systems or studies of routine data. Audit systems (Brazilian Health Ministry; The Confidential Enquiry into Maternal and Child Health [CEMACH]* in the United Kingdom) review individual cases of fetal deaths and have generated useful explanatory hypothesis for causation of deaths. However, since they usually have no control series for comparison, they can do no more than generate hypothesis.** Studies based on data from health information systems have been used in descriptive and analytical studies of fetal mortality, but they offer limited exposure information as depended on administrative data.[1,5,19]

The present paper reports the results of a population-based case-control study of risk factors for antepartum fetal deaths as part of the Study on Perinatal Mortality in São Paulo.***

METHODS

The study area consisted of 14 administrative districts in the South region of the city of São Paulo (2,465,800 inhabitants). A cohort was defined by linking electronic files of live birth and death certificates for the period between August 1st, 2000 and January 31, 2001. Eligible cases were fetal deaths defined according to ICD-10[15] (fetuses of 500 g and over or 22 weeks and over). The sample size considered: ratio of two controls per case, 80% of power, 95% precision confidence level to detect an odds ratio of two for exposures (15% of controls were considered exposed). Controls were obtained by sampling every 63 of all 23,185 infants who survived at least 28 days.

*The Confidential Enquiry into Maternal and Child Health. 2003. Available from http://www.cemach.org.uk [accessed in 2005 Sep 19]
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***Research conducted under the supervision of Prof. Dr. Arnaldo Augusto Franco de Siqueira, and developed at the Departamento de Epidemiologia, Departamento de Saúde Materno-Infantil of Faculdade de Saúde Pública/Universidade de São Paulo (USP), Departamento de Medicina Preventiva of Faculdade de Medicina/USP, and at the Epidemiology Unit/London School of Hygiene & Tropical Medicine.

Information on cases and controls was obtained from birth and death certificates, home interviews with mothers, and a protocol was used to abstract data from obstetric and neonatal hospital records. Home births were excluded (11 cases and one control). Of 213 potential cases, losses were due to mothers that could not be found or refused to participate (8.5%), or the hospital records were not found or refused access to records (11%). For 369 potential controls, these were responsible for 6% and 10%, respectively. Of 172 fetal deaths with complete home visit and hospital record information, eight were classified as intrapartum based on the obstetric records, and another eight were classified as antepartum based on limited information. The final analysis therefore included 164 antepartum fetal deaths and 313 controls.

The proportion of low birth weight was similar between the subjects included and those not included in the study for cases and controls suggesting the absence of major selection bias.

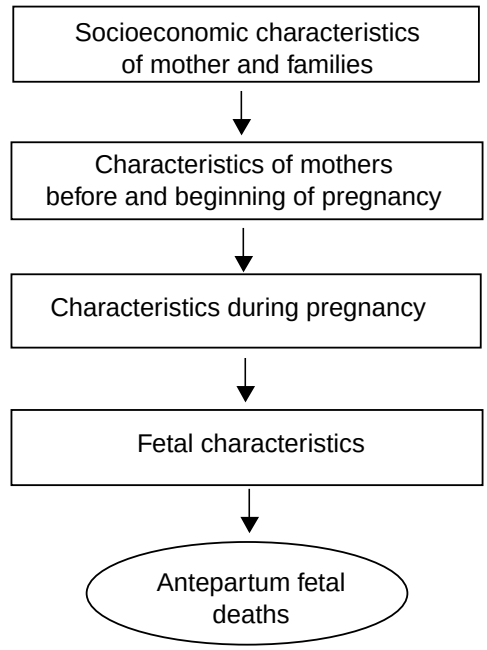

Figure - Conceptual framework.

Variables were grouped in four blocks according to a hierarchical conceptual framework (Figure). Block 1 consisted of socioeconomic and demographic characteristics of mothers and families. These included: ownership of consumer goods; monthly family income (in units of minimum wages); head of the household (mother, spouse or another person) and occupation of the head of the household (adapted from the British occupational classification[3]). Mother's marital union was classified into: no union, union of less than one year, and union of at least one year's duration at birth; education was grouped as number of years of formal education. Crowding represented more than three residents per room. Mother's skin color was self-defined and categorized as white/non-white. Domestic violence was considered as part of the social context, and classified as absent or present, according to the *Abuse Assessment Screening*.[16] Family's membership in a private health care plan was also included in this block.

Block 2 consisted of characteristics of the mothers before pregnancy. These included known obstetrical history risk factors: maternal age, parity, previous fetal loss (spontaneous and induced abortions), previous low birth weight infant, all classified as present or absent. BMI was calculated from reported pre-pregnancy weight and height of mothers. Mother's, family's and father's reaction to pregnancy; pregnancy planning and whether induced abortion was considered or attempted were also included.

Block 3 consisted of conditions occurring during pregnancy and included vaginal bleeding and hypertension (hospital records). Diabetes, renal disease, urovaginal infection, and blows directed to the abdomen (mother's report). Cigarette and alcohol consumption during pregnancy and mother's reported hospitalization during pregnancy were categorized as yes or no. Prenatal care was considered adequate when the first visit occurred in the first trimester of pregnancy, with at least four visits, and at least one visit collected blood and urine and measured mother's blood pressure and fetal heart beats.

Block 4 consisted of characteristics of the fetus: sex, presence of fetal malformation (from hospital records) and intrauterine growth restriction (based on Williams[22] curve of fetal growth). Information on gestational age was collected but this variable was not included in the analysis, because preterm birth in antepartum death may be a consequence rather than a risk factor.

Simple regression analysis was carried out to obtain crude odds ratios (OR) and to select the variables associated with antepartum fetal death ($p<0.20$). These variables were modeled with unconditional logistic regression and adjusted OR[14] was obtained within each block. After this adjustment, variables in each block with p-value less than 0.05 were selected and a new regression analysis was performed starting with the more distal block (socioeconomic and demographic characteristics, block 1) and adding each of the more proximal blocks in order (first block 2, characteristics of mother before pregnancy, then block 3, factors during pregnancy and finally block

Table 1 - Proportion of cases and controls characteristics and risk factors for antepartum fetal death. São Paulo, Brazil, 2000-2001.*

Variable	Case (%)	Control (%)
Block 1 - Socioeconomic and demographic data		
Household head - years of study		
12 yrs and over	3 (1.8)	14 (4.5)
Less than 12 yrs	161 (98.2)	299 (95.5)
Mother's skin color (missing excluded)		
White	66 (40.2)	147 (47.0)
Non-white	97 (59.1)	163 (52.1)
Head of the household		
Mother	19 (11.6)	26 (8.3)
Spouse	105 (64.0)	244 (78.0)
Other	40 (24.4)	43 (13.7)
Crowding		
Less than 1	42 (25.6)	92 (29.4)
1 to 2	106 (64.6)	203 (64.9)
3 and over	16 (9.8)	18 (5.7)
Delivery in public paid hospital		
Yes	119 (72. 6)	210 (67.1)
No	38 (23.2)	91 (29.1)
Missing	7 (4.2)	12 (3.8)
Mother's years of study		
4 yrs and over	135 (82.3)	278 (88.8)
Less than 4	29 (17.7)	35 (11.2)
Mother's union		
1 yr and over	96 (58.5)	243 (70.6)
Less than 1 yr	20 (12.2)	22 (7.0)
No union	48 (29.3)	48 (15.3)
Block 2 - Mothers characteristics before pregnancy		
Parity		
1 to 3	79 (48.2)	155 (49.5)
None	62 (37.8)	128 (40.9)
4 and over	23 (14.0)	30 (9.6)
Pregnancy planning		
Planned	48 (29.3)	116 (37.1)
Unplanned	116 (70.7)	197 (62.9)
Previous low birth weight pregnancy		
No	134 (81.7)	281 (89.8)
Yes	30 (18.3)	32 (10.2)
Family's reaction to pregnancy		
Happy	99 (60.4)	211 (67.4)
Unhappy/indifferent	65 (39.6)	102 (32.6)
Block 3 - Mothers conditions during pregnancy		
Alcohol consumption		
No	123 (75.0)	257 (82.1)
Yes	41 (25.0)	56 (17.9)
Cigarette consumption		
No	120 (73.2)	254 (81.1)
Yes	44 (26.8)	59 (18.8)
Violence directed against abdomen		
No	158 (96.3)	312 (99.7)
Yes	6 (3.7)	1 (0.3)
Hospitalization		
no	131 (79.9)	275 (87.9)
Yes	33 (20.1)	38 (12.1)
Vaginal bleeding		
No	142 (86.6)	307 (98.1)
Yes	22 (13.4)	6 (1.9)
Hypertension		
No	110 (67.1)	291 (93.0)
Yes	54 (32.9)	22 (7.0)
Diabetes		
No	152 (92.7)	309 (98.7)
Yes	7 (4.3)	1 (0.3)
Not known	5 (3.0)	3 (0.97)
Prenatal care		
Adequate	57 (34.8)	208 (66.4)
Not adequate	98 (59.8)	101 (32.3)
None	9 (5.5)	4 (1.3)
Block 4 - Fetal characteristics		
Congenital malformation		
No	149 (90.8)	304 (97.1)
Yes	15 (9.1)	9 (2.9)
Intrauterine growth restriction		
No	89 (54.3)	254 (81.1)
Yes	61 (37.2)	37 (11.8)
Missing	14 (8.5)	22 (7.0)

*Variables associated with antepatum fetal death in the block

4, fetal characteristics). Population attributable fraction (PAF) was also calculated for the variables in each block using the best estimate of effect with Rockhill method.[17] The best estimate effect (OR and PAF) of a particular variable was considered adjusted by the preceding and the added variables. The PAFs are adjusted for previous but not subsequent blocks and cannot be added. The criterion for variables staying in these models during this process was a Wald p-value less than 0.05. The best fitting model was defined using Wald and likelihood ratio tests.[9]

The Research Bioethics Committee of Faculdade de Saúde Pública of Universidade de São Paulo and the ethics committees of participating hospitals approved the study. Consent was verbally given for the home interviews and written for the hospital record review.

RESULTS

Fetal mortality rate was 8.4/1,000 births. Fetal deaths were 63% of all perinatal deaths; 95% of all fetal deaths were antepartum and roughly a third occurred at 28 weeks gestation or over. The mean birth weight was 1,763 g, low birth weight was 71% and 75% were preterm.

In block 1, variables measuring economic status were not statistically significant, whereas those measuring partnership status, mother's education and head of household education were associated with the outcome. The following variables were not significant and thus not selected: family income, number of rooms, socioeconomic classification, ownership of private health insurance and head of household occupation. The multiple regression analysis within Block 1 showed that the following were not significant: head of the household with less than 12 years of study, mother's skin color, spouse being head of the household, crowding, delivery in public heath system hospital. The variables selected as significant ($p<0.20$) for the next step were: no and recent union (less than one year's duration) and mothers having less than four years of study (Table 1).

Regarding characteristics of the mother before pregnancy (Block 2), maternal age over 35 years old showed an increased risk but not statistically significant (OR=1.36; 95% CI: 0.8; 2.3). Negative perception of own health before pregnancy, high or low BMI, previous fetal loss or induced abortion, having considered or attempted a termination of the pregnancy, father's negative reaction to this pregnancy showed $p>0.20$ and were not selected for the next step. After adjustment within the block, family's negative reaction, unplanned pregnancy and high parity were not selected to the next step of analysis. Only history of a previous low birth weight infant was significantly associated to the outcome ($p<0.05$) at multiple regression analysis within the block (Table 2).

The variables related to mothers' conditions during pregnancy (Block 3) not statistically significant in the simple analysis and not selected were multiple gestation, kidney disease and reported urovaginal infection. Alcohol and cigarette consumption during pregnancy, violence against the abdomen and hospitalization during pregnancy lost significance within the block adjustment. The variables statistically significant at multivariable analysis within the block were: vaginal bleeding, hypertension, diabetes during pregnancy, and absence or inadequate prenatal care (Table 2).

To further explore the relation of prenatal care with bleeding and hypertension, it was estimated the risk associated with these conditions in the presence and absence of adequate prenatal care (frequency of diabetes was too low for subgroup analysis). The OR for bleeding in women with adequate prenatal care was 3.9 (95% CI: 1.3; 12.0); all fetuses died if women had bleeding and inadequate/no prenatal care. Regarding hypertension, the OR was 5.6 (95% CI: 2.8; 11.3) in women with adequate prenatal care; 8.7 (95% CI: 2.6; 29.1) with inadequate care and all fetuses of those with no care died.

Among fetal characteristics (Block 4), presence of congenital malformations and intrauterine growth restriction were statistically significant associated with fetal death (Table 2) but not sex.

The selected variables from Block 1 (mothers' marital status and educational status) and Block 2 (previous low birth weight) remained statistically significant in the regression analysis. To these variables were added the selected variables from Block 3 and a new regression analysis was performed. Mothers' marital status, low birth weight and variables from Block 3 remained statistically significant, while mother's low educational status lost its significance (Table 3).

The final step was a regression analysis performed with statistically significant variables from Blocks 1, 2 and 3 adding the selected variables from fetal characteristics (block 4). Only the variable "previous low birth weight" lost its significance (OR=1.8; CI 95%: 0.9; 3.5), all others variables remained significantly associated with antepartum fetal deaths (Table 3).

Hosmer-Lemeshow goodness-of-fit statistic was [$\chi^2(6df)=2.40$], a non-significant difference ($p=0.88$)

Table 2 - Crude and adjusted odds ratios of characteristics and risk factors for antepartum fetal death. São Paulo, Brazil, 2000-2001.

Characteristic/Variable	Crude OR	p-value	95% CI	Adj. OR	p-value	95% CI
Block 1 - Socioeconomic and demographic						
Household head - years of study						
12 yrs and over	reference	–	–	reference	–	–
Less than 12 yrs	2.5	0.14	0.7; 8.9	3.4	0.19	0.6; 20.2
Mother's skin color (missing excluded)						
White	reference	–	–	reference	–	–
Non-white	1.3	0.15	0.9; 1.9	1.2	0.40	0.8; 1.8
Head of the household						
Mother	reference	–	–	reference	–	–
Spouse	0.59	0.1	0.3; 1.1	1.11	0.82	0.4; 2.9
Other	1.27	0.52	0.6; 2.7	1.23	0.60	0.6; 2.7
Crowding						
Less than 1	reference	–	–	reference	–	–
1 to 2	1.14	0.54	0.7; 1.8	1.02	0.94	0.6; 1.9
3 and over	1.95	0.09	0.9; 4.2	1.64	0.33	0.6; 4.4
Delivery in public paid hospital						
Yes	reference	–	–	reference	–	–
No	0.74	0.17	0.5; 1.2	0.74	0.46	0.3; 1.6
Missing	1.03	0.95	0.4; 2.7	1.02	0.97	0.4; 2.8
Mother's years of study						
4 yrs and over	reference	–	–	reference	–	–
Less than 4	1.7	0.05	1.0; 2.9	1.9	0.03	1.1; 3.5
Mother's union						
1 yr and over	reference	–	–	reference	–	–
Less than 1 yr	2.3	0.01	1.2; 4.4	2.7	<0.01	1.4; 5.4
No union	2.5	<0.001	1.6; 4.1	2.3	0.07	0.9; 5.4
Block 2 - Mothers' characteristics before pregnancy						
Parity						
1 to 3	reference	–	–	reference	–	–
None	0.95	0.81	0.6; 1.4	1.0	0.95	0.6; 1.7
4 and over	1.5	0.19	0.8; 2.8	1.3	0.47	0.7; 2.4
Pregnancy planning						
Planned	reference	–	–	reference	–	–
Unplanned	1.4	0.10	0.9; 2.1	1.4	0.16	0.9; 2.2
Previous low birth weight pregnancy						
No	reference	–	–	reference	–	–
Yes	1.8	<0.01	1.1; 3.4	1.9	0.03	1.1; 3.5
Family's reaction to pregnancy						
Happy	reference	–	–	reference	–	–
Unhappy/indifferent	1.4	0.13	0.9; 2.0	1.1	0.45	0.7; 1.8
Block 3 - Mothers' conditions during pregnancy						
Alcohol consumption						
No	reference	–	–	reference	–	–
Yes	1.5	0.07	1.0; 2.4	1.3	0.32	0.7; 2.3
Cigarette consumption						
No	reference	–	–	reference	–	–
Yes	1.6	0.04	1.0; 2.5	1.5	0.12	0.9; 2.6
Violence directed against abdomen						
No	reference	–	–	reference	–	–
Yes	11.8	<0.01	1.4; 101.4	7.5	0.08	0.8; 73.7
Hospitalization						
No	reference	–	–	reference	–	–
Yes	1.8	0.02	1.1; 3.0	1.5	0.22	0.8; 2.7
Vaginal bleeding						
No	reference	–	–	reference	–	–
Yes	7.9	<0.001	3.1; 20.5	7.3	<0.001	2.6; 20.3
Hypertension						
No	reference	–	–	reference	–	–
Yes	6.5	<0.001	3.6; 11.5	5.5	<0.001	3.0; 10.0
Diabetes						
No	reference	–	–	reference	–	–
Yes	14.2	0.001	1.7; 119.8	11.5	0.03	1.3; 103.7
Not known	3.4	0.08	0.8; 14.5	1.9	0.52	0.3; 12.7
Prenatal care						
Adequate	reference	–	–	reference	–	–
Not adequate	3.5	<0.001	2.3; 5.4	2.7	<0.001	1.7; 4.2
None	8.2	<0.001	2.3; 28.7	4.4	0.05	0.9; 19.5
Block 4 - Fetal characteristics						
Congenital malformation						
No	reference	–	–	reference	–	–
Yes	3.4	<0.01	1.4; 8.0	3.2	0.01	1.3; 7.8
Intrauterine growth restriction						
No	reference	–	–	reference	–	–
Yes	4.7	<0.001	2.8; 7.8	4.7	<0.001	2.9; 7.5
Missing	1.8	0.09	0.9; 3.7	1.7	0.13	0.8; 3.6

Table 3 - Adjusted odds ratios, confidence intervals and population attributable etiological factors in the hierarchical modeling process for risk factors of antepartum fetal death. São Paulo, Brazil, 2000-2001.

Variable	OR	95% CI	PAF
Block 1 - Socioeconomic and demographic characteristics			
Mothers' marital status			26%
Recent union	2.5	1.3; 4.8	
No union	2.7	1.7; 4.3	
Mothers education			9%
<4 years study	2.0	1.2; 3.5	
Block 2 – Mothers' characteristics before and at the beginning of pregnancy*			
Previous low birth weight	2.4	1.4; 4.2	11%
Block 3 – Mothers' conditions during pregnancy**			
Diabetes	13.2	1.5; 118.3	5%
Vaginal bleeding	6.6	2.4; 18.3	11%
Hypertension	5.9	3.6; 10.6	27%
Prenatal care			40%
Not adequate	2.4	1.5; 3.8	
None	3.3	0.8; 13.7	
Block 4 – Fetal characteristics***			
Congenital malformation	3.7	1.4; 10.7	7%
Intrauterine growth restriction	5.1	3.0; 10.1	30%

PAF: Population attributable etiological factors
Adjusted by: *Blocks 1 + 2; **Blocks 1 + 2 + 3; ***Block 1 + 2 + 3 + 4

between the predicted and observed probability, which suggests a good fit of the final model.[9] The population attributable fraction for mothers having no/recent union was 26% and for low education of mother was 9%. The PAF for history of previous low birth weight was 11% (Block 2) and for factors during pregnancy (Block 3), the highest clinical variables were diabetes (5%), bleeding (11%), and hypertension (27%). Population attributable fraction for inadequate/no prenatal care presented the highest value (40%) for intrauterine growth restriction was 30% and for congenital malformation was 7% (Table 3).

DISCUSSION

Intrapartum deaths are an important component in fetal mortality. Although they are still frequent in developing countries, the present study showed that more than 90% of deaths were antepartum. These results indicate that access to delivery services is provided by the public health system in the city of São Paulo. The risk of antepartum fetal death was increased in mothers with medical complications such as: diabetes (13-fold), hypertension, bleeding (both 6-fold) and in fetuses experiencing intrauterine growth restriction (5-fold), or with congenital malformation (4-fold). Inadequacy of prenatal care, absence of longstanding union (2.5-fold), previous low birth weight (2.5-fold) and low maternal education (2-fold) also had major impact on the outcome.

The present study has limitations. As information on outcome was collected from hospital records, some fetal deaths may have been misclassified. As a retrospective study, many exposures were reported rather than observed or measured, and are also prone to misclassification, recall bias and potential residual confounding by incomplete measurement of known confounders. The measurement of intrauterine growth restriction is associated to gestational age, which may be overestimated if the fetus dies and remains in the uterus. On the other hand, selection bias is unlikely: this case-control study was nested in a well-defined population and non-responders were similar to responders. The power was limited for the study of rare exposures (e.g. abdominal aggression had a high OR but a wide confidence interval and was seen in six cases and one control only).

Relationships between risk factors and antepartum fetal deaths are complex: variables may have a direct effect, be mediated by others or a marker for something else. For instance, inadequate prenatal care may be measuring inadequacy of screening/diagnosis/management of preventable maternal conditions and/or acting as a proxy for social characteristics associated with fetal death. The study data analysis may not have fully addressed the complexity of fetal mortality chain of causation.

Women with union included both married and cohabitating couples. It was found that single women and mothers with short duration union had a higher risk of the outcome, which is consistent with other fetal death studies[7] and studies on pre-term births.[23]

Mother's skin color was not significantly associated with antepartum fetal death. Similar result was obtained in another Brazilian study[2] for fetal deaths. Higher fetal mortality rate was found among black mothers in USA[20] even when adjusted for prenatal and unfavorable gestational conditions. Occupation of head of household was also not associated with the outcome, and similar results were found in Barcelona.[3] Though a study in Sweden[18] found that association, this was the only socioeconomic variable included in the analysis.

Mother's low education (less than four years of schooling) was associated with antepartum fetal death, and this finding was similar to other studies.[3,7] However, the present results were no longer significant after introducing prenatal care. Possibly the education effect expressed itself at least in part through inadequacy or absence of prenatal care. An association between low maternal education and inadequate prenatal care has been found in Brazilian studies.[12,13]

Previous fetal loss is a well described[8] risk factor; however, in the study data, previous fetal death did not increase risk significantly (OR=1.3; 95% CI: 0.45; 3.5); but the subsample size was small (eight cases and 12 controls) with wide confidence intervals. Previous low birth weight infant was the only aspect of reproductive history associated with risk of antepartum fetal death.

There is consensus that maternal age over 35 increases the overall risk of fetal death moderately,[8,11] but this was not found in the present study. Two possible explanations are the lack of power (only 15 cases and 22 controls), or variable characteristics of older mothers in different contexts. Pre-pregnancy obesity has been found to be associated with antepartum fetal death.[8] It was found no association but there were only eight cases and 11 controls with BMI over 30. Some studies[5,11] showed an increase of fetal deaths among high parity mothers and other studies showed an increase of fetal deaths in nulliparous women[10] but these studies included antepartum and intrapartum fetal deaths.

Künzel & Misselwitz[11] found a large increase in risk of term antepartum fetal death in mothers with high psychological and social burden. It was explored the reaction to pregnancy of family and father and whether pregnancy was planned or termination attempted but no significant associations were found. Smoking and heavy consumption of alcohol are well known to increase the risk of fetal death; these effects increase with the level of consumption and this association is believed to be causal.[6,8,10] In the study results smoking was marginally significantly associated in the bivariate analysis but it lost its significance in the multivariable analysis; the study may not have the power to detect a small effect. Alcohol consumption was only very marginally associated with antepartum fetal death but it was probably underreported (fewer than 5% reported having more than one drink a week).

Association between having had a previous low birth weight infant and fetal death (including antepartum and intrapartum) was observed in Latin America[7] and between previous intrauterine growth restriction and antepartum fetal death in Sweden.[19] Intrauterine growth restriction and fetal death share underlying causes, for example placental abnormalities.[21,24] This might explain why history of previous low birth weight lost significance once intrauterine growth restriction of the index fetus was included in the model.

Complications of pregnancy are recognized risk factors, particularly bleeding,[4,7,11,18] diabetes[4,7,18] and hypertension[6,7,18,19,21] and the present study corroborated it. This indicates why better quality prenatal care could result in significant reduction of antepartum fetal death.

The study results showed that health care played a significant role in the outcome.[4,7] Hospitalization during pregnancy was significantly associated with fetal death in the bivariate analysis; but it was no longer significant when adjusted for complications of pregnancy. Absence or inadequacy of prenatal care was associated with fetal deaths, which is consistent with other studies.[4,7] In the present study, adequacy of prenatal care was defined to include undergoing some essential procedures (laboratory tests, blood pressure measurements, counting fetal heart beats) together with the number of visits and early initiation. Adequate prenatal care reduced the risk of fetal death in women with diabetes, hypertension and bleeding. In the absence of prenatal care all pregnancies of women with bleeding and hypertension resulted in fetal deaths; and an increased risk (36%) was observed in women with hypertension and inadequate prenatal care. High population attributable fraction values of prenatal care indicate that almost half of fetal deaths might be amenable to intervention with access to better quality prenatal care.

Fetal characteristics were also associated with antepartum fetal death: 7% of antepartum fetal deaths were explained by congenital malformations (OR=4) and 30% by intrauterine growth restriction (OR=5). This latter frequently is related to problems of maternal-fetal blood flow and placenta vascularization or implantation.[24] Although strongly associated to antepartum fetal death, these conditions are not easily detected and managed clinically during pregnancy, needing high quality prenatal care.

Finally, the study findings clearly showed the importance of access and adequacy of prenatal care in the pathway of antepartum fetal death. It also indicated the importance of identifying social vulnerabilities, single mothers or those with recent union. Moreover, identification and ready intervention in gestational conditions such as hypertension and intrauterine growth restriction would reduce fetal mortality. Prenatal care in urban areas with reasonable access to health services could easily identify these mothers' conditions and improve the quality of care provided.

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