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Risk factors associated to fetal death

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Objective: The purpose of this study was to investigate risk factors associated to fetal death in a Brazilian population. **Design:** A case control study. **Setting:** The Hospital Maternidade Leonor Mendes de Barros in São Paulo. **Participants:** 122 pregnant women with diagnosis of fetal death and gestation age of 20 or more weeks and 244 controls of pregnant women who delivered liveborns. **Variables studied:** The fetal death (dependent variable), independent variable (the social demographic factors, clinical and obstetrical history, prenatal care indicators and pathological conditions). **Results:** The risk factors associated to fetal death were abruptio placentae, syphilis, few prenatal care visits, one or more previous stillbirths, hospitalization during pregnancy, diabetes, age above or equal to 25 years, hypertension during pregnancy, anemia and age below 20 years. **Conclusions:** Results of the current study might be useful to orientate a primary prevention health program, specially those concerning antenatal care.

Uniterms: Stillbirth. Fetal death. Mother and child health. Risk factor.

INTRODUCTION

The perinatal mortality is an important health indicator for the evaluation of the pregnancy and puerperium process. During the last years a decrease in its rate has been observed worldwide due to a significant decrease of the intrapartum fetal mortality and early neonatal mortality rates, secondary to progresses in childbirth and neonatal care. However, a corresponding reduction in the antepartum fetal mortality has not been achieved.¹

In order to have a decrease of the antepartum fetal mortality rate in a population, it is necessary to know the etiology of fetal death and its associated risk factors. It is also necessary to know the relative importance of these causes and factors in each specific population, in order to

direct health actions to avoid the most prevalent causes and to propose strategies for attenuating or eliminating the risk factors associated to fetal death.²

There are several studies on maternal, fetal and other causes of fetal death, but only recent studies have been trying to identify its risk factors. In this way, some studies have tried to establish an association between fetal death and maternal age, parity and smoking, investigating the presence of possible markers for the occurrence of fetal death.^{3,4} A case-control study for determinants of fetal death, performed in Greece between 1989 and 1991, found a significantly higher risk for the variables early gestation age, lower level of maternal education and higher maternal age.⁵

Another case-control study carried out in five perinatal centers of the USA, in the period from 1982 to 1986, evaluated risk factors for fetal death in 403 cases of stillbirth and found that maternal age of 35 or above, black skin color, pre gestation weight of 85Kg or higher and smoking habit were significantly more frequent in cases than in controls. In the final statistical analysis they were considered as risk factors for fetal death.⁶ It still remains

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unexplained what mechanism operates in the association between maternal age and parity with fetal mortality.³

Concerning smoking, this mediation has been explained by the higher likelihood that women who smoke present placental complications, especially abruptio placentae causing fetal death due to hypoxemia,⁷ and placental insufficiency with consequent intra uterine growth retardation.³

A Brazilian study performed in Campinas showed that the main risk factors for the occurrence of fetal death were previous stillbirth, no prenatal care, hypertension and maternal age above 35 years.⁸

According to the medical literature, it is known that many factors have been identified as risk factors for fetal death, and many of them could be preventable, controlled or treated. In addition, it is necessary to study the relative importance of these several risk factors in different populations. Thus the purpose of this study was to investigate the risk factors for antepartum fetal death in a low income Brazilian population.

METHODS

This was a case-control study. The sample size was estimated as 122 cases and 244 controls, considering the proportion of cases and controls exposed to hypertension as a risk factor respectively of 13.5 and 3.9%,⁹ a case to control ratio of 1:2, an Alpha error of 5% and a power (1 - Beta) of 80%.

The sample of cases was selected according to the admission order of women at the Admission Unit of Hospital Maternidade Leonor Mendes de Barros, which gives care to the low income female population of the east zone of São Paulo city, in the period from August of 1996 to May of 1997. They were pregnant woman with diagnosis of fetal death occurred before the onset of labor, and gestation age of twenty weeks or higher. For the sample of controls the next two pregnant women with a live fetus, admitted to the hospital after each case, with diagnosis of labor and that had a live newborn, were selected. This study was developed with women who participated voluntarily, after they have been cleared on the study details and signed an informed consent. The project was approved by the Committee of Ethics in Research of the institution.

The dependent variable was the fetal death and the independent variables studied were concerned with the social demographic factors, clinical and obstetrical history, prenatal care indicators and pathological conditions during the current pregnancy.

For data collection a structured questionnaire and a form were used. They contained the results of laboratory exams, ultrasound evaluation and clinical data. These instruments were reviewed concerning the quality and legitimacy of information, and the data were coded and stored in a computer file, after performing consistency tests.

Initially a univariate analysis was performed, comparing the frequency of the different categories of the independent variables, both for cases and for controls. The Odds Ratio and its respective 95% CI were estimated for all possible risk factors. Finally a multivariate analysis by logistic regression was performed in order to check on the possible confusion between some variables. The statistical packages EPI.INFO 6.02 and SPSS.PC+ were used for these procedures.

RESULTS

The results related to the descriptive analysis of the population of women with fetal death are presented in another article.² The percentage distribution of women studied according to age can be seen in Table 1. There was no statistically significant trend of higher occurrence of fetal death with the increase of age. However, the estimated risk of fetal death was approximately double among women below 19 years old, compared to the age group between 20 and 24 years, and also higher above 25 years. The age group of highest risk was that above 35 years, with an almost three times greater risk for the occurrence of fetal death than in the reference group.

There was no statistically significant difference between the groups concerning marital status, family income, skin color, paid work and education level. No association between smoking habit and the occurrence of fetal death was observed, which means smoking habit did not increase the risk significantly. When evaluating the women's, distribution according to the number of pregnancies, there was also no statistical difference between the groups, the same happening for the number of previous abortions and history of fetal malformation.

However, a strong association between the history of previous stillbirth and the occurrence of fetal death was observed. More than 6% of the cases reported two or more stillbirths, and only 1.2% of the controls. The estimated relative risk of fetal death increased with the number of stillbirths, a statistically significant trend (Table 2). The percentage distribution of women according to the time at the beginning of prenatal care can be seen in Table 3. There was no significant difference between the groups.

Table 1
Distribution of women according to age and occurrence of fetal death.

Age (years)	Cases	Controls	OR	95% CI
≤ 19	21.3	18.5	2.07	1.01-4.23
20-24	19.6	35.2	1.0	Reference
25-29	23.7	20.1	2.12	1.06-4.25
30-34	19.6	16.8	2.10	1.01-4.37
≥ 35	15.8	9.4	2.96	1.30-6.77
Total	122	244		

$\chi^2_{\text{trend}} = 3.10$

$p = 0.078$

Table 2
Distribution of women according to number of previous stillbirths and occurrence of fetal death.

Nº of stillbirths	Cases	Controls	OR	95% CI
None	77.5	93.9	1.0	Reference
1	16.3	4.8	4.09	1.49-11.43
≥ 2	6.2	1.2	6.29	0.99-67.07
Total*	80	166		

* Information available only for women with at least two pregnancies

$\chi^2_{\text{trend}} = 13.92$

$p < 0.001$

Table 4 shows the percentage distribution of women according to the number of prenatal care visits. It is observed that approximately 60% of the cases had zero to four visits, against only about 25% of the controls. The estimated relative risk of occurrence of fetal death was more than seven times higher when only 1 to 4 prenatal visits took place than when there were more than seven visits. This difference remained even after allowing for gestation age. There was a significant trend in which the higher the number of visits, the lower the risk of fetal death was.

When evaluating pregnant women who related being admitted to hospital during pregnancy for clinical or obstetric treatment, it was observed that this fact was associated to a more than three times higher risk of occurrence of fetal death than when the hospital admission had not occurred (Table 5). When an abruptio placentae occurred, the risk of fetal death was about 22 times higher than when this obstetrical condition was absent (Table 6).

Table 6 shows the estimated relative risks of fetal death for the presence of some pathological conditions during the current pregnancy. Among them, hypertension during pregnancy, present in almost 42% of cases, showed a risk of occurrence of fetal death around twice as high. Concerning other pathological conditions present or diagnosed during admission for delivery, diabetes, syphilis

and anemia showed significantly by higher estimated relative risks of fetal death, around 2.5 times, ten times and twice respectively.

In the multivariate analysis, the independent variables that were significantly associated with the occurrence of fetal death were the diagnosis of diabetes during the hospital admission for delivery, maternal anemia and hospital admission during pregnancy; and the history of previous stillbirth for women with more than one pregnancy (Table 7). The variable abruptio placentae in current pregnancy was not included in the regression model used, considering its obvious causal association with occurrence of fetal death.

DISCUSSION

The interest in performing this study was to investigate which risk factors were associated to fetal death in a low income Brazilian female population. The results show that the main risk factors for fetal death identified were maternal age below 20 and above 24 years, history of previous stillbirths, some maternal pathological conditions and indicators of the medical care received during pregnancy.

Table 3
Distribution of women according to the period of pregnancy when starting prenatal care and occurrence of fetal death.

Onset of prenatal care (month)	Cases	Controls	OR	95% CI
02	34.8	31.7	1.0	Reference
03	33.0	26.4	1.14	0.62-2.09
04	16.5	19.4	0.78	0.37-1.60
³ 5	15.6	22.5	0.63	0.30-1.30
Total*	109	227		

$\chi^2_{\text{trend}} = 2.287$

$p = 0.130$

* 13 cases and 17 controls did not have prenatal care

Table 4
Distribution of women according to the number of prenatal visits and occurrence of fetal death.

Number of prenatal visits	Cases	Controls	OR	95% CI
> 7	6.8	17.6	1.0	Reference
5 - 7	33.3	58.4	1.47	0.60-3.72
1 - 4	49.6	17.2	7.43	2.96-19.23
None	10.3	6.7	3.94	1.21-13.13
Total*	117	238		

* Missing information for 5 cases and 6 controls

$\chi^2_{\text{trend}} = 30.46$

$p < 0.00001$

Table 5
Distribution of women according to hospitalization during pregnancy and occurrence of fetal death.

Hospitalization	Cases	Controls	OR	95% CI
No	86.5	95.6	1.0	Reference
Yes	13.5	4.4	3.41	1.38-8.50
Total	111	228		

* Missing information for 11 cases and 16 controls

To investigate the causes of fetal death in a population is as important as to try to determine its risk factors, facilitating health interventions directed to wards avoiding the known causes and/or decreasing the exposure to the risk factors specifically identified in this population.

The risk factors for fetal death identified in this study, in decreasing order of risk, were: occurrence of abruptio placentae, diagnosis of syphilis, a small number of prenatal visits, history of one or more stillbirths, hospital admission during pregnancy for any reason, diagnosis of diabetes during admission for delivery, maternal age above 24 years, hypertension during pregnancy, anemia during admission for delivery and maternal age below 20 years.

The history of previous stillbirth as a risk factor for fetal death is reported by several authors, in studies performed in developed and developing countries,^{9,10}

reinforcing the results of this study, which also identified the history of previous stillbirth as significant for the occurrence of fetal death not only in the univariate analysis, but also in the multivariate one which took into account only women with more than one pregnancy.

It is already known that the lowest risk age group for clinical and obstetrical complications during pregnancy is that between 20 and 24 years of age, increasing towards both extremes of reproductive age, and that the highest risk is after 35 years, exponentially increasing with age. This corresponds exactly to the findings of the present study concerning the risk of fetal death, corroborating the results of other current studies,^{3,5} although the trend of risk increase with the progressive increase of maternal age was not significant.

It is also known that, when some pathological conditions are present during pregnancy, the risk of

Table 6
Distribution of women according to some pathological conditions during current pregnancy and occurrence of fetal death.

Condition	Cases	Controls	OR	95% CI
Hypertension at delivery	31.2	21.3	1.67	0.99-2.81
Hypertension during pregnancy	41.9	25.3	2.13	1.20-3.78
Diabetes at delivery	12.3	5.3	2.49	1.08-5.79
Diabetes during pregnancy	5.7	4.3	1.22	0.35-3.80
Urinary tract infection during pregnancy	24.5	33.7	0.64	0.35-1.15
Cardiopathy during pregnancy	2.5	0.8	3.10	0.35-37.50
Syphilis at delivery	4.2	0.4	10.38	1.14-493.12
Abruptio placentae	8.2	0.4	21.7	3.00-945.31
Fever during pregnancy	6.1	4.3	1.47	0.49-4.32
Anemia at delivery	22.9	12.3	2.12	1.16-3.90

• For all conditions, the reference is its absence during current pregnancy.

Table 7
Variables significantly associated to fetal death by multivariate analysis.

Variable	adjusted OR	95% CI
Previous stillbirths	5.19	2.18-12.38
Hospitalization during pregnancy	3.09	1.30-7.35
Diabetes at delivery	2.97	1.26-7.02
Anemia	2.60	1.31-5.16

occurrence of fetal death increases, and such an association was also present in this study regarding hypertension, anemia, diabetes and hospital admission during pregnancy, which is supported by the medical literature.³

During the investigation of causes,² as well as the determination of risk factors, the diagnosis of hypertension during pregnancy showed a strong association with fetal death. This suggests that the early diagnosis of hypertension during pregnancy and an appropriate medical intervention could help to reduce the risk of fetal death associated to this cause.

For early detection of pathological conditions during pregnancy it is necessary to have available an appropriate program of prenatal care, offered to the population with enough quantity and quality, especially to those of low income that need it. In this study, a small number of prenatal visits was associated to a higher estimated risk for the occurrence of fetal death. This evaluation was also performed with the stratification of women according to gestation age, in an attempt to

correct for the possibility of methodological mistake in the comparison of the two groups, since it would be expected that a pregnancy with low gestation age would have a smaller number of visits than a pregnancy at term. The same association was observed with this stratification, although it was significant only for the group with gestation age higher than 32 weeks.

The low frequency and the bad quality of prenatal care substantially influence the increase in perinatal mortality rates. It is an important task of prenatal care to reduce the perinatal mortality rate.^{11,12}

When evaluating all risk factors identified in this study, it is recognized that some are avoidable (syphilis, anemia, low number of prenatal visits), others are likely to be controlled and/or treated (hypertension, diabetes) and, finally, some can not be influenced at all (history of 2 or more stillbirths, age below 20 years or above 24 years, abruptio placentae). In the specific case of abruptio placentae, however, its incidence could be reduced with the treatment and control of associated hypertension. When hypertension, diabetes or another risk condition are present, early routine evaluation of the fetal vitality should start, as well as proper control and treatment.¹³

It may be said that this study has increased the knowledge of the risk factors for late antepartum fetal death in a low income Brazilian population. It has shown that health interventions which propose strategies for elimination or control of the possible risk factors associated to fetal death are necessary, since the majority of them in the population studied are avoidable or susceptible to control or treatment.

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RESUMO

Objetivo: Investigar os fatores associados à morte fetal em uma população brasileira. **Tipo de Estudo:** Caso-controle **Local:** Hospital Maternidade Leonor Mendes de Barros, São Paulo. **Participantes:** 122 gestantes com diagnóstico de óbito fetal e idade gestacional de vinte semanas ou mais e 244 controles constituídos por gestantes que deram à luz a recém-nascido vivo. **Variáveis estudadas:** Variável independente (morte fetal), variáveis independentes (fatores demográfico-sociais, clínicos obstétricos, indicadores de cuidados pré-natal, condições mórbidas). **Resultados:** Os fatores de risco identificados foram: presença de descolamento prematuro de placenta, sífilis, pequeno número de consultas de pré-natal, antecedente de um ou mais natimortos, internação hospitalar durante a gestação, diabetes, idade igual ou superior a 25 anos, hipertensão na gestação, anemia e idade abaixo de 20 anos. **Conclusões:** Os resultados deste estudo poderão ser úteis para orientação de programas de prevenção primária, principalmente quanto à assistência pré-natal.