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Fetal deaths in Brazil: a systematic review

Óbitos fetais no Brasil: revisão sistemática

ABSTRACT

OBJECTIVE: To review the frequency of and factors associated with fetal death in the Brazilian scientific literature.

METHODS: A systematic review of Brazilian studies on fetal deaths published between 2003 and 2013 was conducted. In total, 27 studies were analyzed; of these, 4 studies addressed the quality of data, 12 were descriptive studies, and 11 studies evaluated the factors associated with fetal death. The databases searched were PubMed and Lilacs, and data extraction and synthesis were independently performed by two or more examiners.

RESULTS: The level of completeness of fetal death certificates was deficient, both in the completion of variables, particularly sociodemographic variables, and in defining the underlying causes of death. Fetal deaths have decreased in Brazil; however, inequalities persist. Analysis of the causes of death indicated maternal morbidities that could be prevented and treated. The main factors associated with fetal deaths were absent or inadequate prenatal care, low education level, maternal morbidity, and adverse reproductive history.

CONCLUSIONS: Prenatal care should prioritize women that are most vulnerable (considering their social environment or their reproductive history and morbidities) with the aim of decreasing the fetal mortality rate in Brazil. Adequate completion of death certificates and investment in the committees that investigate fetal and infant deaths are necessary.

DESCRIPTORS: Fetal Death, epidemiology. Fetal Mortality, trends. Cause of Death. Risk Factors. Death Certificates. Mortality Registries. Health Information Systems. Review.

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RESUMO

OBJETIVO: Analisar frequência e fatores associados ao óbito fetal na literatura científica brasileira.

MÉTODOS: Revisão sistemática de estudos brasileiros sobre óbito fetal publicados entre 2003 e 2013. Foram analisados 27 artigos originais em três diferentes abordagens: quatro sobre qualidade da informação; 12 estudos descritivos e 11 sobre fatores associados aos óbitos fetais. Foram consultadas as bases de dados PubMed e Lilacs, com extração de dados e síntese realizada por dois ou mais pesquisadores, de forma independente.

RESULTADOS: A qualidade de preenchimento da declaração de óbito fetal mostrou-se ainda deficiente, tanto na completitude de variáveis, principalmente sociodemográficas, como na definição de causa básica. A mortalidade fetal apresentou queda no Brasil, mas persistiram desigualdades. As causas do óbito, quando adequadamente investigadas, indicaram morbidades maternas passíveis de prevenção e tratamento. Os principais fatores associados ao óbito fetal foram pré-natal inadequado ou ausente, baixa escolaridade, morbidades maternas e história reprodutiva desfavorável.

CONCLUSÕES: O pré-natal deve priorizar mulheres mais vulneráveis, socialmente ou em relação à história reprodutiva e morbidades, para diminuir a taxa de mortalidade fetal no Brasil. É necessária a qualificação do preenchimento da declaração de óbito e investimento nos comitês de investigação de óbito fetal e infantil.

DESCRITORES: Morte Fetal, epidemiologia. Mortalidade Fetal, tendências. Fatores de Risco. Causas de Morte. Atestado de Óbito. Registros de Mortalidade. Sistemas de Informação em Saúde. Revisão.

INTRODUCTION

The fetal mortality rate (FMR) is considered one of the best indicators of the quality of health care provided during pregnancy and childbirth.[a] FMR is calculated using the number of total fetal deaths in the numerator and the number of total births (live and dead births) in the denominator but by varying the criteria for gestational age and weight to define fetal death.[a]

WHO[b] (2011) estimated that approximately 2.6 million fetal deaths (considering infant weight > 1,000 g or gestational age > 28 weeks) occurred worldwide in 2009. Between 1995 and 2009, FMR showed a 14.0% decrease, from 22.1 per 1,000 total births to 18.9 per 1,000 births.[b] The number of fetal deaths in the third trimester of pregnancy was slightly smaller than the three million neonatal deaths that occurred worldwide.[38] Despite this magnitude, this indicator was not included by the United Nations among the Millennium Development Goals,[23] and fetal births have remained ignored by public health policies and programs, both internationally and domestically.[17,c] FMR is low in developed countries, varying between two per 1,000 births and seven per 1,000 births, whereas in Brazil, FMR was at an intermediate level in 2010 at 10.97 per 1,000 births.[24]

According to the latest data available in Brazil,[d] the absolute number of fetal deaths (considering infant

[a] Ministério da Saúde, Secretaria de Vigilância em Saúde, Secretaria de Atenção à Saúde. Manual de vigilância do óbito infantil e fetal e do Comitê de Prevenção do Óbito Infantil e Fetal. 2.ed. Brasília (DF); 2009 [cited 2012 Apr 10]. (Série A. Normas e Manuais Técnicos). Available from: http://bvsms.saude.gov.br/bvs/publicações/manual_obito_infantil_fetal_2ed.pdf

[b] World Health Organization, Department of Reproductive Health and Research. National, regional, and worldwide estimates of stillbirth rates in 2009 with trends since 1995: policy brief. Geneva; 2011 [cited 2013 Dec 19]. Available from: http://www.who.int/reproductivehealth/publications/maternal_perinatal_health/rhr_11_03/en/index.html

[c] Lansky S. fetal mortality: invisible and preventable deaths. In: Bittencourt DAS, Dias MAB, Wakimoto MD, organizadores. Vigilância do óbito materno, infantil e fetal e atuação em comitês de mortalidade. Rio de Janeiro (RJ): EAD/ENSP; 2013.

[d] Ministério da Saúde, DATASUS. Sistema de Informações de Mortalidade - SIM. Brasília (DF); c2008 [cited 2013 Apr 10]. Available from: http://www2.datasus.gov.br/DATASUS/index.php?area=060701

weight of 500 g or gestational age of 22 weeks) decreased from 38,759 to 31,613 between 2001 and 2011. FMR in Brazil has some limitations and should only be used in the Brazilian states in which this rate is calculated using the direct method. Even so, it can be generally estimated using vital statistics. FMR decreased from 12.3 per 1,000 live births to 10.7 per 1,000 births in the same period.[d,e] In the early 2000s, 30.0% of the data on birth weight were unknown. In 2011, this percentage decreased to 9.0%, and it was reported that approximately 30.0% of fetal deaths in Brazil were associated with infants weighing ≥ 2,500 g.

A review of perinatal deaths occurring in Brazil between 1990 and 2002[14] found few specific studies on this topic, with population and methodological differences such as the definition and calculation of some variables. In the 1990s, FMR was estimated at 14.0 per 1,000 births, and FMR was higher in northeast Brazil and lower in South Brazil. When secondary data were used, the level of data completeness was poor, and most underlying causes were listed as undefined. The studies on prevention identified that most fetal deaths occurred before birth, suggesting deficient prenatal care. The factors associated with fetal death were maternal age > 35 years, low income, low education level, inadequate prenatal care, and previous fetal death. However, these factors have been identified in one or at the most two studies, having little consistency as scientific evidence.

The objective of this study was to review the frequency and factors associated with fetal death in the Brazilian scientific literature.

METHODS

A systematic review of the literature evaluated fetal death as a primary or secondary outcome in Brazil between 2003 and 2013.

Three main factors were used as eligibility criteria: studies on the quality of information (variables: level of completeness, reliability, and validity of death certificates), descriptive studies (variables: description of FMRs and temporal trends, description of underlying causes, and application of a classification of preventable deaths), and studies (transverse and longitudinal) on the factors associated with fetal deaths. The studies involving populations with specific morbidities, basic research (e.g., on chemical mediators and cell biology), diagnostic tests, clinical trials, case reports, dissertations, and theses were excluded. Review studies were also excluded. Studies on perinatal mortality were included when they provided individualized data on fetal death.

The literature search was conducted in the Lilacs database (via the Virtual Health Library) and Medline (via PubMed), without language restriction. In Lilacs, the search strategy was (fetal death OR fetal mortality OR stillbirth) AND Brazil, in the abstract or subject fields. The search for Brazilian states (replacing the keyword "Brazil") was included to increase the sensitivity of the search. For Medline, the strategy was (fetal death OR fetal mortality OR stillbirth OR natimortality) AND Brazil. An additional manual search was performed in the references of the included studies.

Initially, two examiners evaluated the titles. The abstracts of the studies with titles approved by at least one examiner were read. The studies with an abstracts approved by both examiners were included. In cases of disagreement, a third examiner read the abstract to make the final decision. The reasons for exclusion are listed in the flowchart (Figure).

After selecting the abstracts, the full text was read to confirm the eligibility of the studies and proceed with the collection of relevant information. The studies were read and independently evaluated by at least two examiners, and disagreements were resolved by a third examiner. The data on author, location, population characteristics, outcome, type of study design, criteria of fetal deaths, and main results were collected in accordance with a pre-established worksheet. The authors FMSB and SCF read all the included studies and reviewed the spreadsheet.

The methodological quality of the studies was not a criterion for inclusion because the intention of analysis was to analyze the nature of studies on fetal death in Brazil, revealing aspects related to the methodology used.

Initially, 321 studies were identified in Medline and 105 were identified in Lilacs. The search for Brazilian states retrieved three studies that had not been identified previously. In analysis of titles and abstracts, there was disagreement between the two independent examiners regarding 12 studies retrieved from Medline. After analysis by a third examiner, five of the 12 studies were excluded. In the Lilacs database, the evaluation of three studies was discordant, and one was excluded.

Considering the two databases, duplicates were excluded, leaving 29 studies to be read in full; of these, 25 were selected. Two additional studies were included after the manual search of the references. The Figure shows the flowchart for the search and selection of the 27 studies.

Among the 27 studies selected, 13 solely focused on fetal deaths, seven studies evaluated perinatal deaths,

[e] Ministério da Saúde, DATASUS. Sistema de Informações de Nascidos Vivos - SINASC. Brasília (DF); c2008 [cited 2013 Apr 10]. Available from: http://www2.datasus.gov.br/DATASUS/index.php?area=060702

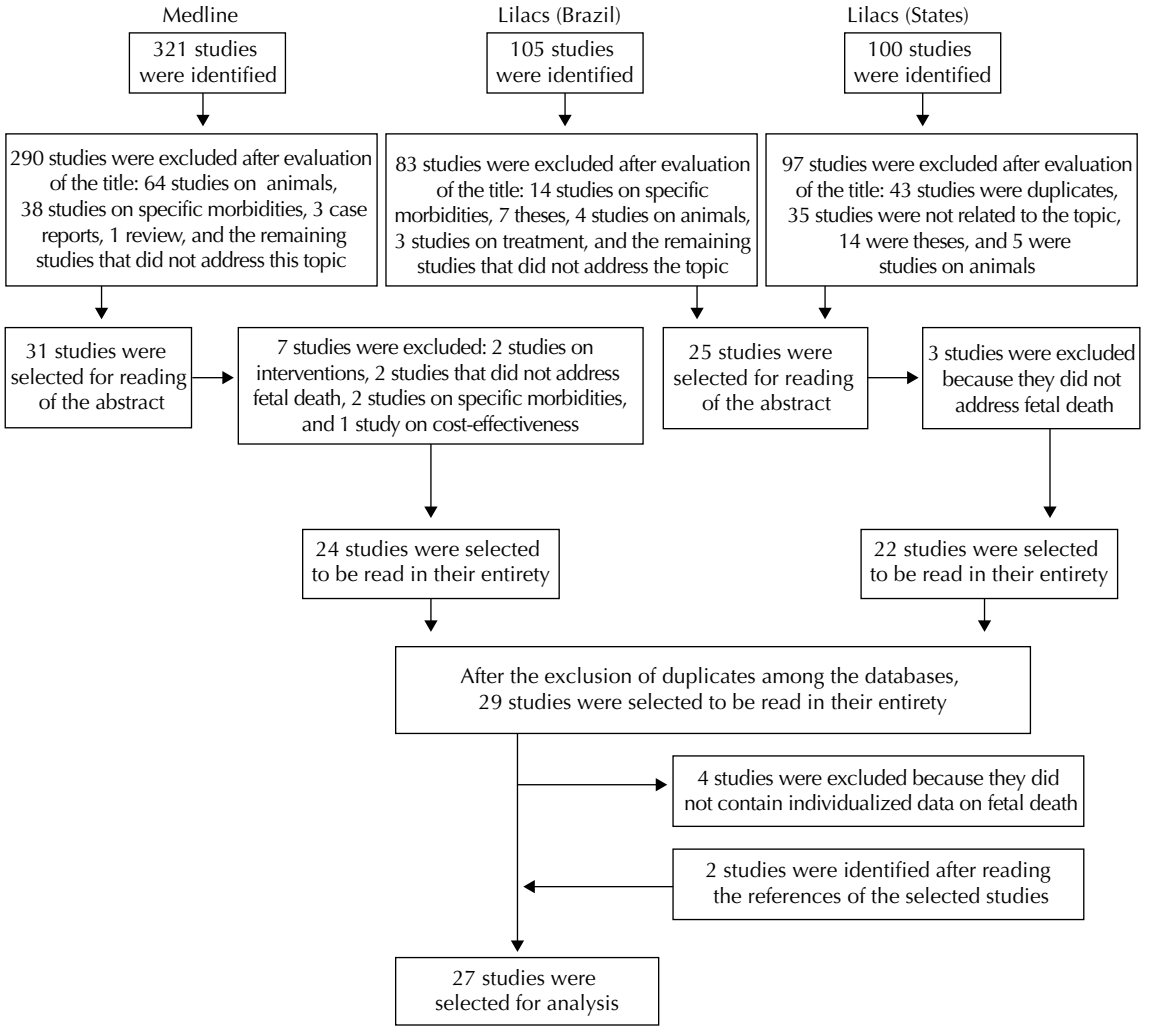

Figure. Flowchart of the selection of studies for systematic review.

and the others evaluated other outcomes. The scientific production in the Southeast region was predominant (13/27). The Northeast and South regions contributed with five and six studies, respectively, and three studies covered the nation as a whole. No studies conducted in the Midwest and North regions were found. The journals with the most publications on this topic belonged to the area of public health, with 10 studies.

The studies selected and their main results are summarized according to their main approach. Table 1 presents the four studies that addressed the quality of information, Table 2 presents the 12 descriptive studies, and Table 3 shows the 11 studies that evaluated the factors associated with fetal deaths. When a study had more than one approach, the approach that the authors defined as the main objective was selected. The characteristics of the studies are classified according to venue and chronological order.

RESULTS

Quality of information

Four studies were identified; of these, two[2,6] were conducted in the city of Sao Paulo, SP, Southeastern Brazil, and presented a very poor level of completeness of death certificates (DC) for important variables, particularly sociodemographic variables. The level of completeness of the variable "fetal weight" was approximately 100% in 2008 in comparison with 37.0% in 2001-2003. For the other variables, incompleteness often exceeded 50.0%, and the percentage of underlying causes was not specified.

Almeida et al[2] evaluated the difference in quality and the agreement between different data sources (death certificates or medical records), different issuers (death verification service or hospital), and institutions (Brazilian Unified Health System [SUS] or others). The

quality was better in hospitals; among these, the quality was better in institutions not affiliated with SUS. Except for sex and weight, the variables had excellent agreement, with values between 2.9% and 82.0%. The agreement was low for the underlying causes, and according to these authors, the autopsies performed by the death verification services did not contribute to elucidating the causes of fetal death.

In Ribeirao Preto, in the state of Sao Paulo,[5] the completion of nine fields on early neonatal and fetal death certificates during an eight-year period was evaluated. On the fetal death certificates, only the field "sex" was adequately completed, and completion of the field "birth weight" was regular. For the field "mother's age", incompleteness changed from regular to poor. For the fields "mother's education" and "live and dead births", completeness was inadequate throughout the evaluation period and incompleteness varied between 60.0% and 80.0%.

A study conducted in the Northeast[31] on the cross correlation of data from the Hospital Information System (HIS) and Mortality Information System (MIS) identified an additional 165 cases of stillbirth, indicating underreporting of approximately 10.0% cases in MIS. Underreporting was higher in smaller municipalities.

Descriptive studies

Twelve studies were retrieved: five in the Southeast, three in the South, two in the Northeast, and two of a national scope.

Table 1. Characteristics of the studies that evaluated the quality of information on fetal deaths. Brazil, 2003-2013.

Author, year of publication	Location, study period, and sample	Outcome evaluated	Criterion of fetal death	Methods	Results
Beringhs et al[6] (2008)	City of Sao Paulo, 2001-2003 FD = 6,722 fetal DC	Level of completeness of Part V of fetal death certificates	Weight > 500 g	SEADE Foundation No score attributed the level of completeness	Level of completeness: gender (98.0%), parity (70.0%), underlying cause of fetal death (46.7%), fetal weight (37.3%), type of delivery (25.0%), age (19.9%), and maternal education (16.7%)
Almeida et al[2] (2011)	City of Sao Paulo, first semester of 2008 FD = 710	Quality of information of fetal death certificates: validity and reliability	Not specified	SEADE Foundation - Level of completeness: excellent (> 95.0%), good (90.0%-95.0%), moderate (70.0%-89.0%), poor (50.0%-69.0%), very poor (< 50.0%) - Calculation of agreement, sensitivity, and specificity - Evaluation by SUS institutions/institutions other than SUS, and issuer of DC (hospitals *versus* DVS)	- Completeness: worse in DC completed by DVS, worse in SUS hospitals Overall rating: excellent for gender and weight; good for gestational age; moderate for type of pregnancy, very poor for live and dead births (43.1%/31.5%), maternal age (47.2%), type of delivery (23.5%), and parental education (17.2%) - Underlying cause not specified in 49.5% of cases - Low agreement for maternal variables and underlying causes of fetal death
Barbuscia et al[5] (2011)	Ribeirao Preto, Sao Paulo, 2000-2007 FD = 1,226	Level of completeness of neonatal and fetal DC	Weight > 500 g or GA > 22 weeks	SEADE Foundation and MIS - Level of completeness: good (> 90.0%); regular (71.0%-90.0%), poor (≤ 70.0%)	Level of completeness of fetal DC Good for gender; regular for birth weight, gestational age, type of pregnancy, and childbirth, poor for maternal age, live and dead births, level of education
Rafael et al[31] (2011)	Maranhao, 2008 FD (MIS) = 1,530 FD (HIS) = 786	Underreporting of fetal and infant deaths	GA > 22 weeks	HIS and MIS Cross-correlation of data to retrieve data on fetal deaths not previously reported to MIS	FMR before/after data recovery: 12.0 ‰/13.3 ‰ Underreporting of data on stillbirths: 9.7%

DC: death certificate; GA: gestational age; FD: fetal death; MIS: Mortality Information System; HIS: hospital information system; SUS: *Sistema Único de Saúde*; DVS: death verification service; FMR: fetal mortality rate

Table 2. Characteristics of the descriptive studies that evaluated fetal deaths, Brazil, 2003-2013.

Author, year of publication	Location, study period, and sample	Outcome evaluated	Criterion of fetal death	Methods	Results
Nurdan et al[29] (2003)	Microregion with 10 municipalities, state of Minas Gerais 1995-2000 LB = 11,948/FD = 190	Underlying causes of fetal death	GA > 20 weeks and/or weight > 500 g	Registry records (death certificates) and medical records Hospital-based	FMR = 15.6‰ Antepartum deaths (86.3%) Unknown causes (61.6%) and DPP (18.4%) Fetuses at term (40.0%)
Duarte et al[11] (2004)	Ribeirao Preto January 1991 to December 2000 Births = 33,360	Time-series studies on perinatal, fetal, and early neonatal deaths and delivery route	GA > 20 weeks or weight > 500 g	Medical records, autopsy reports Hospital-based	FMR: ↓33.3 ‰ (1991) to 13.0 ‰ (2000) No change in the percentage of cesarean sections in the period
Camargo[7] (2008)	State of Sao Paulo, 2000-2006	Characteristics of fetal death Level of data completeness	GA ≥ 22 weeks, any weight	SEADE Foundation Population-based	Improvement in the level of completeness of DC for weight (85.3%) and maternal age (84.0%) M/F ratio = 117/100. TMF ↓9.8‰ to 8.0‰ Fetuses to term: 16.0%/Weight ≥ 2,500 g: 24.0% Correlation between maternal age (years) and FMR: 20-34: 8.0‰; 35-39: 13.5‰; 40-44: 19.0‰; > 44: 50.0‰ More frequent GA range: 32-36 weeks Causes: intrauterine hypoxia (30.0%), NS (26.0%), placenta, membrane, and umbilical cord complications (16.1%), maternal conditions (15.0%)
Amaral et al[3] (2011)	Campinas, Sao Paulo, 2005 LB = 4,491 FD = 32	Near miss audit, maternal and perinatal deaths	Weight ≥ 500 g or GA ≥ 22 weeks	Clinical data collected prospectively Population-based	FMR = 7.1‰ Causes: intrauterine hypoxia (46.9%); malformation (25.0%); not identified (28.1%)
Fonseca & Coutinho[15] (2008)	Jacarepaguá, city of Rio de Janeiro 1999-2003 LB = 19,340 PD = 512/FD = 377	Causes of perinatal deaths (fetal and early neonatal) and prevention of perinatal death	Weight ≥ 500 g and GA ≥ 22 weeks	Research records + medical records + prenatal cards Hospital-based (exclusively SUS)	FMR = 18.0‰. Weight ≥ 2,500 g: 24.0%/GA ≥ 37: 22.0% Causes of FD of pre-term infants: maternal complications (35.0%), placenta, membrane, and cord complications (26.0%), not defined (21.0%) Causes of FD at term: maternal complications (27.0%), placenta, membrane, and cord complications (25.0%), not defined (17.0%), asphyxia (12.0%)
Matijasevich et al[25] (2008)	Pelotas, Rio Grande do Sul, 1982, 1993 and 2004 LB = 15,602 FD = 193	Tendency and differences in perinatal deaths in 3 cohorts	GA > 28 weeks or weight > 1,000 g	Interviews, registry records, review of medical records Population-based	TMF ↓1982 = 16.1‰; 2004 = 9.6‰; FMR of antepartum death: ↓13.1‰ to 8.4‰; FMR of intrapartum death: ↓2.5 ‰ to 0.7‰ Minor decrease associated with low income

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Trindade et al[39] (2011)	Pato Branco, Paraná, 2000-2008 FD = 91	Root causes of fetal death	GA > 22 weeks and/or weight ≥ 500 g	MIS data No reports of missing or corrected information	FMR: 2000 = 11.5‰; 2008 = 11.0‰ Causes: placenta previa (38.5%), NS (17.6%), maternal hypertension (13.2%)
Vieira et al[41] (2012)	Florianópolis, Santa Catarina, 2000-2009 FD = 111 with autopsy (total of 173)	Underlying causes and prevention of fetal deaths	GA ≥ 22 weeks or weight > 500 g	Medical records + DC + autopsy records Classification used: ReCoDe system Hospital-based (university hospitals)	Clinical evaluation: identification of causes in 65.8% of cases: fetal malformation, maternal hypertension, placental and umbilical cord complications, infection; pathological confirmation in 66.6% of cases: infection, malformation, placental complications. ReCoDe – valuation of IGR, only 9.0% undefined
Silva Filho & Maia[35] (2004)	Mombasa, Ceará, 2000-2001 FD = 28	Underlying causes of fetal death	Weight ≥ 500 g and/or GA ≥ 22 weeks	Medical records and DC Hospital-based	Approximately 40.0% of cases with weight ≥ 2,500 g Approximately 90.0% of cases with ill-defined causes
Jacinto et al[19] (2013)	Salvador, Bahia, 2000-2009	Tendency of perinatal, early neonatal, and fatal deaths, underlying causes and prevention	GA ≥ 22 weeks with weight ≥ 500 g	NISLB and MIS Integrated, autoregressive, and moving average curves and linear coefficient of determination (R^2) Classification: Wigglesworth	Most with antepartum FD. Gradual decrease of FMR, reaching 11.9‰ in 2009 Decreased rate of underreporting, except on education and ethnicity Causes: P20 (44.7%), P02 (18.3%), P00 (15.2%); 30.0% of cases with weight > 2,500 g
Chiavegatto Filho et al[8] (2012)	Brazil 2000-2009 FD = 339,883	Sex ratio (SR) for fetal death	GA ≥ 20 weeks or weight ≥ 500 g and/or height ≥ 25 cm	MIS	SR = 1.188 Larger SR associated with low education, maternal age of 10–14 years, GA < 22 weeks, and low birth weight
Veloso et al[40] (2013)	Brazil: state capitals	Tendency of low birth weight and multiple births	Not specified	MIS and NISLB Time-series studies using Joinpoint regression	FMR decreased from 14.1‰ in 1996 to 9.3‰ in 2010. Worst results in the north and northeast and best results in the south Negative correlation between low birth weight in live newborns and FD

IGR: intrauterine growth restriction; DC: death certificate; PPS: premature placental separation; GA: gestational age; FD: fetal death; PD: perinatal death; NS: not specified; LB: live births; SR: sex ratio; MIS: Mortality Information System; NISLB: National Information System on Live Births; FMR: fetal mortality rate

Table 3. Characteristics of the studies that evaluated the factors associated with fetal death, Brazil, 2003-2013.

Author, year of publication	Location, study period, and sample	Outcome and factors studied	Criterion of fetal death	Methods	Results
Neves et al[28] (2004)	Juiz de Fora, Minas Gerais July 1998 to June 1999 FD = 111	- Fetal death - Pregnancy, prenatal care, sedentary work, smoking, malformations	Weight > 1,000 g and/or GA ≥ 28 weeks	Questionnaire + medical records case-control study Population base Multivariate analysis	FMR = 13.07‰ Risk factors: hemorrhage in the third quarter of pregnancy (OR = 38.6), diabetes (OR = 9.9), hypertension (OR = 7.1), having fewer than six consultations during prenatal care (OR = 4.2)
Almeida et al[1] (2007)	14 districts in the city of Sao Paulo August 2000 to January 2001 FD = 172 Controls = 313	- Antepartum fetal death (164) - Socioeconomic factors, reproductive characteristics, maternal morbidity, prenatal care, smoking and alcohol use, IGR, fetal malformation, and gender	Weight > 500 g or GA ≥ 22 weeks	MIS + NISLB + interviews Case-control study Population base Hierarchical multivariate analysis	Attributable fraction of the identified risk factors: inadequate prenatal care (40.0%), IGR (30.0%), hypertension (27.0%), union instability (26.0%), bleeding (11.0%), prior low birth weight (11.0%), low education (9.0%), malformation (7.0%), diabetes (5.0%) Losses: 20.0%
Medeiros et al[27] (2009)	14 districts in the city of Sao Paulo August 2000 to January 2001 PD = 318 FD = 162	- Perinatal death (FD = 172) - Socioeconomic factors, reproductive characteristics, maternal morbidity, prenatal care, smoking and alcohol use, IGR, fetal malformation, and gender Environmental traffic pollution	GA ≥ 22 weeks	MIS + NISLB Case-control study Population base Hierarchical multivariate analysis using different models to evaluate fetal and neonatal death	Risk factors: being a single mother (OR = 2.24), previous low birth weight (OR = 2.19), hemorrhage (OR = 6.14), hypertension (OR = 6.61), inadequate prenatal care (OR = 2.33), fetal malformations (OR = 4.17), delivery complications (OR = 3.31) No association with pollution Losses: > 15.0%
Fonseca & Coutinho[16] (2010)	Jacarepaguá, city of Rio de Janeiro October 2002 to October 2004 LB = 7,134 FD = 140	- Fetal death - Socioeconomic factors, psychosocial factors, biological and behavioral factors of the mother, reproductive factors, prenatal care, IGR	Weight ≥ 500 g and/or GA ≥ 22 weeks	Interviews + review of medical records Hospital-based (SUS) case-control studies Hierarchical multivariate analysis with 2 models	Risk factors: maternal morbidity (OR = 2.1), previous stillbirth (OR = 5.9), domestic violence (OR = 2.0), IGR (OR = 2.2) Protective factors: stable relationship (OR = 0.5), employment (OR = 0.6), presence of a partner at admission (OR = 0.3), adequate prenatal care (OR = 0.3) Losses: 4.0%
Oliveira et al[30] (2010)	City of Rio de Janeiro July 1999 to March 2001 FD = 91 LB = 9,041	- Fetal and infant death experienced by women aged ≤ 35 years - Socioeconomic and demographic factors, maternal characteristics, prenatal care and delivery, infant weight, GA, gender	Weight ≥ 500 g or GA ≥ 22 weeks	Medical records + interviews Population base Cross-sectional study Hierarchical analysis	FMR = 9.6‰ Risk factors: high blood pressure and pre-existing diabetes (OR = 2.43), GA < 37 weeks (OR = 12.3), weight < 2,500 g (OR = 5.7) Protective factor: adequate prenatal care (OR = 0.40) No significant correlation between adolescence and fetal death

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Restrepo-Méndez et al[32] (2011)	Pelotas, Rio Grande do Sul, 1982, 1993, and 2004 Single birth from mothers aged ≤ 30 years	- Infant and fetal deaths - Adolescence, adjusted for socioeconomic and gestational factors	GA > 28 weeks and/or weight > 1,000 g	Interview + medical records Population base Cohort study Multivariate analysis	No significant correlation was found between adolescence and fetal death, although the correlation was suggestive of protection: OR = 0.6 (95%CI 0.4;1.0)
Klein et al[21] (2012)	Caxias do Sul, Rio Grande do Sul March 1998 to May 2004 LB = 10,980 FD = 138	- Fetal death - Sociodemographic factors, reproductive factors, maternal morbidity, malformations, infant weight, GA	GA ≥ 20 weeks, and/or weight ≥ 500 g	Review of medical records Hospital-based (SUS) case-control studies Hierarchical multivariate analysis	FMR = 17.0‰ Risk factors: having fewer than 6 prenatal consultations (OR = 5.1), previous stillbirths (OR = 11.5), hypertensive syndrome (OR = 2.7), and malformations (OR = 9.7)
Dumith et al[12] (2012)	Rio Grande, Rio Grande do Sul, 2007 LB = 2,500	- Perinatal outcomes - Factor: physical activity adjusted for age, prenatal care, education, income, parity	GA ≥ 20 weeks, and/or weight ≥ 500 g	Interview Population base Cross-sectional study Hierarchical multivariate analysis	FMR = 15.0‰ Physical activity showed protection, with borderline significance: OR = 0.43 (p = 0.05)
Andrade et al[4] (2009)	Recife, Pernambuco, June 2004 to March 2005 LB = 4.632 FD = 116	- Fetal death - Biological factors, demographic factors, clinical factors, lifestyle, obstetric care, prenatal care, health service use, birth weight, fetal gender	Weight ≥ 500 g and / or GA ≥ 22 weeks	Hospital records, medical records, interviews, and DC Case-control study Hospital base (SUS) Hierarchical multivariate analysis	FMR = 24.4‰; 95.7% of antepartum death Risk factors: malformations (OR = 7.5), having less than 6 prenatal consultations (OR = 4.4), hemorrhage (OR = 2.9), pilgrimage (OR = 2.9), age ≥ 35 years (OR = 2.2), education < 8 years (OR = 1.6; 95%CI 1.02;2.6)
Rigotto et al[33] (2013)	Ceará 2000-2010	- Fetal death and other complications - Pesticides	–	NISLB + MIS Ecological: linear regression comparing municipalities	Gradual increase in FD in municipalities with high exposure to pesticides; $R^2 = 0.75$
Siqueira et al[37] (2010)	Brazil, 26 states, except Federal District, 2001 LB = 3,115,474 FD = 38,759	Reproductive outcomes, including fetal death - Use of pesticides	–	NISLB + MIS Ecological study Multivariate analysis	No correlation was observed between fetal death and use of pesticides

IGR: intrauterine growth restriction; DC: death certificate; GA: gestational age; FD: fetal death; LB: live births; OR: odds ratio; MIS: Mortality Information System; NISLB: National Information System on Live Births; SUS: *Sistema Único de Saúde*; FMR: fetal mortality rate

In Minas Gerais, in the microregion of Caratinga,[29] a high percentage of full-term fetal deaths was observed (59.79%). In addition, 86.3% deaths occurred before delivery, and for 61.57% cases, the underlying causes of death were unknown.

The FMR in SUS hospitals in Ribeirao Preto[11] decreased from 1991 to 2000 regardless of the percentage of cesarean sections, the numbers of which remained unchanged, suggesting that this decrease was correlated with improved obstetric care.

The FMR in Sao Paulo decreased by approximately 20.0% between 2000 and 2006[7] and increased along with an increase in maternal age. These studies showed improvement in the completion of the variables "weight", "gestational age", and "maternal age" but not other variables. The percentage of non-specific causes and intrauterine hypoxia remained high.

In Campinas, in the state of Sao Paulo,[3] a population-based study conducted in 2005 indicated that intrauterine anoxia was the most frequent cause (46.9%) of fetal death, followed by malformations (25.0%).

The results of a study conducted in a large maternity hospital in the city of Rio de Janeiro, RJ, Southeastern Brazil[15] indicated that 84.0% of the fetal deaths occurred before hospital admission. The search of medical records and prenatal care cards decreased the ill-defined causes to less than 20.0%. For both preterm and full-term fetal deaths, maternal complications were the first underlying cause (37.0% and 27.0%, respectively), followed by complications related to the placenta, umbilical cord, and membranes.

In the city of Pelotas, RS, Southern Brazil, three birth cohorts were compared.[25] This is one of the few studies that used an old criterion for classifying stillbirths (28th gestational week or weight > 1,000 g). The decrease in FMR was more pronounced between 1982 and 1993. The decrease occurred in all weight ranges, and intrauterine growth restriction (IGR) also decreased. However, inequalities associated with family income persisted. In 2004, FMR was higher in families with income of less than three minimum wages. One study[25] used the classification of Wigglesworth for death prevention[42] and indicated a 72.0% decrease in intrapartum stillbirths and 36.0% decrease in fetal deaths before delivery.

In the city of Pato Branco, PR, Southern Brazil,[39] the average FMR was 9.3 per 1,000 births between 2000 and 2008. The most frequent underlying cause was placenta previa (38.5%), and the classification of 17.0% cases was not specified.

In Florianópolis, SC, Southern Brazil, a single study used the ReCoDe classification[18] for death prevention and evaluated cases with complete clinical and pathological data (64.0% of the total) from a university hospital for a period of 10 years.[41] The clinical evaluation indicated that malformations, maternal hypertension, and placental disorders were the underlying causes of fetal death, while the pathological examination revealed infection, malformations, and placental disorders. The two classifications complemented each other, decreasing the percentage of ill-defined causes. The ReCoDe classification had the best performance, with IGR as the cause of death in 32.5% cases and only 9.9% of non-defined deaths.

In the city of Mombaça, CE, Northeastern Brazil, only 28 hospital-based fetal deaths were reported, with a poor level of completeness of medical records, and the underlying cause of fetal death was not identified in more than 90.0% of cases.[35]

In the city of Salvador, BA, Northeastern Brazil, a time-series study showed that fetal death was the main cause of perinatal death, with a small tendency toward decline. There was a poor level of completeness for data on fetal deaths in MIS, particularly data associated with maternal age and education (40.0% and 17.0%, respectively). The most frequent cause of fetal death was intrauterine hypoxia, represented by 44.7% of the cases.[19]

The sex ratio of fetal deaths in Brazil was estimated at 1,188, according to maternal and fetal characteristics.[8] This ratio was higher than that for live births and even higher among mothers at age extremes, among mothers with low education, in case of a short gestational period, and for low-birth-weight fetuses. In addition, the sex ratio was high for most underlying causes, suggesting the vulnerability of male fetuses.

Veloso et al[40] evaluated the tendency of low birth weight between 1996 and 2010 in the Brazilian capitals and found a negative correlation between the percentage of low weight (which increased until 2004) and FMR. FMR decreased from 14.1 per 1,000 live births to 9.3 per 1,000 births, and in 2011, this indicator was higher in the Northeast (12.9 per 1,000 births) and lower in the South (8.5 per 1,000 births). The annual percentage of decrease in FMR was heterogeneous among the different Brazilian regions: North (-2.68%), Northeast (-1.17%), Midwest (-2.13%), and South (-3.83%). In the Southeast, the annual decrease was 4.5% by 2005, stabilizing thereafter.

Associated factors

Eleven studies were identified: five in the Southeast, two in the Northeast, three in the South, and one covering the entire Brazilian territory. Most studies used hierarchical multivariate analysis, and the factors investigated were maternal age, education, employment (type and employment status), ethnicity, psychosocial factors

(presence of a partner, domestic violence), smoking and alcohol abuse, reproductive characteristics (parity, previous outcomes), prenatal care, maternal morbidity (hypertension, diabetes, bleeding), maternal nutritional status, physical activity, and biological variables of the fetus (weight, gestational age, intrauterine growth).

In Juiz de Fora, MG, Southeastern Brazil,[28] for stillbirths aged more than 28 weeks, maternal morbidities (hypertension, diabetes, and bleeding in the third trimester) and the presence of fewer than six prenatal consultations were positively correlated with fetal death.

In the city of Sao Paulo,[1] fetal deaths prior to labor were significantly correlated with the following variables: education < 4 years (OR = 2.0), being single (OR = 2.7), previous child with low birth weight (OR = 2.4), gestational bleeding (OR = 6.6), hypertension (OR = 5.9), diabetes (OR = 13.2), inadequate prenatal care (OR = 2.4), malformation (OR = 3.7), and IGR (OR = 5.1). The variable "gestational age" was considered to be a consequence and not a determinant of fetal death and was therefore not included. The most attributable fractions were inadequate prenatal care, IGR, maternal hypertension, and marital instability. A correlation between maternal hypertension and prenatal care was observed. Accordingly, the odds ratio among hypertensive women with inadequate prenatal care was 8.7, which was much higher than that for hypertensive women with adequate prenatal care (OR = 5.6).

In addition, in Sao Paulo, the correlation between traffic pollution and perinatal death was evaluated.[27] However, for fetal death in isolation, no correlation was found between these variables.

In a SUS maternity hospital in the city of Rio de Janeiro,[16] the following protective factors were identified: marital stability, employment stability, being accompanied upon admission to the maternity hospital, and adequate prenatal care. The risk factors were maternal morbidity, IGR, previous stillbirth, and violence during pregnancy. Weight and gestational age were not included because these variables are not conceptually involved in the genesis of fetal death.

Another study conducted across all the maternity hospitals in the city of Rio de Janeiro[30] investigated adolescence and fetal and infant outcomes. However, no correlation was found between fetal deaths and adolescence. Hypertension and pre-existing diabetes, gestational age < 37 weeks, and birth weight < 2,500 g increased the risk of fetal death, whereas adequate prenatal care played a protective role.

The cohorts in Pelotas, Rio de Janeiro, were also investigated with regard to the correlation between adolescence and risk of fetal death.[32] In the three cohorts, adolescence suggested protection against fetal death, without statistical significance. FMR among adolescent mothers decreased from 9.8 per 1,000 births in 1982 to 7.4 per 1,000 births in 2004.

In a SUS maternity (50.0% of health care coverage) in Caxias do Sul, RS, Southern Brazil,[21] the associated factors were the presence of fewer than six prenatal consultations, previous stillbirths, hypertensive syndrome, and malformations.

In Rio Grande, RS,[12] physical activity during pregnancy was correlated with several maternal and perinatal outcomes. The association was protective against fetal death (OR = 0.43) but reached a borderline significance. This was the only study to address this factor.

In a high-risk maternity hospital in Recife, PE, Northeastern Brazil,[4] the following factors were correlated with fetal death: having fewer than six prenatal consultations, gestational hemorrhagic syndrome, medical consultation before admission to the maternity hospital, and congenital malformations. The variable "maternal age" was questionable (OR = 2.2; 95%CI 1.0;4.9). The sex ratio was 1:1, and the percentage of indeterminate underlying causes was high (53.3%).

Two ecological studies evaluated the association of agrochemicals/pesticides with fetal death, with conflicting results. A time-series study conducted in the lower Jaguaribe area of Ceará state[33] between 2000 and 2010 showed a gradual increase in fetal death associated with exposure to pesticides. Another study addressed infant and fetal death in Brazil in 2001[37] and found no correlation between these two variables and fetal death.

DISCUSSION

The FMR decreased in almost all the studies evaluated; however, this decrease was heterogeneous. Among SUS users, it became evident that fetal mortality was higher in groups with a lower socioeconomic status. Therefore, it is possible that universal access to health care has not been achieved, indicating inequalities in health. In the studies that described weight ranges, the percentage of stillborns with weight ≥ 2,500 g varied between 24.0% and 40.0%. According to Lansky, these fetuses have a great potential for survival, highlighting the seriousness of the problem in Brazil.[c]

Among the 27 studies published between 2003 and 2013, only 13 specifically focused on fetal death, supporting the low visibility of this topic despite its great importance.[c] As with other topics related to maternal and child health,[14,36] the studies predominantly addressed the Southeast region, followed by the South region. These regions have lower FMR but are home to the greatest number of research institutions.

The evaluated studies were mostly published in public health journals, indicating that other topics are prioritized in periodicals that address obstetrics and maternal and child health.

The quality of information contained in fetal death certificates, despite some improvement, remains deficient. A poor level of completeness of data on sociodemographic variables, including age and maternal education, was observed. Therefore, the use of MIS to evaluate the correlation between social inequalities and fetal deaths is unfeasible, as previously noted by Romero & Cunha[34] in relation to infant deaths in Brazil. Notably, the level of completeness of fetal death certificates was poorer than that reported by these authors for death certificates of infants aged under one year, corroborating the low visibility of fetal deaths.[c] Although cases of fetal deaths have decreased, underreporting occurs. However, data retrieval using the HIS-SUS system is possible, at least considering births from women using this health care system.[31]

Evaluation of the underlying causes is challenging, considering that the percentage of ill-defined causes is high and that although it was assessed in a single study, agreement was low. The recurrent diagnosis of intrauterine hypoxia, despite its presence as a constant cause of death in ICD-10, barely contributes to the understanding of the phenomenon. In addition, most studies did not even specify whether hypoxia occurred before or during birth and simply reported the code P20, a limitation that had already been indicated by Lansky.[c] Studies that investigated the underlying causes by review of either medical records or autopsy records indicated two findings: the contribution of IGR as a proximal factor and the increased allocation of maternal causes, including hypertensive diseases, diabetes, and syphilis, as the cause of fetal death.

In addition to the ongoing training of doctors in relation to the completion of death certificates, fetal and infant death investigation committees are important for the improvement of data quality information systems.[a] Although the original death certificates cannot be changed, it is possible to correct the data on MIS after review of the death certificates. In the WHO report[f] on strengthening civil registration and vital statistics, the use of data on causes of death to evaluate health at the local, regional, and national levels is emphasized.

The classifications of death prevention have hardly been used, and Wigglesworth's classification,[42] adapted by Kelling, was predominantly used.[20] Analysis of death prevention is important because it can guide managers to important resources for improving prenatal care and childbirth. The most frequent category was antepartum fetal death, suggesting greater deficiency in prenatal care. However, few studies have investigated the history of patients before their admission to the maternity ward where fetal death was confirmed, preventing the confirmation of this finding. This limitation of Wigglesworth's classification had already been noted; therefore, other studies are necessary to better define the context of fetal death.

With regard to the study of determinants, the case-control design and hierarchical analysis were predominant. A review by Di Mario[10] on fetal death in developing countries between 1996 and 2006 indicated a predominance of case-control studies, whereas in the review of Flenady et al[13] conducted in developed countries, approximately 70.0% of the studies were of the retrospective cohort type, using vital statistics databases.

Among the socioeconomic and demographic determinants of the mother, a low education level and advanced age were associated with fetal death in some studies. In the study by McClure[26] and in the aforementioned reviews,[10,13] maternal age was associated with fetal death, with a high attributable fraction in developed countries, where the prevalence of pregnant women aged more than 35 years is high. A low education level was also correlated with fetal death in these reviews.

Ethnicity and working conditions were addressed less frequently, and only one study (Fonseca & Coutinho, 2010)[10] indicated that employment had a protective effect. Relationship with a partner was associated with fetal death in three studies. Considering that the prevalence of women with no partner or those in unstable relationships can be high among those with a lower socioeconomic status, the fraction attributable to this factor can be high, as observed in the study conducted in the city of Sao Paulo,[1] where the attributable fraction was 26.0%. In a multicenter study conducted in Latin America, the correlation between lack of a partner and fetal death was borderline (RR = 1.12; 95%CI 1.0;1.25).[9] Domestic violence has not been widely investigated; therefore, the results are inconclusive. Ethnicity did not show any correlation with fetal death in our review, and this topic has not been addressed in recent international reviews or in multicenter studies.[9,10,13,26]

Prenatal care evaluated using either quantitative measurements such as the number of visits or adequacy criteria such as the Adequacy of Prenatal Care Utilization Index[22] was a strong correlation factor: this variable plays a protective role when the number of prenatal consultations is adequate but increases the

[f] World Health Organization, Institutional Repository for Information Sharing - IRIS. Strengthening civil registration and vital statistics for births, Deaths and causes of death: resource kit. Geneva; 2013 [cited 2014 Jan 20]. Available from: http://apps.who.int/iris/bitstream/10665/78917/1/9789241504591_eng.pdf

risk of fetal death when the number of consultations is low. The correlation with maternal hypertension was shown by Almeida et al,[1] indicating how prenatal care can affect fetal death.

The study by Almeida et al[1] estimated that inadequate prenatal care had the highest attributable fraction (40.0%). This result is consistent with the review by Di Mario,[10] who found that the attributable fraction for absent or poor prenatal care varied between 15.0% and 72.0%. In addition, Flenady et al[13] found a strong correlation between lack of prenatal care and fetal death (OR = 3.3). However, the attributable fraction was low, probably because of the high coverage of prenatal care in developed countries. In the study by McClure et al[26] conducted in seven low- and middle-income countries, the lack of prenatal care showed the highest correlation among the evaluated factors.

Unfavorable reproductive history of the mother was thoroughly investigated, particularly previous stillbirths, multiparity, and morbidities, and although no consensus was found, this analysis suggests a positive correlation with fetal death, which is corroborated by international reviews.[10,13] With regard to fetal characteristics, the male gender showed vulnerability in the study of Chiavegato et al;[8] however, this result was not corroborated by other studies. Few studies have addressed weight and gestational age, and most included only IGR, defending the causal relationship of the latter, whereas weight and gestational age would be consequences of the process. The international reviews also identified IGR as an important factor, with the attributable fraction being greater than 20.0%.

Maternal nutritional status, which has not been frequently studied in Brazil,[1,27] showed no correlation with fetal death. However, obesity was the modifiable factor with the highest attributable fraction in developed countries.[13]

Smoking, identified as a modifiable factor with a high attributable fraction in populations with a lower socioeconomic status in developed countries,[13] was not widely explored in national studies and was not a determinant of fetal death, probably because of the difficulty in measuring this variable or its absence in vital statistics.

Although our results included a low number of studies, which prevented the realization of a meta-analysis, they provide directions for the investigation of fetal death in Brazil and for investment in public policies.

Factors such as ethnicity, obesity, smoking (and quitting smoking), and intrauterine growth, which have been given little attention, should be addressed in future studies. On the other hand, there is a sufficient amount of scientific evidence on the influence of socioeconomic factors and quality of prenatal care in fetal mortality. Although these two factors may not have a direct biological correlation with fetal death, it is reasonable to assume that providing better prenatal care to vulnerable women and/or to those with adverse reproductive history may decrease FMR in Brazil.

The quality of information on fetal deaths, which allows the realization of epidemiological studies with greater internal validity, and investment in research committees should be prioritized so that fetal mortality can gain visibility as well as to ensure that these problems will be confronted more effectively.

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