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Incidence, causes, and risk factors of stillbirth in an Amazonian context: Saint Laurent du Maroni maternity ward 2016–2021

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ABSTRACT

Objective: We aimed to describe the epidemiology of intrauterine fetal deaths in multiethnic western French Guiana and to assess its main causes and risk factors.

Study design: A retrospective descriptive study was conducted based on data from January 2016 to December 2021. All information on stillbirth with a gestational age ≥20 weeks in the Western French Guiana Hospital Center was extracted. Terminations of pregnancy were excluded. We focused on medical history, clinical investigation, biological findings, placental histology, and autopsy examination to elucidate the cause of death. We used the Initial Cause of Fetal Death (INCODE) classification system for assessment. Univariable and multivariable logistic regression analyses were performed.

Results: Overall, 331 fetuses in 318 stillbirth deliveries were reviewed and compared to live births that occurred during the same period. The rate of fetal death varied between 1.3 % and 2.1 %, with an average of 1.8 % over the 6-year period. Poor antenatal care (104/318, 32.7 %), obesity ≥30 kg/m^2 (88/318, 31.7 %), and pre-eclampsia (59/318, 18.5 %) were the main risk factors associated with fetal death in this group. Four hypertensive crises were reported. According to the INCODE classification, the main causes of fetal death were obstetric complications (112/331, 33.8 %), particularly intrapartum fetal death with labor-associated asphyxia under 26 weeks (64/112, 57.1 %), and placental abruption (29/112, 25.9 %). Maternal-fetal infections were common, particularly mosquito-borne diseases (e.g., Zika virus, dengue, and malaria), re-emerging infectious agents such as syphilis, and severe maternal infections (8/331, 2.4 %). 19.3 % of fetal deaths (64/331) remained unexplained.

Conclusion: Change in lifestyle as well as social deprivation and isolation adversely affect pregnancy in western French Guiana, in the context of a poor health care system that is similar to what is found in the Amazonian basin. Particular attention must be paid to emerging infectious agents in pregnant women and travelers returning from the Amazon region.

Introduction

French Guiana is a French territory in South America with a multicultural and multiethnic population [1]. With an estimated population of more than 49,000 inhabitants, Saint Laurent du Maroni is the second largest city and is located in the west on the border with

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Suriname. Primary health care for this region, which includes most of the west French Guiana population along the lower Maroni River, both from the French and Surinamese sides (about 80,000 inhabitants), is delivered through the West French Guiana Hospital Center. This area has the highest demographic growth of French Guiana [2]. Although French Guiana has the highest GDP and health care expenditures per capita in Latin America, poverty is still widespread: over half of the total population lives under the poverty threshold, a situation that is more frequent in western French Guiana.Western French Guiana has experienced various viral epidemics, such as Chikungunya in 2014, Zika virus in 2016 [3], Dengue virus in 2020 and 2013, and recently the COVID-19 pandemic [4]. Social deprivation and fragility are particularly frequent in this population which is often compounded by limited access to care [5]. Illegal gold mining has led to mercury exposure [6], and geophagy of aluminium-rich clay has been found to cause substantial deficiencies and toxicities in the region [7,8]. All of these factors can adversely affect pregnancy. For example, pregnant women often have micronutrient deficiencies (up to 80 %) [8], and there is a substantial problem of lead poisoning among pregnant women. However, having children is highly valued in Maroon cultures, which is supported by a recent study showing that the ideal number of children reported by men and women was around 10, which explains the high fertility rate of the region [9].

The rate of intrauterine fetal death (IUFD) differs between high- and low-income countries [10]. According to the World Health Organization, 2.6 million stillbirths occur annually in the third trimester, and 98 % of these occur in low- and middle-income countries [11]. The Hospital Center of west french Guiana, with a french health system, made it possible to carry out a complete in the Amazonian environment.

This study aimed to describe the epidemiologic risk factors and causes of IUFD in the population of western French Guiana.

Materials and methods

A retrospective and comprehensive review of all IUFDs at the French Guiana Western Hospital Center (CHOG) over a 6-year period was performed. The CHOG is the referral center for all of western French Guiana and the populations living along the Maroni River. Deliveries from January 2016 to December 2021 were extracted from medical records and tallied. All cases of IUFD were extracted and entered into a database. IUFD was defined as death at the time of delivery at ≥20 weeks of gestation with Apgar scores of 0 at both 1 and 5 min. The gestational age was calculated according to the craniocaudal length at the first trimester. When patients first presented in their second or third trimester, head circumference was measured to estimate gestational age. In cases of IUFD without antenatal ultrasound, the last menstrual period was used. Terminations of pregnancy and miscarriage were excluded. The following information was included from the maternal chart: demographics, medical history, alcohol, drug and tobacco use, prenatal care, ultrasound scans, delivery parameters, biologic testing, and pathologic examination of the fetus and placenta. Given the presence of specific infections in the territory, the CHOG protocol included systematic screening for syphilis, cytomegalovirus, toxoplasmosis, rubella virus, parvovirus, malaria, leptospirosis, Q fever, Chagas, chikungunya, and dengue virus. In 2016, screening for Zika virus was added, and more recently Tonate virus was included in 2019. If no genetic exploration had been performed prenatally, karyotype or microarray in umbilical sampling at delivery was proposed in cases of malformities or dysmorphic elements. The west French Guiana maternity protocol for managing stillbirth is described in Table 1.

Table 1
Elements of a stillbirth evaluation in west French Guiana hospital center.

Elements of a stillbirth evaluation	Details
Clinical evaluation	Medical and obstetric history, maternal medical condition, previous stillbirth, current pregnancy information clinical circumstances accompanying the stillbirth
Ultrasound examination	Placenta (localization and feature), amniotic fluid, fetus
Biological screening	- Kleihauer test - Liver, kidney, and Thyroid function - Protein c reactive - Infection's screening: Syphilis, cytomegalovirus, toxoplasmosis, rubella virus, Parvovirus, Malaria, Leptospirosis, Q fever, Chagas, Chikungunya Dengue virus, Zika virus, Tonate virus. - Screening for hepatitis B and C if not done before. - Blood culture test if fever - Screening for autoimmune diseases: antiphospholipid antibodies, antinuclear antibodies - Hemoglobin and hemoglobin electrophoresis from the patient and her partner and search for thalassemia alpha. - Hemoglobin A1C test - Vaginal culture test and cytobacteriological examination of urine if need - Ionogram, Heavy metal, and vitamin deficiencies evaluation
At delivery	Clinical examination of placenta and membranes (placental abruption, and umbilical cord abnormality) Physical examination of stillborn baby and photographs, document abnormalities +/- Umbilical, cord sampling for infectious agent or genetic testing by karyotype or microarray Bacteriological analyses of placenta Placental pathology X-ray imaging fetal autopsy after consent of parent
Postnatal check-up	Clinical evaluation Antiphospholipid syndrome (anticardiolipin and β 2-glycoprotein antibodies) and thrombophilias screening according to the medical history

Analysis of risk factors for stillbirth

We performed exhaustive collection of data using medical birth register. Each stillbirth was assigned a cause of death according to an algorithm (the Initial Causes of Fetal Death Evaluation, or INCODE) developed by the Stillbirth Collaborative Research Network [12]. It classifies causes of IUFD in seven groups: maternal medical condition, obstetric complications, maternal or fetal hematologic conditions, fetal abnormalities, placental or fetal infection, pathologic placental conditions, and unexplained. Each cause of fetal death was classified as probable or possible. Probable causes were conditions with a high likelihood of having directly caused the IUFD, and possible causes were potentially involved in a pathophysiologic sequence leading to the death. According to INCODE, not all conditions can be classified as probable or possible causes of death according to the best available evidence; in these cases the conditions were considered present [12]. Isolated histologic chorioamnionitis and being small for gestational age were not considered causes of death [12]. Histologic chorioamnionitis associated with funisitis was assigned as a possible cause of fetal death. Each case was examined by one obstetrician and one consultant in fetal medicine. Fetal growth restriction was defined as fetal weight below the 10th percentile according to INTERGROWTH-21st [13]. Stillbirths were compared to live births that occurred during the same period using data from the computerized anonymized registry that compiles all births within the territory.

Statistical analysis

Collected information was extracted from a computerized delivery registry which is managed by a network of perinatal professionals (Reseau Perinat), and anonymized. The Student's t-test was used to compare continuous variables, and comparison of proportions was performed using the chi-square test or Fisher's exact test, as appropriate. The unpaired Student's t-test and the Mann–Whitney U test were used to

compare groups of continuous normally and non-normally distributed variables, respectively. The analysis was performed using STATA® software (v.17). Univariable and multivariable logistic regression analyses were performed using a step-by-step approach. A high proportion of data were missing for body mass index (BMI) and hemoglobin levels at birth. Much smaller proportions of data were missing for other variables. We used multiple imputation to impute missing values. An analysis of complete cases (missing data were coded as "unknown") was also conducted. A two-sided $P < 0.05$ was defined as statistically significant.

Ethical considerations

In compliance with Regulation (EU) 2016/679 of the European Parliament on the protection of personal data, a privacy impact assessment of the study was carried out according to the methodology described by French regulations, the Commission Nationale Informatique et Libertés' méthodologie de référence MR-004. The work was approved by the hospital's ethics committee (decision CHOG-2022–12).

Results

Study population

During the study period, we identified 18,037 deliveries beyond 20 weeks of gestation. In total, 331 fetuses in 318 stillbirth deliveries were reviewed. The rate of fetal death varied between 1.3 % and 2.1 %, with an average of 1.8 % (95 % confidence interval (CI) = 1.6–2; 331/18037) over the past 6 years. Among fetal deaths, 9 twins and 2 triplets were identified. Among the twin pregnancies, 5 were dichorionic and 4 were monochorionic diamniotic. The median maternal age was 28 years (range 22–34), median gravida was 4 (2−7), and median parity was 3 (1−5). Placental pathology was obtained in 57.4 % (190/331) of cases, and fetal karyotyping was obtained in 13.2 % (44/331). Fetal autopsy was performed in only 0.6 % (2/331) of cases because of cultural or religious concerns.

Baseline characteristics and risk factors for fetal death

Table 2 shows univariable comparisons of maternal demographics, medical and obstetric conditions between the stillbirth groups, and deliveries with live births during the same period.

Women in the stillbirth group were more likely to: be aged 35 years and older; be nulliparous; be obese; smoke during pregnancy; have a scarred uterus; have severe anemia under 8 g/dl; have pre-existing hypertension or diabetes; experience a threatened previous stillbirth; have had inadequate antenatal care (i.e., did not attend their first antenatal appointment at 12 weeks of gestation or earlier); and develop hypertensive disorders during pregnancy.

The most common maternal conditions associated with stillbirth in the study population were obesity > 30 kg/m^2 (31.7 %, 101/318), preeclampsia (18.5 %, 59/318), late presentation to prenatal care with a first visit after first trimester (28 %, 89/318), and inadequate pregnancy care with less than 4 visits during pregnancy (32.7 %, 104/318). Furthermore, 11 % (35/318) of patients had no prenatal visits before stillbirth. Among women who experienced stillbirth, one-third of patients (30.8 %, 98/318) had a hypertensive disorder: preeclampsia in 60.2 % (59/98), gestational hypertension in 24.5 % (24/98), and chronic hypertension in 15.3 % (15/98).

Micronutrient and vitamin deficiencies are frequent in west French Guiana and in populations living along the Maroni River: more than half of patients have an iron deficiency and one-tenth have severe anemia. Heavy metal poisoning is also frequent in these populations including lead poisoning >50 µg/L (16.3 %), aluminum toxicosis >0.37 µmol/L (25 %), and zinc toxicosis >24 µmol/L (5.8 %). Further details are shown in Table 3.

Compared with those having live birth during, women who experienced stillbirth are more likely to have scarred uterus, to be nulliparous, more likely to be aged 35 years and older, to be obese, to smoke during pregnancy, to have severe anemia, to have pregestational hypertension or diabetes disorders, or to had previous stillbirth. During pregnancy resulting in fetal death, pregnant women are more likely to

Table 2
Maternal characteristics and risk factors for stillbirth in an amazonian context: saint Laurent du Maroni maternity ward 2016–2021, results from univariable analysis.

Maternal characteristics and comorbidities	Stillbirth ≥ 20 WG, n (%) (n = 331)	Live born ≥ 20 WG (n = 17170)	P value
Maternal age, median (IQR)	28 (22–34)	26 (21–32)	-
Age over 35 years	19.34 (64/331)	13.5 (2328/17170)	**0.002**
Age under 18 years	11.7 (39/331)	12.1 (2085/17170)	0.8
BMI, median (IQR), kg/m2	28.4 (22–32)	26.8 (22–30)	-
Obesity >30 kg/m^2	31.7 (101/318)	26.7 (225/842)	**<0.001**
BMI ≤18 kg/m^2	4.3 (10/228)	3.5 (30/842)	0.5
Gravida, median (IQR)	4.9 (2–7)	4 (2–6)	-
Parity, median (IQR)	3.2 (0–5)	2.7 (1–4)	
Nulliparous	27.8 (92/331)	23.1 (3971/17170)	**0.04**
Scarred uterus	26.6 (88/331)	12.9 (2 221/17170)	**<0.001**
Substance use			
Tobacco use	0.6 (2/331)	0.17 (30/17 170)	0.12[a]
Alcohol use	1.21 (4/331)	0.4(69/17 170)	**0.04****
Drug use	0.3 (1/331)	0.15 (25/17 170)	0.3[a]
Adequate antenatal care	59 (182/308)	62 (10 526/16 950)	**<0.001**
No visit during pregnancy	11 (35/318)	2.14 (344/16 048)	**<0.001**
Previous stillbirth	10.8 (36/331)	1.7 (66/3890)	**<0.001**
Chronic hypertension	10.5 (35/331)	1.5 (262/17170)	**<0.001**
Pregestational diabetes	4.6 (15/325)	3.4 (580/17067)	0.23
Gestational diabetes	4.4 (13/318)	3.2 (545/17170)	0.2
Preeclampsia	18.5 (59/318)	4.6 (798/17170)	**<0.001**
Eclampsia	1.2 (4/318)	0.30 (51/17 170)	**0.02**[a]
Severe anemia ≤8 g/dl	8.1 (26/318)	2.8 (30/1042)	**0.001**
Sickle cell disease	1.8 (6/331)	0.6 (114/17170)	**0.043**
HIV infection	2.1 (7/331)	1.1 (119/17 770)	**0.08**

Discrepancies between the denominator for some of the categories and the number of pregnancies included in the study are due to missing data.
Bold indicates statistical significance.
[a] Fisher's exact

Table 3
Intoxication, micronutrient, and vitamin deficiencies in women with fetal death *in utero* living in west French Guiana and along the Maroni River.

Micronutrient deficiencies	n/N (%)
Severe anemia ≤8 g/dl	26/318 (8.1)
Ferritin ≤30 ng/mL	125/242 (51.6)
Vitamin B12 deficiency	30/204 (14.7)
Hypokalemia <3,5 mmol/L	142/318 (44.6)
Severe hypokalemia <2.5 mmol/L	7/318 (2.1)
Vitamin A deficiency <0,7 µmol/L	13/72 (18)
Vitamin D deficiency <25 nmol/L	6/72 (8.3)
Intoxications and Heavy metal poisoning	
Lead poisoning >50 µg/L	38/232 (16.3)
Aluminum toxicosis > 0,37 µmol/L	21/82 (25.6)
Zinc toxicosis > 24 µmol/L	3/51 (5.8)
Vitamin D toxicosis > 250 nmol/L	2/72 (2.7)

Discrepancies between the denominator for some of the categories and the number of pregnancies included in the study are due to missing data (N = the number of women in whom the analysis was performed, n = number of pathological tests)
Nutritional deficiencies and intoxications were not documented in control group.

receive inadequate antenatal care (not to attend their first antenatal appointment at 12 weeks of gestation or earlier) or to develop hypertension disorders during pregnancy. Table 4 shows multivariate regression results with adjusted odds ratios.

The most common causes of stillbirth were obstetric complications (33.8 %, 112/331) (Table 5). In this group, intrapartum fetal death with asphyxia associated with labor < 26 weeks (57 %, 64/112) and placental abruption (26 %, 29/112) were the two most prevalent sub-groups. Overall, the rate of placental abruption was 20.5 % (68/331) and the median gestational age was 34 weeks. About 7.3 % (5/68) of the women had a history of placental abruption and 17.6 % (12/68) did not receive prenatal care. Placental abruption was associated with hypertensive disorder in almost half of the patient (32/68, 47 %).

Maternal conditions are the second major cause of stillbirth in the west French Guiana population (24.2 %, 80/331). This mainly includes hypertensive disorder of pregnancy (82.5 %, 66/80), with 72.7 % (48/66) having preeclampsia and 12 % (8/66) gestational hypertension without proteinuria. A fetal growth restriction and/or abnormal doppler could be associated. Four cases were complicated with hypertensive crisis.

In the present study, 6 % (20/331) of deaths were due to fetal abnormalities: 55 % (11/20) were chromosomal abnormalities (aneuploidies and deletions) and 45 % (9/20) were structural anomalies without chromosomal anomaly.

Infections have contributed significantly to stillbirths in the study population. Among infection-related stillbirths (4 %, 13/331), 61.5 % were categorized as probable and 38.5 % were categorized as possible. Emerging infectious diseases such as Zika virus (3/13), and re-emerging infections such as syphilis (5/13), were reported. Three infection-related deaths were due to bacterial pathogens, one resulted from malaria, and one from dengue fever. For Zika virus, fetal infection was confirmed by polymerase chain reaction in placental tissue and amniotic fluid. The fetuses presented severe central nervous system anomalies specific to Zika virus including akinesia and club feet.

Severe urinary (3/8), digestive (1/8), and cutaneous (4/8) maternal infections resulted in fetal death in 2.4 % (8/331) of cases. In total, 16 % (53/331) of cases that had infections that were present from admission to delivery were without an established causal link with fetal death: leptospirosis (11), cytomegalovirus (2), syphilis (7), toxoplasmosis (2), dengue virus (6), Zika virus (6), Tonate virus (1), Q fever (3), and Covid-19 (7). Overall, documented infection was present at admission in 16 % of women who experienced stillbirth. Among them, stillbirth-related infection was retained as possible or probable in 6.3 % (21/313) of cases according to INCODE classification. Finally, 19.3 % (64/331) of fetal deaths remained unexplained.

Table 4
multivariate analysis, risk factors for stillbirth in Saint Laurent du Maroni maternity (January 1, 2016, to December 31, 2021).

Maternal and Obstetric Characteristics	Odds ratio	[95 % conf. interval]
Age over 35 years	1.3	.88–2.16
BMI > 30 kg/m^2	1.1	.76–1.58
Nulliparous	1.7	**1.16–2.62**
Scarred uterus	1.9	**1.26–2.85**
No antenatal visit	17.5	**5.68–53.95**
Previous stillbirth	2.1	**1.07–4.38**
Chronic hypertension	8	**3.64–17.61**
Preeclampsia	2.4	**1.46–4.15**
Severe anemia ≤ 8 g/dl	2.1	**1.00–4.67**
Pregestational diabetes	3.3	**1.01–11.26**

Abbreviations: BMI, body mass index. BMI was calculated as weight in kilograms divided by height in meters squared at beginning of the pregnancy. A high proportion of data were missing for BMI and hemoglobin revels.
Multiple pregnancies are excluded of multivariate analysis. Bold indicates statistical significance.

Table 5
Causes of fetal death in the subgroup with obstetric complications in French Guiana population (January 1, 2016, to December 31, 2021), according to INCODE classification (n = 112).

Obstetric complications	n	Frequency (%)
Fetal maternal hemorrhage	5	4.5
Intrapartum fetal death with asphyxia associated with labor < 26 weeks	64	57
Hypoxic intrapartum fetal death > 26weeks	5	4.5
Placental abruption	29	26
Complications of multiples gestation	6	5.4
Uterine rupture	1	0.9
Uteroplacental insufficiency	2	1.8

Discussion

Principal findings of the study

Our study indicated that obstetrical complications, placental abruption, and hypertensive disorders were the most common causes of fetal death in the area of western French Guiana. The rate of stillbirth (1.8 %) was two to three times higher than that reported in metropolitan France [14], England [15], and Canada [16]. For 2019, Hug et al. estimated that two million babies were born stillborn at 28 weeks of gestation or more, for a global rate of 13.9 stillbirths per 1000 total births (90 % uncertainty interval 13.5–15.4) [17]. This rate varied widely across regions, from 22.8 stillbirths per 1000 total births in west and central Africa to 2.9 in western Europe [17]. The main risk factors were poor pregnancy care, maternal obesity (>30 kg/m; 31.7 %), and anemia (≤8 g/dl; 8.1 %). In infection-related stillbirth cases, the likely causes were mosquito-borne diseases (e.g., Zika virus and malaria) and re-emerging infectious agents such as syphilis. Stillbirth remained unexplained in one of five patients (19.3 %). Social deprivation and a poor health care system are likely to be potentiating factors. The impact of heavy metal poisoning and nutritional deficiencies, which are widespread in this population [8,18], remains unclear. In a study conducted by Rimbaud et al., 25 % of pregnant women living in west French Guiana have a blood lead level ≥ 50 µg/L and 5 % exceed 100 µg/L [18].

Comparison with other studies

Our findings on the impact of vasculo-renal pathology are similar to what has been reported in other studies in similar cohorts [10,16,19]. Obstetric complications, the most prevalent cause of stillbirth, is highly related to multiparty and prematurity. In western French Guiana, social deprivation and immigration are relatively high. This area also has the highest preterm birth rate and perinatal mortality rate among all French territories (13.5 % of newborns were born before 37 weeks of gestation) [5].

The second major cause of fetal death was maternal medical conditions during pregnancy, particularly complications associated with hypertensive disorder. This is likely related in part to the ethnic composition of the population, which is predominantly Afro-Caribbean, as well as the low socioeconomic level. The association between maternal racial origin and adverse outcomes in pregnancy has been described [20]. In a review of preventable stillbirths, more than 200,000 stillbirths have been estimated to be attributable to pre-eclampsia and eclampsia (principally in low-income countries) [11].

The study population showed a low rate of smoking and alcohol consumption during pregnancy. However, pregnant women in French Guiana are known to consume clay [7] which can induce iron deficiency and anemia. Our data shows that 8 % of patients had a hemoglobin level less than 8 g/dl on admission for delivery.

Viral and bacterial infection is a known causative factor for stillbirth within the study region [21–23]. Infection can lead to fetal death

through several mechanisms such as direct fetal infection, placental infection leading to placental insufficiency (syphilis or malaria), severe maternal illness, and infection involved in previable or periviable preterm births. The causal link between infection and stillbirth remains difficult to demonstrate, especially for bacterial pathogens. Saint Laurent hospital, the single reference center in the area, provides care to the entire population of west French Guiana, residents along the Maroni River and sometimes from other parts of Latin America. Some precarious population like illegal gold miners are particularly exposed to several infection (malaria, HIV, leishmaniasis.) and Heavy metal poisoning [24]. Emergent and reemergent infectious diseases such as syphilis [25] and Zika virus are known to cause stillbirth [3,22]. Thus, testing for specific organisms, such as parvovirus and syphilis, has been recommended [23]. Western French Guiana has experienced various viral epidemics, such as Chikungunya in 2014, Zika virus in 2016, dengue virus in 2013 and 2020, and recently COVID-19. However, the presence of these viral agents is insufficient evidence on its own to support infection as a probable or possible cause of death [12,26]. We have previously reported adverse outcomes including stillbirth after leptospirosis infection and dengue infection [27]. In a previous study by Carles et al., fetal death was found to occur in 50 % of cases of infection after symptomatic leptospirosis [28]. Adverse fetal outcomes associated with dengue infection have been described only in symptomatic dengue during pregnancy [29]. There is evidence of an association between COVID-19 in pregnancy and stillbirth [4,30]. It is the consequence of rare cases of fetal infection [31] and mainly due to the placental and maternal consequences of infection. In addition to the direct impact of COVID-19 on pregnancy outcomes, there is evidence that the pandemic indirectly affected women and child health by the modification of healthcare systems and the difficulties of access to care during periods of confinement [32]. For invasive microbial infections, the most common bacteria associated with stillbirths were *Escherichia coli*, group B streptococcus, and enterococcus [33]. Identification of infectious agents can be more challenging in low-income countries because identification requires autopsy, viral and bacterial cultures, and/or equipment to perform viral-specific polymerase chain reaction in fetal vital organs (lung, liver, or brain) [12]. These infections are involved in previable or periviable preterm births. Both intra-amniotic infection and inflammation ascertained by amniocentesis have been identified in patients with cervical insufficiency [34]. Administration of antibiotics (ceftriaxone, clarithromycin and metronidazole) has been associated with treatment success in approximately 60 % of cases [35]. The lack of testing facilities, concerns regarding testing cost, and cultural or religious objections regarding fetal autopsy are limiting factors for evaluation of stillbirth in low- and middle-income countries. In our study, fetal deaths due to infection are probably underestimated. Even with adequate screening procedures, the causal link between infection and stillbirth remains difficult to demonstrate, especially for bacterial pathogens.

Finally, we found that 19 % of fetal deaths were unexplained, a proportion lower than reported by other studies [16,33]. This proportion is known to vary depending on the classification system, and the INCODE classification used here is strongly based on fetal and placental cultures performed after autopsy [12].

Main strengths and limitations of the study

To our knowledge, this is the first study of stillbirth causes and risk factors in western French Guiana and around the Maroni River. The findings may help health providers manage the care of women living in this area or those residing in Amazonian regions with similar ethnic and environmental profiles. Our data collection protocol was broad and systematic to limit the exclusion of important etiologies. Because of economic considerations, few centers in Latin America can provide comprehensive infection screening like that available in experienced centers such as the Pasteur Institute Cayenne. Our findings may be useful to healthcare providers, as well as local and international authorities for the development of appropriate management protocols for pregnant women in these lesser-known areas.

The findings of this study must be considered in light of several study limitations. First, the study is limited by the retrospective chart. Second, the lack of autopsy was an important limitation. In our population, cultural or religious concerns and misconceptions regarding the autopsy procedure are common. Korteweg et al. have found that placental pathology is helpful in identifying a cause of fetal death in 96 % of cases [36]. Information about ethnicity was not collected in the patient medical records and this data could have helped to identify possible ethnic inequalities in stillbirth rates. We focused on medical history, biologic results, and the placenta to identify the cause of death. Moreover, less invasive examination or alternatives, such as postmortem high-field magnetic resonance imaging (MRI), might be an acceptable approach to considerer when patient barriers to fetal autopsy exist. Postmortem MRI can be used to identify major lesions. For example, one study showed results consistent with autopsy findings in 95 % of cases [37]. Using postmortem MRI would likely be beneficial in our region, however, it remains limited due to a lack of resources. Preventive actions include fighting malnutrition, increased screening for sexually transmitted infections and improved access to care. Cross-border cooperation remain crucial to ensure early monitoring of pregnancy to reduce inequality in access to health care in same isolated areas.

Conclusion

Obstetric complications, maternal complications, and infection were found to have important roles in stillbirths in the Amazonian basin. Lifestyle, social deprivation, and a poor health system adversely affect pregnancy in this area. In addition to standard investigations such as fetal autopsy, placental pathology, and genetic testing, patients should be offered broad infection screening with special focus on mosquito-borne diseases (Zika virus, dengue, and malaria) and re-emerging infectious agents such as syphilis. Travelers returning from Amazonian basin should be screened for these infections in case of fetal anomalies. Urgent action must be taken to address the modifiable factors that are directly or indirectly involved in fetal deaths. Finally, prospective comparative studies are needed to better understand the role of intoxication and malnutrition in stillbirths occurring in Amazonian pregnant women.

Declaration of Competing Interest

The authors report no declarations of interest.

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