

## Factors Associated with Fetal Death in Utero: Case - Control Study in a Reference Hospital Structure in Cameroonian Metropolitan Area

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### Summary

**Introduction:** Intrauterine fetal death is the death of the fetus in the uterus beyond 22 weeks of gestational age and/or weighing 500g. It is frequent in developing countries, showing that, efforts and progress still need to be made in the follow-up of high risk pregnancies.

**Objective:** The general objective of our study was to identify the associated factors of intrauterine fetal death at the Yaounde Gynaeco-Obstetric and Pediatric Hospital.

**Methodology:** We conducted a case-control study at the Yaounde Gynaeco-Obstetric and Pediatric Hospital from January 1<sup>st</sup> to April 30<sup>th</sup> 2021. The cases were all women admitted in the service of obstetrics and gynaecology with fetal death from 22 completed weeks of gestation and above confirmed by ultrasound and willing to participate in the study and the controls were any woman admitted in the service who gave birth to a live fetus and willing to participate with maternal age as the paring criteria. We recruited 42 cases for 84 controls making one case for two controls. The statistical analysis was done using SPSS software version 23.0 and excel 2016.

**Results:** The associated factors for intrauterine fetal death found during our study were: being single (ORa=3,6; CI= (1,3-1,9)), less than four antenatal consultations (ORa=3,6 ;

CI= (1,3-10,1)) and being followed by a midwife (ORa=6,6 ; CI= (1,0-41,7)).

**Conclusion:** The associated factors are: being single, less than

four antenatal consultations and being followed by a midwife.

**Keywords:** Intra Uterine Fetal Death; Associated Factors; Cameroon

## Introduction

Fetal death in utero (FIDU) is defined by the World Health Organization (WHO) as the death of an in-utero fetus beyond 22 weeks of amenorrhea or weighing at least 500g. Since the 2014 recommendations, the Collège National des Gynécologues et Obstétriciens Français (CNGOF) has adopted a broader definition by including all in-utero deaths beyond 14 weeks of amenorrhea [1]. In utero fetal death is a serious event with a prevalence of 2% worldwide per year of which 98.0% of cases are in developing countries. The frequency of fetal death varies from one country to another depending on the socio-economic standard of living and the quality of pregnancy management. In Europe, the 2014 study by Delabaerea *et al.* covering 24 countries found a rate of in utero fetal death ranging from 0.17 to 0.49% of births [2]. In Africa, the available data are variable: in 2018 a study showed a prevalence of 3.69% in Equatorial Guinea [3]; 13.98% in Congo in 2016 [4]; 5.22% in Madagascar in 2013 [5]. In Cameroon a study done by Nkwabong *et al.* at the Yaounde University Hospital Centre showed in 2012 a rate of fetal death in utero at 3.40% [6]. High rates in Africa compared to Europe show how much progress and effort still needs to be made in monitoring pregnancies, especially those at risk. Several risk factors have been identified and the most frequent are: obesity, maternal age over 35 years, smoking, hypertension during pregnancy [7]. The etiologies found were: funicular anomalies, maternal haemorrhage, chromosomal and malformative anomalies, infections [7]. The diagnosis of certainty is made by ultrasound and the etiological diagnosis may require specific examinations such as fetal autopsy, placenta analysis, fetal karyotype [7]. Fetal death in utero is responsible for several complications that may jeopardize the maternal vital prognosis. These complications are mainly haemorrhagic by disseminated intravascular coagulation (DIC) and retention of placental debris, infectious (chorioamnionitis) and especially psychological [8]. The psychological consequences will most often have repercussions on subsequent pregnancies. It is therefore urgent and important for the medical team to develop a preventive health policy for fetal death in utero, by identifying the risk factors and etiologies in order to reduce the rate of fetal death in utero. Since the rates are high in Africa, we wanted to assess the extent of the problem in a referral hospital specializing in the health of the mother-child couple. The general objective

of this study was to study the factors associated with fetal death in utero in order to contribute to the improvement of the well-being of the mother-child couple in Yaoundé.

## Methodology

**Setting, type and period of study:** This was a case-control study conducted in gynecology-obstetrics the Yaoundé Gynecology-Obstetrics and Pediatrics Hospital from "January 1 to April 30, 2021.

**Study population and sample:** This study concerned all pregnant women admitted to the Gynaecological-Obstetric and Paediatric Hospital of Yaoundé during the period of our research for fetal death in utero. The latter were compared to a group of controls from the same facility and the same period with maternal age as a matching criterion. Each case of in utero fetal death was matched with two controls. Thus, 42 cases were matched to 84 controls.

**Inclusion and exclusion criteria:** The study included cases of in utero fetal death and their controls selected according to the selection criteria described below, and excluded cases of intrapartum death, therapeutic termination of pregnancy, voluntary termination of pregnancy, death before viability, or any woman who withdrew her consent.

### Definition of cases and controls:

**Case:** Woman admitted to the gynecology and obstetrics department for ultrasound confirmed in utero fetal death beyond 22 weeks of amenorrhea and consenting to participate in the study.

**Controls:** Women admitted to the gynecology and obstetrics department who delivered a live fetus and who consented to participate in the study.

**Data collection and statistical analysis:** Socio-demographic, clinical and therapeutic data were collected on a pre-established data collection form submitted to the women concerned. The data were entered and analyzed using the Statistical Package of Social Sciences (SPSS) software version 23.0. Microsoft Excel

and Word application software were used for data processing. Chi-square test was used to measure the association between categorical variables. Then a univariate analysis followed by a multivariate analysis was done using the multinomial logistic regression method to search for the factors associated with fetal death. The confidence interval was 95%. When the P value was less than 0.05, the result was considered statistically significant.

## Results

Single women were 4.9 times more likely to have an in utero fetal death. There was no association between region of origin, place of residence, occupation, education level of the patients and the occurrence of in utero fetal death (Table 1).

**Table 1:** Socio-demographic characteristics

Variables	Case	Witnesses	OR [95% CI]	p-value
	N= 42 n (%)	N=84 n (%)		
<b>Age groups (in years)</b>				
[15-20]	1 (2,4)	6 (7,1)	0,3 [0,0-2,7]	0,256
[20-25]	10 (23,8)	15 (17,9)	1,4 [0,6-3,5]	0,287
[25-30]	14 (33,3)	19 (22,6)	1,7 [0,7-3,9]	0,142
[30-35]	9 (21,4)	25 (29,8)	0,6 [0,3-1,5]	0,219
[35-40]	5 (11,9)	13 (15,5)	0,7 [0,2-2,2]	0,402
[40-45]	3 (7,1)	6 (7,1)	1,0 [0,2-4,2]	0,654
<b>Marital status</b>				
Single	36 (85,7)	46 (54,8)	<b>4,9 [1,9-13,0]</b>	<b>0,001</b>
Married	6 (14,3)	38 (45,2)		
<b>Place of residence</b>				
Urban	31 (73,8)	69 (82,1)	0,6 [0,3-1,5]	0,195
Rural	11 (26,2)	15 (17,9)		
<b>Region of origin</b>				
Adamaoua	0 (0)	1 (1,2)	1,5 [1,3-1,7]	0,667
Center	15 (35,7)	24 (28,6)	1,4 [0,6-3,1]	0,268
East	1 (2,4)	1 (1,2)	2,0 [0,1-33,2]	0,557
Far North	0 (0)	4 (4,8)	1,5 [1,3-1,7]	0,193
Coastal	6 (14,3)	6 (7,1)	2,2 [0,6-7,2]	0,166
North	0	3 (3,6)	1,5 [1,3-1,7]	0,293
West	15 (35,7)	34 (40,5)	0,8 [0,4-1,7]	0,375
Northwest	2 (4,8)	9 (10,7)	0,4[0,9-2,0]	0,222
South	3(7,1)	1 (1,2)	6,4[0,6-63,4]	0,108
Foreign	0(0,0)	1 (1,2)	1,5[1,3-1,7]	0,667
<b>Profession</b>				
Housekeeper	9 (21,4)	21 (25,0)	0,8 [0,3-2,0]	0,417
Public sector employee	4 (9,5)	17 (20,2)	0,4 [0,1-1,3]	0,100
Private sector employee	6 (14,3)	6 (7,1)	2,2 [0,7-7,2]	0,166
Informal sector employee	12 (28,6)	26 (31,0)	0,9 [0,4-2,0]	0,476
Pupil/Student	11 (26,2)	14 (16,7)	1,8 [0,7-4,3]	0,152
<b>Level of study</b>				
Not in school	0	4 (4,8)	1,5 [1,3-1,7]	0,193
Primary	10 (23,8)	10 (11,9)	2,3 [0,9-6,1]	0,074
Secondary	12 (28,6)	32 (38,1)	0,6 [0,3-1,4]	0,196
Superior	20 (47,6)	38 (45,2)	1,1 [0,5-2,3]	0,474

Nulliparity and previous in utero fetal death were associated with the occurrence of in utero fetal death and increased the risk of its occurrence by 2.1 [C.I. 1.0-4.5] and 3.4 [C.I. 1.2-9.8] respectively. Women with fewer than four antenatal contacts, fewer than three

doses of intermittent preventive treatment for malaria, and those attended by midwives had 3.7 [CI 1.5-8.8], 2.5 [CI 1.2-5.4], and 5.5 [CI 1.0-29.8] times the risk of in utero fetal death respectively (Table 2).

**Table 2:** Clinical characteristics of patients

Variables	Case	Witnesses	OR [95% CI]	p-value
	N= 42 n(%)	N=84 n(%)		
<b>Body Mass Index</b>				
Underweight	0	2 (2,4)	1,5 [1,3-1,7]	0,443
Normal	10 (23,8)	29 (34,5)	0,6 [0,3-1,4]	0,153
Overweight/Obesity	32 (76,2)	53 (63,1)	1,9 [0,8-4,3]	0,100
<b>Gestité</b>				
Primigeste(G1)	12 (28,6)	17 (20,2)	1,6 [0,7-3,7]	0,204
Paucigest(G2-G4)	16 (38,1)	41 (48,8)	0,6 [0,3-1,4]	0,171
Multigeste(G5-G6)	9 (21,4)	18 (21,4)	1,0 [0,4-2,4]	0,596
Large Multigeste (G7)	5 (11,9)	8 (9,5)	1,3 [0,4-4,2]	0,448
<b>Parity</b>				
Nullipare(P0)	20 (42,9)	25 (28,6)	<b>2,1 [1,0-4,5]</b>	<b>0,040</b>
Primiparous(P1)	9 (21,4)	20 (23,8)	0,9 [0,4-2,1]	0,476
Paucipare(P2-P4)	9 (23,8)	30 (35,7)	0,6 [0,2-1,3]	0,124
Multipare(P4-P6)	2 (7,1)	7 (8,3)	0,8 [0,2-3,4]	0,559
Large multiparous (P7)	2 (4,8)	2 (3,6)	1,3 [0,2-8,4]	0,559
<b>History of fetal death in utero</b>	10 (23,8)	7 (8,3)	<b>3,4 [1,2-9,8]</b>	<b>0,019</b>
<b>History of abortion</b>	14(33,3)	25(29,8)	1,2 [0,5-2,6]	0,416
<b>History of caesarean section</b>	2(4,8)	10(11,9)	0,4 [0,8-1,8]	0,163
<b>Nature of the pregnancy</b>				
Singleton	39 (92,9)	79 (94,0)	0,8 [0,2-3,6]	0,535
Multiple	3 (7,1)	5 (6,0)		
<b>Number of ANC* performed</b>				
< 4	16 (38,1)	12 (14,3)	<b>3,7 [1,5-8,8]</b>	<b>0,003</b>
≥ 4	26 (61,9)	72 (85,7)		
<b>First NPC* in the first quarter</b>	17 (40,5)	43 (51,2)	0,6 [0,3-1,4]	0,172
<b>ANC* provider</b>				
Gynecologist-obstetrician	19 (45,2)	49 (58,3)	0,6 [0,3-1,2]	0,115
General practitioner	2 (4,8)	8 (9,5)	0,4 [0,1-2,3]	0,289
Midwife	5 (11,9)	2 (2,4)	<b>5,5 [1,0-29,8]</b>	<b>0,041</b>
Nurse	16 (38,1)	25 (29,8)	1,4 [0,7-3,1]	0,229
<b>Iron/folicacidsupplementation</b>	38 (92,7)	72 (85,7)	2,1 [0,6-7,9]	0,205
<b>Use of LLINs**.</b>	36 (87,8)	76 (90,5)	0,8 [0,2-2,5]	0,430
<b>Number of IPTs***.</b>				
< 3 doses	24 (58,5)	30 (36,1)	<b>2,5 [1,2-5,4]</b>	<b>0,015</b>
≥ 3 doses	17 (41,5)	53 (63,9)		

ANC = antenatal consultation, IPT = intermittent preventive treatment, LLIN = long-lasting insecticidal net

Regarding fetal characteristics, sex and presentation were not related to the occurrence of in utero fetal death, but male sex was the most represented with a percentage of 59.5% and 79.1% of cases were born in cephalic presentation. Prematurity multiplied the risk of in utero fetal death by 7.8 [CI: 3.3-17.8]. A weight of

less than 2500g was associated with in utero fetal death with a risk multiplied by 6.7 [CI : 3.0-15.2] (Table 3).

In multivariate analysis, the independent factors associated with in utero fetal death were single status, fewer than four prenatal visits, and midwives as providers of prenatal visits ( $p < 0.05$ ) (Table 4).

**Table 3:** Population distribution by fetal characteristics

Variables	Case	Witnesses	OR [95% CI]	P-value
	N= 42 n(%)	N=84 n(%)		
<b>Sex</b>				
Male	25(59,5)	50(59,5)	1,0(0,5-2,1)	0,575
Female	17(40,5)	34(40,5)	1,3(0,6-2,8)	0,284
<b>Gestational age</b>				
[22-37 [SA	29(69,0)	18(20,9)	<b>7,8( 3,4-17,8)</b>	<b>0,020</b>
[37-42 [SA	13(31,0)	66(79,1)	<b>0,1(0,1-0,3)</b>	
<b>Presentation</b>				
Cephalic	34(79,1)	74(88,1)	0,6(0,2 -1,5)	0,303
Headquarters	7(16,7)	9(10,7)	1,9(0,7-5,4)	0,162
Transverse	1(2,4)	1(1,2)	1,0(0,1-11,2)	0,739
<b>Weight</b>				
< 2500g	26(61,9)	15(17,9)	<b>6,7(3,0-15,2)</b>	<b>0,031</b>
> 2500g	16(38,1)	69(82,1)	<b>0,2(0,1-0,3)</b>	

**Table 4:** Multivariate analysis

Variables	Case	Witnesses	OR [95% CI]	p-value
	N=42 n (%)	N= 84 n (%)		
<b>Marital status</b>				
Single	36 (85,7)	46 (54,8)	<b>3,6 [1,3-9,9]</b>	<b>0,015</b>
<b>History of fetal death in utero</b>	10 (23,8)	7 (8,3)	3,0 [0,9-9,7]	0,070
<b>Number of ANC* performed</b>				
< 4	16 (38,1)	12 (14,3)	<b>3,6 [1,3-10,1]</b>	<b>0,013</b>
<b>ANC* provider</b>				
Midwife	5 (11,9)	2 (2,4)	<b>6,6 [1,0-41,7]</b>	<b>0,045</b>
<b>Number of IPTs***.</b>				
< 3 doses	24 (58,5)	30 (36,1)	1,4 [0,6-3,7]	0,415
<b>Nulliparity</b>	20(42,9)	25(28,6)	1,7 [0,7-4,2]	0,252
<b>Gestational age 37 SA&lt;</b>	29(69,0)	18(20,9)	5,2 [2,1-13,1]	0,061
<b>Fetal weight 2500g &lt;</b>	26(61,9)	15(17,9)	4,8 [1,9 – 9,8]	0,072

## Discussion

### Socio-demographic characteristics

**Age:** We found that pregnant women with in utero fetal death had an age range between 15 and 44 years. This age is comparable to the 15 to 45 years found by Diallo *et al.* in 2015 at the Regional Hospital of Mamou [9]. In our study, the age range of 25 to 30 years was the most represented (29.5%) but was not associated with the occurrence of fetal death in utero. This can be explained by the fact that this is the reproductive age.

**Educational level:** In our study, we found a predominantly secondary and higher educational level (80.9%) unlike Kangulu *et al.* in 2016 who found a primary level in majority [4]. This can be explained by the fact that our patients live in the city and had the opportunity to be educated.

**Place of residence:** Rural residence was also identified as an associated factor by Kangulu *et al.* in 2016 with 3.7 times more risk of in utero fetal death [4] unlike our study which showed that majority of the patients resided in urban area (79.4%) and this was not associated with in utero fetal death.

### Factors associated with in utero fetal death

**Marital status:** Single women were the most affected in our series (85.7%) which is comparable to the study conducted in Guinea in 2018 by Soumah *et al.* [3] who found 79.3% of single women in their population. We found during our study that unmarried women were 4.9 times more likely to have a fetal death in utero. This phenomenon could be explained by the fact that they were carrying an unwanted pregnancy and found themselves without any financial assistance due to the abandonment of the parents and/or the genitor, and were therefore unable to carry out their prenatal follow-up correctly.

**History of fetal death in utero:** A history of fetal death in utero is a significant associated factor of fetal death in utero. These results were confirmed in two meta-analyses by Flénady including five studies and finding a 2.6-fold increase in the risk of death in subsequent pregnancies (95% CI 1.5-4.5) [10]. Our study found that a history of fetal death in utero multiplies the risk of fetal death in the next pregnancy by 3.4 [1.2-9.8] with a significant p value of 0.019.

**Parity:** We found nulliparous as a factor associated with in utero fetal death which multiplied the risk by 2.1. Flénady *et al.* in 2011 [10] showed that there was an increased risk of fetal death of 1.42 (95% CI 1.33-1.51). These patients represent a population more exposed to certain pathologies such as pre-eclampsia which is a cause of fetal death in utero.

**Pregnancy monitoring:** Poor pregnancy monitoring increases the risk of in utero fetal death [5, 11]. The new recommendations of the World Health Organization state that at least eight good quality prenatal visits should be made. Pregnancy follow-up should be done by a gynecologist, intermittent preventive treatment should be taken every month from sixteen weeks of amenorrhea with at least three doses. In our context, these new recommendations are not yet really applied and we still consider the four refocused consultations. This justifies the fact that we have had fewer than four prenatal consultations and less than three doses of intermittent malaria treatment and being followed by a midwife who is not suitable for consultation as a factor associated with fetal death in utero.

**Fetal characteristics:** Our study was able to establish an association between prematurity and fetal death in utero. Prematurity was associated with fetal death in utero in 69.0% of cases. This result is comparable to that found by Andriamandimbison *et al.* in Madagascar in 2013, who showed that fetal death in utero was associated with prematurity in 64.4% of cases [5]. This is due to the fact that when fetal death is diagnosed the delivery was done at that gestational age. Fetal weight was associated with in utero fetal death when the weight was less than 2500g and increased the risk by 6.7 times. Tensay *et al.* in 2017 in his study on determinants of in utero fetal death found that fetuses with weight less than 2500g died more compared to those with weight more than 2500g (OR = 0.27, 95% CI 0.14-0.53) [12]. Our results can be explained by the fact that the weight depends on the gestational age and the majority of our cases of fetal death in utero were premature babies who could not reach the normal weight of a full term fetus which is 2500g and also the occurrence of hypertensive pathology which can cause fetal suffering and impede fetal growth.

**Limitations of the study:** Inability to verify the veracity of information derived from the interview.

## Conclusion

This study was conducted to investigate the factors associated with fetal death in utero at the Yaounde Gynaecological-Obstetric and Paediatric Hospital. It was found that the associated factors are: celibacy, less than four prenatal contacts and follow-up by a midwife. Any pregnant woman presenting these factors must benefit from a closer follow -up by respecting the schedule of prenatal consultations as recommended by WHO and be followed by a gynaecologist or a better trained midwife.

## Conflict of Interest

No conflict of interest declared.



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