Perinatal mortality following perinatal asphyxia & birth environment: Case-control study

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Abstract. Perinatal asphyxia (PA) is a major health problem, responsible for high mortality and a wide range of morbidity. Several factors play a part in the occurrence of perinatal mortality during asphyxia. The aim of this work was to identify factors predictive of perinatal mortality following PA, using an unmatched case-control study. Thus, 31 cases and 126 controls were identified with a total of 157 newborns suffering from PA. It was carried out during April 1 to June 30, 2022, at the Mohammed VI University Hospital in Marrakech. The socio-demographic, clinical, and biological data of the newborns were collected using an evaluation grid. In this series, the sex ratio was 0.96 and the case-fatality rate 20%. The results showed that the factors showing a statistically significant association in the genesis of mortality in PA cases were : intrauterine growth retardation [(ORA= 4711,799), 95%, IC : (48,964 , 453416,766)] ; maternal history [(ORA =31,876, 95%,CI : (1,346; 755,149)] ; Apgar index after 5 min less than or equal to 3: [(ORA=139,75) ,95%, CI : (16,523 ; 1182,01)]; and congenital malformations : [(ORA=241,435) ,95%, CI : (6,044 ; 9644,748)]. Consequently, addressing these factors is crucial to identify high-risk newborns at an early stage and to implement appropriate measures. The goal is to eliminate avoidable morbidity and disability.

Key words: Apgar index, intrauterine growth retardation, newborn, perinatal asphyxia, perinatal mortality, risk factor.

Introduction

The moment of birth is a very sensitive phase in a human life. In certain situations, the onset of perinatal asphyxia (PA) threatens the well-being of the newborn. PA is an anomaly resulting from an alteration in maternal-fetal exchanges, of significant duration and intensity [1, 2]. As a result, the newborn can hardly, or can't breathe at birth [1]. The World Health Organization (WHO) defines PA as the failure to establish or initiate normal breathing at birth [1, 3]. PA combines clinical and biological criteria such as fetal heart rate (FHR) abnormalities, cardiorespiratory and neurological depression (an APGAR score of less than 7 at 5 minutes of life), with evidence of acute hypoxia responsible for severe acidemia (arterial blood pH <7 and/or a base deficit ≥ 12 mmol/l) [1, 4, 5]. Consequently, PA can lead to various complications in newborns, including multi-organ failure, damage to the hemostatic system, anoxic-ischemic encephalopathy leading to cerebral palsy, and perinatal mortality [3, 6, 7, 8, 9]. The factors causing PA can have a maternal, fetal, or funicular origin. They can also be linked to the birth environment which includes a lot of factors as delivery complications, obstetrical practices, availability of specialized care and immediate care, (Infection, hypothermia etc.). These factors can contribute to the occurrence of perinatal asphyxia and its potential consequences [7, 10, 11, 12, 13]. Despite the development of mother-child health care, PA is still responsible for high neonatal morbidity and mortality rates. Indeed, every year, PA causes around 4 million neonatal deaths worldwide [9, 14]. These rates increase considerably in low-income countries. In Morocco, it is a serious problem, affecting 8 to 10 full-term newborns per 1,000, compared with 2 to 3 cases per 1,000 in developed countries [6, 15]. Most of deaths can be avoided by the management of risk factors, a high-quality care throughout the perinatal period, and the implementation of appropriate interventions [9, 14, 16]. Therefore, the aim of the present study is to determine the predictive factors of perinatal mortality in cases of PA recorded in the maternity ward of the Mohammed VI Hospital Center in Marrakech.

Article Maps

The aim of the present research is to determine the risk factors for mortality following PA. This article is structured as follows:
First, we introduced the study with a concise and comprehensive abstract, offering a global overview of our work. Next, we presented the context of PA as a major health problem, highlighting the importance of studying the risk factors associated with perinatal mortality following asphyxia. We then described the methodology adopted to achieve our research objective. Therefore, we analyzed and discussed the results of our study, highlighting the significant risk factors contributing to mortality by PA. We then presented our conclusions and recommendations based on the results obtained. Before concluding our article with the references, we expressed our gratitude to the participants in the study, and all people who helped and facilitated its realization.

1 Material and methods:

1.1 Study framework and design:

This is a retrospective analytical case-control study including cases of perinatal asphyxia recorded in the maternity ward of the Mohammed VI University Hospital Center (CHU) in Marrakech, during the period from April 1, 2022 to June 30, 2022. It was carried out using an

observation book containing all the information needed to analyze the causes and predictors of mortality in the context of perinatal asphyxia: maternal, obstetric, and neonatal factors.

1.2 Study location:

The study was carried out in the birthing room of the Mohammed VI Hospital Center, Marrakech. This is a third-level reference maternity which is also the destination for complicated births from other establishments throughout the Marrakech-Safi region. The maternity hospital handles a very large number of deliveries every year. According to the Marrakech regional health department, in 2022, 17 464 births were recorded, which facilitated the achievement of the main objective of this study.

1.3 Target population:

In this study, all newborns born in the context of PA were included. They were diagnosed based on one or more clinical criteria (abnormal fetal heart rate and/or APGAR score of less than 7 at 5 minutes), in the absence of a technical platform for gasometry. However, we excluded asphyxiated newborns suffering from major malformations incompatible with life (1 case of anencephaly) and asphyxiated newborns whose records were incomplete. Therefore, the cases included were fresh stillbirths (whose fetal heart sounds were perceived during labor) and asphyxiated newborns who died in the delivery room either immediately after birth or after an attempt at resuscitation. Controls were newborns who were discharged alive after 2 hours of monitoring in the delivery room. For each case identified, four controls were selected. Thus, 31 cases and 126 controls were identified during the study period from April 1 to June 30, 2022, with a total of 157 newborns suffering from PA.

1.4 Study variables:

The effect/dependent variable was perinatal mortality in the context of PA. The exposure/independent variables were, maternal factors: the mother's sociodemographic variables (age, origin), presence or absence of previous history; existing medical, surgical, and obstetrical history; course of last pregnancy; current pregnancy (gestational age, follow-up, term, whether at risk or not, existence of pathologies during pregnancy or not); obstetrical factors (presence of dystocia, mode of delivery); and funicular and neonatal factors (premature rupture of membranes, quality of amniotic fluid, volume of amniotic fluid, newborn's term , weight, sex, Apgar at birth after 5 minutes, neurological examination, notified pathologies, malformations).

1.5 Data analysis and processing:

The processing and analysis of the data collected was carried out using IBM SPSS Statistics software (version 20). For data processing, the reasoning used was as follows:
- Descriptive analysis was carried out for sociodemographic data, clinical characteristics, and maternity care. Qualitative variables were expressed as headcounts and proportions, while quantitative variables were presented as means with standard deviations.
A univariate analysis, the chi-square (χ^2) test, was used to explore the associations present between perinatal mortality following asphyxia and each of the qualitative variables.

Simple then multiple logistic regression was used to determine the factors associated with perinatal mortality, calculating adjusted ORs and their 95% confidence intervals. The threshold of statistical significance was set at 0.05.

1.6 Ethical consideration:

All research involving human beings raises moral and ethical issues. Ethical provisions are therefore applied to protect the rights of patients and participants in the preliminary investigation. Authorizations were obtained from the Regional Directorate of the Health Ministry in Marrakech and from the Management of the Mohammed VI Hospital Center to gain access to maternity wards and conduct this study (authorization number: 2899/ 196 /01 April. 2022)).

2 Results

2-1 Maternal characteristics:

The average age of the parturient who gave birth to the newborns studied was 28, with a minimum age of 17 and a maximum age of 43.

In addition, the majority of these parturient were between 20 and 39 years 83.40% (n= 131) (figure N 1).

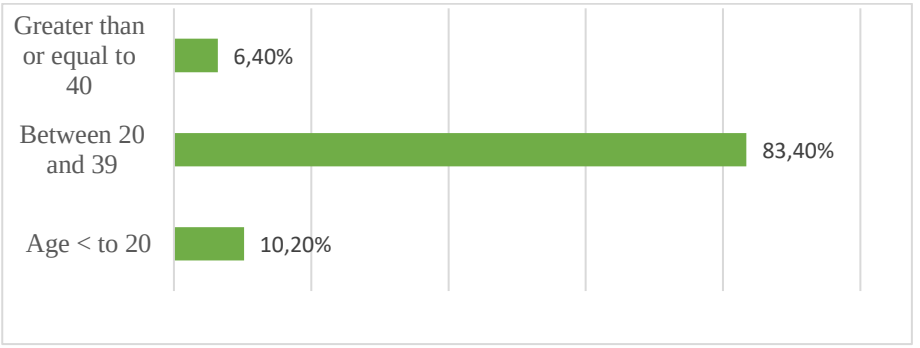

Figure N 1. Age distribution of parturient of the newborns studied (Mohammed VI University Hospital Maternity Hospital, 2022).

Analysis of the results of the present study also revealed that 61.10% (n=96) of newborns were born of a high-risk pregnancy, and that 53.50% (n=84) of pregnancies were monitored (figure N 2).

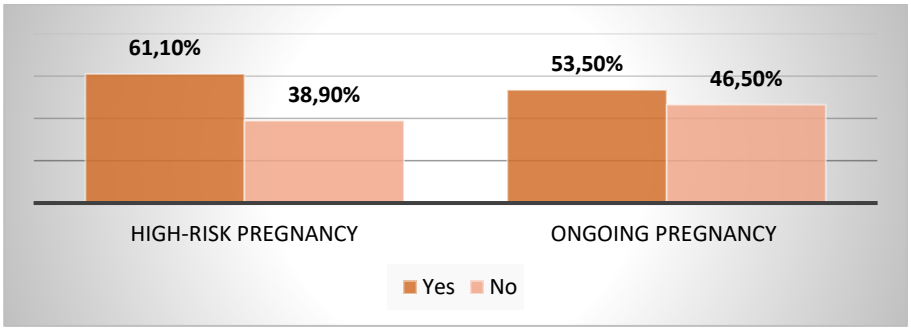

Figure N 2. Distribution of mothers of newborns studied by pregnancy type and follow-up (Mohammed VI University Hospital Maternity Hospital, 2022).

2-2 Characteristics of the neonatal population:

Au total, 31 cas et 126 témoins ont été recensés durant la période d'étude, avec un total de 157 nouveau-nés atteints d'asphyxie périnatale.
Le sexe ratio a été de 0,96.

Chez les nouveau-nés à l'étude, plus qu'un tier des nouveau-nés soit 34,40% (n=40) sont prématuré.

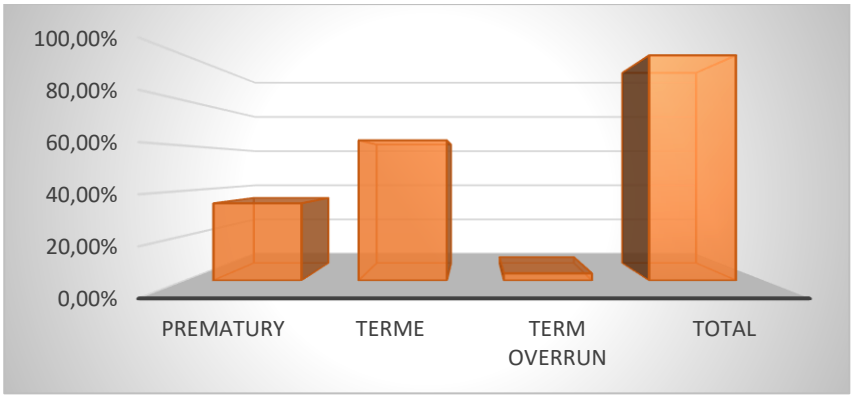

Figure 3. Distribution of neonates studied according to gestational age studied (Mohammed VI University Hospital Maternity Hospital, 2022).

In our sample, 49.70% (n=78) of the newborns studied had a low birth weight.

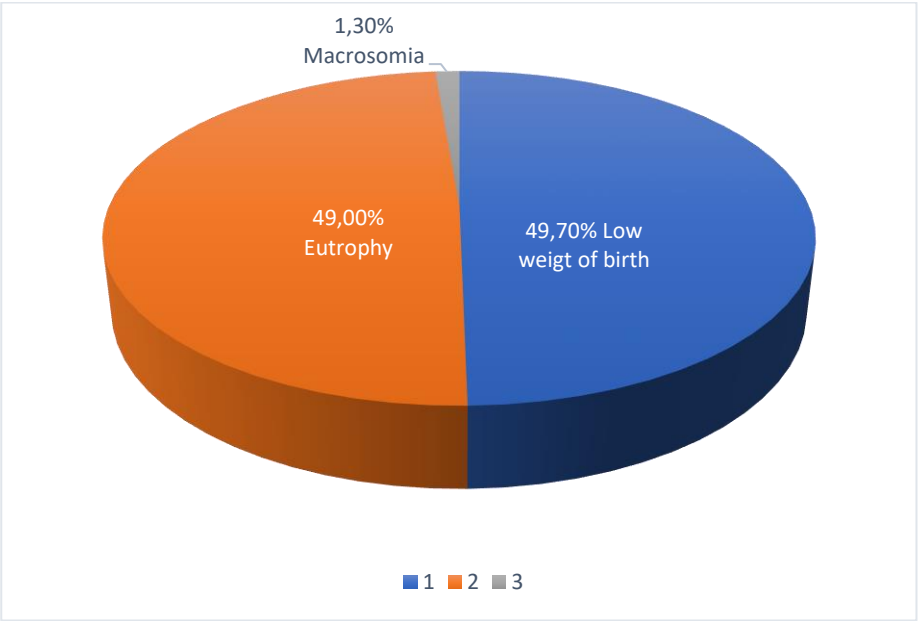

Figure 4. Distribution of newborns by birth weight studied (Mohammed VI University Hospital Maternity Hospital, 2022)

2-3 Relationship between perinatal mortality and maternal factors, including socio-demographic characteristics and antecedents:

The results of our study show significant associations between perinatal mortality and certain maternal demographic variables, as well as medical and obstetric history. We observed a significant association between the presence of maternal history (P value= 0.004), and more specifically the history of fetal death *in utero* (P value= 0.042) with perinatal mortality. However, no association was found between perinatal mortality and other antecedents such as gestational diabetes, pre-eclampsia, and anemia, as well as parturient age and origin (P value> 0.05).

The results of our study show a significant association between perinatal mortality and antecedent fetal death in utero (P value= 0.042). However, no association was found between perinatal mortality and parturient age (P value> 0.05).

Table N 1. Relationship between perinatal mortality and maternal factors (Mohammed VI University Hospital, Maternity Hospital, 2022).

Predictors	**Attributes**	**Cases (n=31)**		**Controls (n=126)**		**P value (5%)**
		Numbers	%	Numbers	%	
Mom's age	Age <20	2	6,45	14	11,11	**0.280**
	Between 20 and 39	27	87,09	97	80,15	
	Age > 40	4	12,90	6	4,76	
Origin	Urban	15	48,33	52	41,26	**0.443**
	Rural	18	58,06	65	51,58	

Antecedents	Yes	18	58,06	25	19,84	**0.004**
	No	22	74,19	91	72,22	
Type of antecedent	Fetal death in utero	10	32,25	7	5,55	**0.042**
	Scarred uterus	7	22,58	9	7,14	**0.077**

2-4 Relationship between maternal factors, including pregnancy characteristics and mode of delivery, and perinatal mortality:

The results for this category of variables reveal significant associations between perinatal mortality and: mode of delivery (P value = 0.000), anemia (P value= 0.009), threat of premature delivery (P value= 0.015), prolonged labor (P value= 0.033), and term of pregnancy (P value = 0.040). On the other hand, no association was reported between perinatal mortality and each of these variables: gestational diabetes, pre-eclampsia, antenatal hemorrhage, and retroplacental hematoma. In fact, all these variables showed a P value greater than 5%.

Table N 2. Association between perinatal mortality and maternal factors related to pregnancy and mode of delivery (Mohammed VI University Hospital, Maternity Hospital, 2022).

Predictors	Attributes	Cases(31)		Controls (n=126)		P value **(5%)**
		Numbers	%	Numbers	%	
Current Pregnancy Pregnancy age	Term	14	45,6	98	77,77	**0.040**
	Post term	1	3,22	4	3,17	
	Premature	16	51,61	24	19,04	
Twin pregnancy	Yes	1	3,22	0	0	**0.086**
	NO	30	96,77	126	100	
Follow-up pregnancy	Yes	15	51,61	68	53,96	**0.186**
	NO	15	48,38	58	46,03	
Pregnancy at risk	Yes	20	64,51	76	60,31	**0.088**
	NO	11	35,48	50	39,68	
Complications associated with pregnancy and delivery						
Gestational Diabetes	Yes	6	19,35	21	16,66	**0.670**
	NO	25	80,64	105	83,33	
Preeclampsia	Yes	2	6,45	16	12,33	**0.137**
	NO	29	93,54	110	87,30	
Thrombocytopenia	Yes	3	9,67	1	0,79	**0.021**
	NO	30	0,96	117	92,85	
HR incompatibility	Yes	1	3,22	2	1,58	**0.753**
	NO	30	96,77	117	92,06	

Threat of premature delivery	Yes	15	0,48	2	19,84	**0.015**
	NO	16	51,6	116	80,15	
Anemia	Yes	8	25,80	25	5,55	**0.009**
	NO	32	1,03	101	87,30	
Retroplacental hematoma	Yes	0	0	7	1,58	**0.405**
	NO	31	100	115	91,26	
Antenatal hemorrhage	Yes	3	9,67	4	3,17	**0.280**
	NO	28	0,90	122	96,82	
Dynamic dystocia	Prolonged labor	2	6,45	4	3,17	**0.036**
	Blocked work	4	12,90	1	0,002	
	Hyperkinesia	1	3,22	5	3,96	
Uterine pre rupture	Yes	1	3,22	125	0,79	**0.325**
	NO	30	96,77	14	99,20	
Mode of delivery	Childbirth pathway Instrumental delivery	8	25,80	14	11,11	**0.000**
	Unassisted vaginal delivery	5	16,12	4	11,11	
	Cesarean delivery	18	25,80	102	80,95	

2-5 Relationship between perinatal mortality and neonatal & funicular factors:

According to the chi-square (χ^2) test, the results of the perinatal mortality association with the variables forming the neonatal and funicular factors highlight statistically significant associations. These are: intra-uterine growth retardation (P value = 0.000), APGAR of the newborn after 5 minutes of life (P value = 0.000). Specifically, APGAR less than or equal to 3. The association was also significant with neonatal respiratory distress (P value= 0.002), and the existence of congenital malformations (P value= 0.033). However, no association was found between perinatal mortality and each of the following independent variables: premature rupture of membranes beyond 24 hours, and pathological amniotic fluid (P value> 0.05). (Table N 3)

Table 3. Relationship between neonatal and funicular factors and perinatal mortality (Mohammed VI University Hospital, Maternity Hospital, 2022).

Predictors	Attributes	Cases(31)		Controls (n=126)		P value **(5%)**
		Numbers	%	Number2	%	
Neonatal factors						
Sex	Feminine	16	51,61	63	50	**0.813**
	Male	15	48,38	61	48,41	
Weight	Hypotrophy	16	51,61	53	49,20	**0.141**
	Eutrophy	11	35,48	62	52,38	
	Macrosomia	0	0	2	1,58	
	Normal	3	9,67	20	20,63	
Intrauterine growth retardation	Yes	7	22,58	2	1,58	**0.000**

	No	29	93,54	115	94,44	
Neonatal Infection	Yes	3	9,67	5	3,96	**0.423**
	No	28	90,32	112	91,26	
Malformation	Yes	5	16,12	4	3,17	**0.033**
	No	26	83,87	113	96,82	
Funicular factors						
Premature rupture of membranes beyond 24 hours	Yes	6	19,35	23	18,25	**0.512**
	No	25	80,64	94	81,74	
Amniotic Fluid volume	Hydramnios	6	19,35	1	0,79	**0.001**
	Oligohydramnios	1	3,22	5	3,96	
	Normal Volume	24	77,41	120	95,23	
Amniotic Fluid Quality	Tinted liquid	13	41,9	26	20,63	**0.131**
	Meconium fluid	4	12,90	5	3,96	
	Clear fluid	14	45,16	95	75,39	
APGAR after 5min	Less than or equal to 3	21	67,74	10	7,93	**0.000**
	Between 4 and 6	9	29,03	55	43,65	
	Greater than or equal to 7	1	3,22	56	44,44	
Neonatal respiratory distress	Yes	28		61		**0.002**
	No	9	29,03	59	**46,82**	

2-6 Predictors of perinatal mortality following asphyxia:

Broadly speaking, the results of the logistic regression reported in Table 4 indicate a significant association between perinatal mortality (PM) and a set of independent variables studied, including:
Intrauterine growth retardation (P value= 0.002). The adjusted OR was [(ORA= 4711.799), P value<5%, CI: (48.964, 453416.766)], which means that newborns with intrauterine growth retardation have 4711.799 times more risk of perinatal mortality than newborns without growth retardation. Furthermore, 22.38% (n=7) of cases were stunted, while only 1.51% (n=2) of controls were stunted.

Maternal history revealed a significant association (p-value = 0.017) with the occurrence of perinatal mortality. It was found that women with a history had a 31.876-fold higher risk of perinatal mortality than mothers without a history, with an AOR of [(AOR =31.876, p<5%, CI: [1.346; 755.149)]. In fact, 58% (n=18) of cases came from a pregnancy with a history, compared with 19.84% of controls (n=25).

In addition, the results of the present study showed a highly significant association between an APGAR score of less than or equal to 3 in 5min of life, and perinatal mortality. This predictor factor recorded an ORA of [(ORA =139.75), (p value= 0.000), CI: [16.523; 1182.01)]. Moreover, 70.96% of cases (n= 22) presented an Apgar score < 3 versus 34% (n= 12) of controls.

In contrast, mode of delivery was overall significant at the 5% threshold. However:

- "Instrumental vaginal delivery" showed a statistically significant association with perinatal mortality, with p-value of 0.032 without ORA significance. (ORA : 0.12132),P-value <5% , CI : (0.00732, 2.0118)].
- Caesarean delivery also showed a statistically significant association with PD, for both p-value and ORA without confidence interval significance [(ORA: 5.78012), P value 0.001, CI: (0.73269,45.5988)].

Table N 4. Predictive factors of perinatal mortality following asphyxia perinatal asphyxia Multivariable regression model (Mohammed VI University Hospital, Maternity Hospital, 2022).

Factors	Modalities	P-value (5%)	COR	Confidence interval 95%		AOR	Confidence interval 95%	
				min	max		min	max
Mom's age	Age <20	0,166	,290	,002	43,800	0,215	0,031	1,504
	Between 20 and 39		2,352	,053	103,950	0, 520	0,138	1,956
	Age > 40		1	1	1	1	1	1
Provenance	Urban	,256	,017	3,861	,256	3,279	,270	39,870
	Rural		1	1	1	1	1	1
Antecedents	Yes	,030	,017	,000	,680	31,876	1,346	755,149
	No		1	1	1	1	1	1
Type of Antecedent	Scarred uterus	,031	,008	,000	,647	87,591	2,197	3492,545
	Thrombopenia	,037	,001	,000	,663	717,051	1,440	357036,441
	Threat of premature delivery	,021	2,48	1,147	5,36	1251,344	3,488	448946,353
	No antecedent	1	1	1	1	1	1	1
Pregnancy age	Term	1	1	1	1	1	1	1
	Post term	0.144	0.576	0.275	1.21	,200	,000	376,504
	Premature	0.939	1.091	0.116	10.29	2,089	,001	3609,982
Intrauterine growth retardation	Yes	0.002	12.409	2.4600	62.59	4711,799	48,964	453416,766
	No	1	1	1	1	1	1	1
Malformation	Yes	0.043	4.107	1.046	16.13	241,435	6,044	9644,748
	No	1	1	1	1	1	1	1
Mode of delivery	Childbirth pathway Instrumental	0.032	4.812	1.144	20.25	0.12132	0.00732	2.0118
	Cesarean delivery	0.001	13.226	3.838	45.57	5.78012	0.73269	45.5988
	Unassisted vaginal delivery	1	1	1	1	1	1	1
Apgar after 5min	Less than or equal to 3	0,000	0,007	0,001	0,061	139,75	16,523	1182,01
	Betwin 4 and 6	0,308	0,314	0,034	2,913	3,185	0,343	29,551
	Normal	1	1	1	1	1	1	1

1 : Réf.

3 Discussion:

This study aimed to identify factors predictive of perinatal mortality following PA; Thus,
157 newborns with PA were included, with 31 cases and 126 controls. The sex ratio was 0.96, indicating that both sexes were affected in almost the same way by AP. This sex ratio is consistent with that found in the neonatal population included in other studies [1, 4,6]. In Badawi and al.'s work, male sex predominated. Consequently, he confirmed that male sex increases the risk of PA and perinatal mortality by 50% [6].
During the study period, perinatal asphyxia contributed to a significant mortality rate in our series. This situation is like that of many maternity hospitals in other developing countries, such as: Madagascar (18.10%), Nigeria (23.9%), and Congo Brazzaville (30.4%) [12, 14, 17]. In contrary, developed countries have a lower rate. For example, in France, PA causes less than 0.1% of newborns mortality [14, 18, 19], which can be explained by the high-level technology available in developed countries. Indeed, the inadequacy of PA diagnostic resources (gasometry technical platform) will delay the diagnosis and cause an increase in the mortality and morbidity rates [20, 21].
In addition, the study of associations between risk factors and perinatal mortality highlighted some producer factors with a strong statistical association with perinatal mortality. These include intrauterine growth retardation (IUGR), the presence of congenital malformations, the Apgar score, and maternal medical and/or obstetric history such as scar uterus and thrombocytopenia.
On one hand, intra-uterine growth retardation showed a highly significant association with the occurrence of perinatal mortality. This result can be justified by low birth weight and energy reserves of newborns, which makes them more sensitive to uterine contractions during labor and to the rapid drop in fetal blood pH. Consequently, they present greater risk of PA, cardiorespiratory adaptation at birth, and early neonatal death [6, 22, 23, 24].
On the other hand, the Apgar index after 5 minutes of life is an important indicator of the newborn's state of health. It provides information on potential cardiorespiratory problems. Thus, low Apgar values indicate severe respiratory distress and a poor prognosis. In this study, there was a strong significance between an Apgar score below 3 and the occurrence of mortality, which is consistent with previous studies [23, 26, 27]. Casey and al. demonstrated an increased risk of death associated with low Apgar scores. In their study on newborns asphyxiated, they found a mortality of 244 per 1000 in term newborns with an Apgar score between 0 and 3 at five minutes, while they reported only 0.2 per 1000 in those with a score between 7 and 10 [27].
In summary, intrauterine growth retardation (IUGR), the presence of congenital malformations, the Apgar score, and maternal medical and/or obstetric history such as scar uterus and thrombocytopenia, are important factors to consider when assessing the risk of perinatal death in newborns with PA. Careful monitoring of these factors could enable early identification of high-risk neonates and facilitate the implementation of appropriate preventive and curative measures [3, 14, 19].
The perspectives of the present study are to conduct further studies on perinatal mortality, not only that related to asphyxia, but also on overall neonatal mortality. Prospective multicenter studies are highly desirable in order to be able to study the problem in other contexts.

4 Conclusion:

Perinatal asphyxia (PA) is an extremely serious health problem, likely to cause not only perinatal mortality, but also severe, long-term consequences. The birthing unit at the Med VI University Hospital in Marrakech records relatively high rates of PN.

Only if the risk factors identified in this study are considered, and if all pregnant women, especially those with one of the notified risk factors, are adequately and effectively cared for, will it be possible to improve neonatal health in the region, and successfully achieve the third target of the Sustainable Development Goals (SDGs).

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Conflicts of interest:

The authors declare no conflict of interest regarding the publication of this work.

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