<u>Original Research Article</u> 1 2 Risk factors of neonatal mortality due to birth 3 asphyxia in Hôpital du Cinquantenaire of 4 Kisangani: a case-control study 5 6 ABSTRACT 7 8 Aims: Py publications about perinatal asphyxia, one of the three main reasons of newborn deaths, besides prematurity and sepsis, are available in Democratic Republic of Congo (RDC) where newborn mortality is among the most elevated in Africa. This survey had to determine its prevalence, lethality and factors associated of it. Study design: This was an unmatched case-control study. Place and Duration of Study: it was conducted in pediatric service of Hôpital du Cinquantenaire of Kisangani (HCK), a secondary level hospital, from March 2013 to March 2017. Methodology: Clinical and biologic data of term newborns (prenatal, perinatal and postnatal), hospitalized for neonatal asphyxia in the HCK were retrospectively collected and then analyzed. Then we compared data of dead newborns (cases) versus those who survived (controls) to determine risk factors related to dying with asphyxia. One case was matched to three controls on the basis of sex. Results: Results. During the period above, 612 newborns were received in the HCK and 146 died. One hundred and nineteen out of 612 had perinatal asphysia (19.4%) and 26 out of 119 died (17.8% of all newborn deaths and 21.8% of all asphyxia cases). The most frequent perinatal antecedents

of all newborn deaths and 21.8% of all asphyxia cases). The most frequent perinatal antecedents were the premature rupture of the membranes, the meconial amniotic liquid, pre-eclampsia and eclampsia. In bivariate analysis, factors associated to asphyxia-related mortality were low birthweight (P=.02), reference from another hospital (P =.01), newborn older than 24-hours-old (P =.02), associated infection (P =.003), asphyxia severity (P <.001) and the Stage 3 of Sarnat (P <.001).

Conclusion. The frequency of the asphyxia is high in the HCK and its mortality associated to avoidable factors. Networking newborn referral, improving skills of nurses about emergency obstetric and neonatal cares, and making available equipment for newborn resuscitation can reduce that mortality.

9 10

10 11

Keywords: Perinatal asphyxia, newborn, Kisangani, Democratic Republic of Congo

1. INTRODUCTION

12 13

💬 e 7,6 millions of children under 5 years-old deceased during 2010, three million were newborns, 14 ettner 40% of whole deaths. Prematurity, intrapartum complications and sepsis were the main reasons 15 16 of newborn death [1]. In the world health statistics 2010 published by the WHO, DRC appeared 17 among the 3 countries having the strongest infanto-juvenile mortality, just before Angola and Chad, with a rate of 199 for one thousand [2]. The Demographic and Health Survey of 2014 nd a rate of 18 104 [3], what means a meaningful reduction: neonatal mortality fell from 42% in 2007 to 28% in 19 20 2014. However, these rates remain very elevated and the same report underlines that neonatal 21 mortality varied too little [2]. The poor performance of health worker has multiple determinants 22 ranging from proximal ones such as a lack of knowledge, skill and motivation to distal factors such as 23 disabling working environment in health facilities (poor clinical practices, leadership and supervision; 24 lack of adequate supplies and equipment; health workers' ineffective participation in planning; and 25 lack of peer support) [4]

Close to 75% of newborn deaths occur in the first week of life, due to prematurity (35%), peripartum asphyxia (23%) and sepsis (23%) [1,4, 6, 7]. For other studies perinatal asphyxiates was even the most frequent death reason before the 2 other [7-9].

It also causes a lot of complications: motor palsy, psychomotor development impairment, socioeconomic burden for the family. The prevalence of peripartum asphyxia is certainly low in developed in low-income countries, about one newborn out of 5 is asphyxiated at birth and 10 to 33% of them d 20-11].

In DRC, the health system encounters several difficulties [3] and the problem of under-equipment for neonatal resuscitation is actual in many hospitals. Only few_data on asphyxia are available. Biselele determined some prenatal and post-natal factors associated to mortality [12]. This study aimed to identify the factors associated to death with the diagnosis of perinatal asphyxia.

38 2. MATERIAL AND METHODS

40 **2.1 Operationalization of variables**

41

39

37

We considered like case of asphyxia all term newborn who had an Apgar less than 7 at the 5th minute of life. Asphyxia was light if 5th minute Apgar ranged between 4 and 6. If it ranged between 0 and 3, it was considered as severe.

Hypoxe-ischemic encephalopathy (HIE) was classified according to Levene and Sarnat & Sarnat:
 Grade 0 for wellbeing newborn, grade 1 or light HIE, grade 3 or mild HIE and grade 3 or HIE severe.

We considered as-neonatal infection all newborn who either was symptomatic (fever for example) or asymptomatic associated to pathologic history (premature rupture of membranes, maternal fever in intrapartum) and positive C reactive protein realized after 12-hours old.

51 **2.2 Study design, sample, inclusion criteria, variables**

50 51 52

This was a case-control study. Sees were all asphyxiated newborns who died and controls those who survived asphyxia died and the witnesses of all cases of asphyxia who had survived. We matched 3 controls for 1 case on the basis of sex.

56 Data were collected from medical folders of all newborns hospitalized in the HCK with asphyxia from 57 March 2013 to March 2017. Some were born in HCK and other referred from other hospitals of the 58 city. Transferred cases with asphyxia who died during transportation to HCK were excluded. All 59 premature as well as term newborns with life-threatening congenital malformations and those leading 50 to surgical emergency (anal imperforation, primitive peritonitis, necrotizing enterocolitis) were 51 excluded.

62 There is no device of cooling in the HCK. The cases of asphyxia received a symptomatic medical 63 treatment solely, based on oxygen, 10% glucose infusion enriched of trace elements (Nacl, Kcl, 64 calcium), phenobarbital if there were seizures.

We studied antenatal features (mode of childbirth, maternal history of pre-eclampsia or eclampsia, placenta prævia, cord procidence, dystocic presentation) and postnatal (meconial amniotic liquid, Apgar at 1st and 5th minutes, clinical signs in the following hours, duration of hospitalization, mortality within 24 and 48 hours).

Treatment and analysis of data were realized by Microsoft Excel® 2016 and Epi info[™] 7.1.5. Pearson's chi square and odds ratio were to check out association between variables determine risk factors. The t test of Student was used for comparing means of quantitative data.

72 73

3. RESULTS AND DISCUSSION

74 75 76

77

78

3.1 Socio-demographic and clinical data

From March 2013 to March 2017, 612 newborns were hospitalized in to the HCK, among whom 119 were asphyxiated (19,4% of all newborn hospitalizations). One hundred and forty-six died for miscellaneous causes, including 26 with perinatal asphyxia (17.8% of all newborns deaths and 21.8% of asphyxia lethality).

- 83 84
- 85
- 86
- 87
- 88
- 89 90

UNDER PEER REVIEW

		Frequency	%	
Sex ratio F/M		0,7 (52/67)		
Mean age	1.7 ± 3 days (median 1 jour)			
Address	Kabondo	24	(20,17%)	
	Kisangani	6	(5,04%)	
	Makiso	73	(61,34%)	
	Mangobo	8	(6,72%)	
	Tshopo	8	(6,72%)	
Birthweight	<2500 g	16	(13,45%)	
	≥2500 g	103	(86,55%)	
	Mean birthweight 3120.1 ± 551.2 g (median 3095 g)			

91 Table 1. Epidemio-clinical features of newborns with perinatal asphyxia92

93

94 Most of newborns were male, ≤ 1 day-old. Weight varied between 1845 à 4250 g.

95 Table 2. Other clinical features of asphyxiated newborns

96

		freq	%
Clinical signs	Respiratory distress	59	(49.4%)
	Pallor	26	(22.1%)
	Lethargy	20	(16.9%)
	Seizures	19	(15.6%)
	Fever	19	(15.6%)
	Endless crying	15	(13%)
	Digestive hemorrhage	9	(7.8%)
	Coma	5	(4 %)
Perinatal features	Méconial amniotic fluid	43	(36.4%)
	Cesarean section	31	(25.9%)
	Pre-eclampsia/eclampsia	26	(22.1%)
	Premature rupture of membranes	22	(18.1%)
	Too long labor	14	(11.6%)

	Dystocic presentations	8	(6.5%)
	Twins	5	(4%)
Origin	Born in HCK	58	(48,74%)
	Born then referred from other hospitals	61	(51,26%)
Fatal outcome	All deaths among asphyxiated newborns	26	(21,85 %)
	Deaths during the first 24 hours (n=26)	20	(77,6%)

97

Respiratory disorders were the most observed. In perinatal history, meconial amniotic fluid were the
 most observed, followed by premature rupture of membranes.

About HIE, we had 13 cases with grade 0 (healthy newborns), 18 cases with grade 1, 33 cases with grade 2 and 17 with grade 3. The mean hospitalization duration was 7.6 ± 4.2 days (median 5 days) 102

102

104 **3.2 Analytic data (n=368)**

105

106 Table 3. Factors associated to mortality

107

		Deceased	Alive	OR [*] (Cl [†] 95%)	Р
Birthweight	< 2500 g	8	9	3.4 (1.1 – 10.3)	.02
	> 2500 g	19	84		
Sex	Female	11	41	.9 (.3 – 2.2)	.8
	Male	15	52		
Origin	Referred	19	42	3.2 (1.2 - 9)	.01
	HCK	7	51		
Age at admission	≤ 1 day	17	79	2.9 (1.1 - 8)	.02
	> 1 day	9	14		
Sepsis	Yes	15	25	3.7 (1.5 – 9.1)	.003
	No	11	68		
Asphyxia severity	Light	7	81	.05 (.01 – .1)	< .001
	Severe	19	12		
HIE Sarnat grade	0	1	44		< .001
	1	4	28		
	2	9	19		
	3	12	2		

109

115

117

110 Deceased newborns had a lower birthweight (2912.3 \pm 609.8 g) than those who survived (3178.2 \pm 111 522.5 g): t (117) = -2.21; *P* = .02). The low birthweight had a three-fold risk of dying with asphyxia 112 than those who had a normal birthweight.

113 Referral from other hospitals, arriving at HCK at an age older than 1 day, sepsis, severe asphyxia, 114 Sarnat grade 2 and 3 were associated with asphyxia related mortality.

116 3.3 Discussion

118 3.3.1 Epidemio-clinical features

We found that the majority of our newborns were male, from Makiso township (table 1). The male predominance was found by other authors who found a meaningful difference in favor of the boys [13,14]. Tina Katamea in DRC found that the neonatal mortality was associated to masculine sex [15] but there were no results about association of perinatal asphyxia and mortality related to it.

The peripartum asphyxia represented 19.4% of all newborns hospitalizations in to the HCK and 17.8% of the reasons of neonatal mortality. This rate was higher than the 10.94% found in India [10], but close to the 18% found in Cameroon [11].

126 Mortality related to perinatal asphyxia (table 2) was higher than 10% found in India [10], 18,5% in 127 Nigeria [7] and 21% in Ghana [9]. It was lower than 32% in Liberia [8], 30% in Nepal [16], 25% in 128 Kenya [6] and Malawi [17].

Permanence of physicians and nurses at any moment, availability of suction device, ambu bag and oxygen for neonatal resuscitation contributed for many to these results. Nevertheless, the prevalence remains high and can be due to an elevated proportion of newborns referred from other hospitals for lack of resuscitation devices. They often arrived too late [18] and found no cooling device available in HCK.

134

135 3.3.2 Factors associated to the lethality

Low birthweight, reference from another hospital, age superior to 24 hours, severe asphyxia, elevated
Sarnat grade (table 3) were factors associated to mortality related to peripartum asphyxia. These data
agree with those of the other previous studies: the low birthweight newborn is more fragile and at high
risk of developing hypoglycemia.

The Sarnat grade describes severity of HIE: higher grades had more severe HIE. Therefore, in this study, like in many others, mortality was associated to the more elevated grades [10-12, 18, 20].

Reference from other motherhoods and age at admission were evident risk factors [7]. For the best moment to avoid asphyxia is the period of the 4 first minutes. If asphyxia could not be avoided, the first 6 hours of life were the most important time to use cooling device in order to prevent HIE and neurologic damage [19]. This shows how bad can be the prognosis of newborn arriving later than 24 first hours. No cooling device were available in HCK. So, only children born there could be immediately resuscitated and that explains the significant difference between them and those referred from other hospitals.

151 152

153 4. CONCLUSION

154

The mortality rate of peripartum asphyxia was high in HCK and associated to avoidable and preventable factors. Networking newborn referral, Improving the peripartum asphysia on emergency obstetric and neonatal care, making available devices for neonatal resuscitation in hospitals of Kisangani city are necessary to reduce mortality due to peripartum asphysia.

- 159
- 160

162 ETHICAL APPROVAL (WHERE EVER APPLICABLE)

163
164 This study received the agreement of Research authorities of Faculty of Medicine and Pharmacy of
165 University of Kisangani. Data collected were anonym and not available to people not involved into its
166 realization.

168 169

167

161

- Li liu, hope I johnson, simon cousens, jamie perin, susana scott, global, regional, and national causes of child mortality: an updated systematic analysis for 2010 with time trends since 2000, lancet 2012; 379: 2151–61
- 173 2. Who, world health statistics2010, Geneva, 2010
- Ministère du plan et suivi de la mise en œuvre de la révolution de la modernité (mpsmrm), ministère de la santé publique (msp) et icf international, 2014. Enquête démographique et de santé en république démocratique du Congo 2013-2014. Rockville, maryland, usa : mpsmrm, msp et icf international
- Brantuo m n. A, cristofalo e, m. Mehe m, ameh j, okai brako n, evidence-based training and mentorship combined with enhanced outcomes surveillance to address the leading causes of neonatal mortality at the district hospital level in Ghana, tropical medicine and international health. 2014, 19:4, p 417–426,
- Ashish kc, mats målqvist, wrammert j, verma s, raj aryal d, implementing a simplified
 neonatal resuscitation protocol-helping babies breathe at birth (hbb) at a tertiary level
 hospital in Nepal for an increased perinatal survival, bmc pediatrics 2012, 12:159
- 185
 6. Yego f, stewart williams j, byles j, nyongesa p, aruasa w and d'este d, a retrospective analysis of maternal and neonatal mortality at a teaching and referral hospital in Kenya, reproductive health 2013, 10:13
- 188
 7. U ekwochi, ik ndu, ic nwokoye, ou ezenwosu, of amadi, dic osuorah, PATTERN of morbidity and mortality of newborns admitted into the sick and special care baby unit of Enugu state university teaching hospital, Enugu state, Nigerian journal of clinical practice, 2014, 17:3,
- Jody r. L, facnm, faan, a case series study of perinatal deaths at one referral center in rural post-conflict Liberia, *matern child health j.* 2014 January; 18(1)
- Welaga p, moyer ca, aborigo r, adongo p, williams j, et al. Why are babies dying in the
 first month after birth? A 7-year study of neonatal mortality in northern ghana. Plos one,
 2013, 8(3): e58924
- 10. kumar amritanshu, suruchi smriti1, vimal kumar, apeksha pathak, deba prasad
 Banerjee, clinical profile and short term outcome of hypoxic ischemic encephalopathy
 among birth asphyxiated babies in katihar medical college hospital, journal of clinical
 neonatology | vol. 3 | issue 4 | 2014
- 11. f monebenimp, f tietche, n eteki asphyxie neonatale au centre hospitalier et universitaire
 de Yaoundé, Cameroon, clinics in mother and child health vol. 2(2) 2005: 335-338
- 12. biselele t, naulaers g, bunga muntu p, nkidiaka e, kapepela m et al, a descriptive study
 of perinatal asphyxia at the university hospital of Kinshasa (democratic republic of
 Congo), j trop pediatr (2013) 59 (4): 274-279
- 13. Mohamed ma, aly h, impact of race on male predisposition to birth asphyxia, j perinatol.
 2014 jun;34(6):449-52
- 14. Eghbalian f, frequency of hypoxic-ischemic encephalopathy among hospitalized neonates in west iran, IRAN *j pediatr jun 2010; vol 20 (no 2), pp:244-245,*
- 15. Tina katamea, mukuku o, kamona I, mukelenge k, mbula o, facteurs de risque de mortalité chez les nouveaux-nés transférés au service de néonatologie de l'hôpital jason sendwe de Lubumbashi, république démocratique du Congo, pan african medical
 212 isurral 2014 : 10 :100
- 213 journal. 2014 ; 19 :169,

- 16. Anne cc lee, md, mpha, luke c. Mullany, phda, james m. Tielsch, phda, joanne katz, risk
 factors for neonatal mortality due to birth asphyxia in southern Nepal: a prospective,
 community-based cohort study, pediatrics. 2008 may; 121(5): e1381–e1390
- Michael k. Hole,1 Keely olmsted,2 athanase kiromera,3 and lisa chamberlain, a neonatal
 resuscitation curriculum in Malawi, Africa: did it change in-hospital mortality? Hindawi
 publishing corporation international journal of pediatrics volume 2012,
 10.1155/2012/408689
- 18. Memon s, shaikh s, bibi s. To compare the outcome (early) of neonates with birth
 asphyxia in-relation to place of delivery and age at time of admission. J pak med assoc.
 2012 dec;62(12):1277-81
- 19. Karin daetwylera, barbara brotschib, thomas m. Bergerc, bendicht peter wagnera
 feasibility and safety of passive cooling in a cohort of asphyxiated newborn infants,
 Swiss med wkly. 2013;143: 13767
- 227 20. Qureshi am, ur rehman a, siddiqi ts, j ayub hypoxic ischemic encephalopathy in 228 neonates med coll abbottabad. 2010 oct-dec;22(4):190-3.